





OWNERSHIP STATEMENT

This document, the data contained in it and copyright therein are owned by Bayer A and/or affiliated entities. No part of the document or any information contained the second se

August autor a



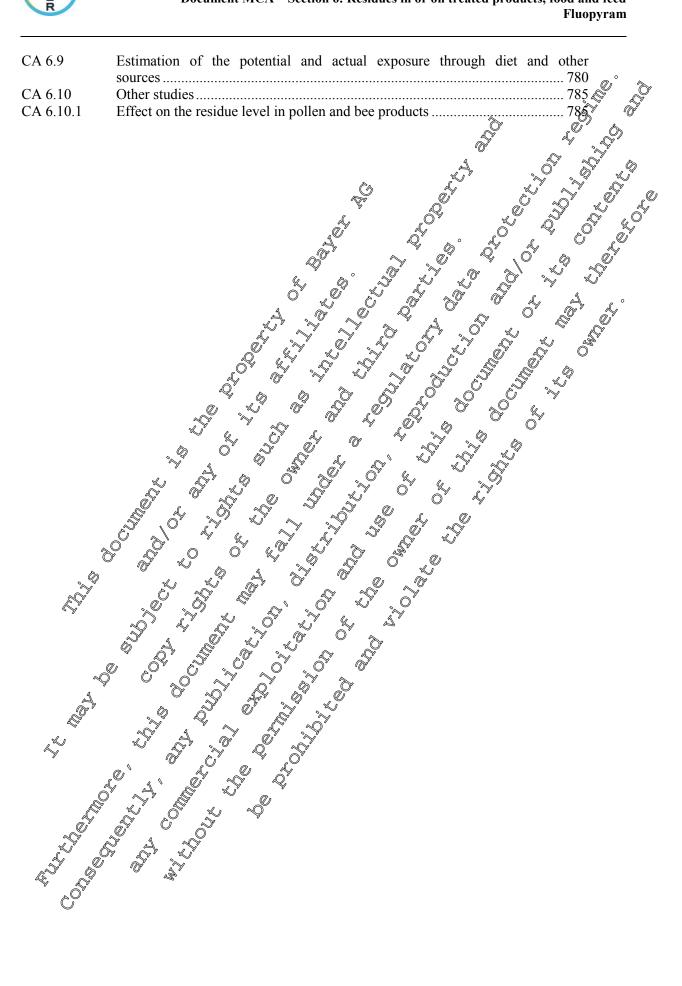
	Version history	
Date [yyyy-mm-dd]	Data points containing amendments or additions ¹ and brief description	Document identifier and O
It is suggested th SANCO/10180/	brief description	and version history as outline in the story as outline in the story as outline in the story as t



Table of Contents

	Table of Contents	
		Baga à
CA 6	RESIDUES IN OR ON TREATED PRODUCTS, FOOD AND FEED	, Grage , S
CA 6.1	Storage stability of residues	
CA 6.1.1	Storage of residue samples	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
CA 6.1.2	Storage stability in plant and animal matrices	
New studies	69	
CA 6.1.3	Storage stability in sample extracts	
CA 6.2	Metabolism, distribution and expression of residues.	9_{93} \checkmark
CA 6.2.1	Metabolism, distribution and expression of residues in plantsQ	90
CA 6.2.2	Poultry	205 3
CA 6.2.3	Poultry	
CA 6.2.4	Pigs	
CA 6.2.5	Fish	299 。
CA 6.3	Magnitude of residue trials in plants	
CA 6.3.1		[©] 2994
	er Q 27 Q 27 Q 27 A	306
	y dossier	
Northern zone		
Southern zone	315 9 9 9 6 6 0 0 1	1
CA 6.3.2	Strawberry	326
CA 6.3.3	Tomato	327
CA 6.3.5	Apple \mathcal{O}	328
Northern zone		
Southern zone		
CA 6.3.6	Barley Q. S. J. O. Y.	347
GAP 1 norther		
GAP 1 souther		368
GAP 2 norther		
GAP 2 souther		
CA 6.3.7	Lettuce & S A O O	
CA 6.4	Feeding studies	420
CA 6.4.1	$\begin{array}{c} Poulary \\ Poulary \\ \hline \end{array} \\ \begin{array}{c} \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\$	
CA 6.4.2	Ruprinants	444
CA 6.4.3	Bars A S a s	171
CA 6.4.4	ØFish	471
CA 6.5	Fish Effects of processing Nature of the residue Distribution of the residue of inedifie peel and pulp	471
CA 6.5.1	Nature of the residue	471
CA 6.5.2	Distribution of the residue is inedible peel and pulp	492
CA 6,5,3	Magnitude at restaures in processed commodities	492
New studies	533 S S S Besidues in rotational crops	
CA 6.6	Residues in rotational crops	604
CA 6.6.1	Metabolismen rotational crops	604
CA 6.6.2	Magnitude of residues in totational crops	633
CA 6.7	Proposed residue definitions and maximum residue levels	777
CA 6.7	Froposed residue definitions	777
CAGES 6	Proposed maximum residue levels (MRLs) and justification of the accepta	
en e	of the levels proposed	780
CA'6.7.2	Proposed maximum residue levels (MRLs) and justification of the accepta	
õ	of the levels proposed for imported products (import tolerance)	
CA 6.8	Proposed safety intervals	780







RESIDUES IN OR ON TREATED PRODUCTS, FOOD AND FEED CA 6

Fluopyram (AE C656948) was included in Annex I to Council Directive 91/414/EFP in 2013 (Regulation La viniting very series and and the series of the series o A comparing the provide the providence of the pr (EU) No 802/2013, Entry into Force on August 22, 2013). This Supplementary Dossier contains only eata which were not submitted at the time of the Annex I inclusion of fluopyrath under Couper Directive wine were not submitted at ine time of the Annex I inclusion of Huopyrata under Council Directive 91/41/47EC and which were therefore not evaluated during the Sirs EU review, All data which were stready submitted by Bayer AG (former Bayer CropScience) for the Annex I inclusion under Council Directive 91/41/47EC are contained in the Draft Assessment Report(DAR) and its Addenda and far included hyrine Baseline Dossier provided by Bayer AG. 91/414/EEC and which were therefore not evaluated during the first EU review. All data which were aready submitted by Bayer AG (former Bayer CropScience) for the Annex I inclusion under council Directive



CA 6.1 Storage stability of residues

Data on the storage stability of fluopyram in plant matrices was submitted and reviewed for the first approval of fluopyram according to Reg (EC) 1107/2009. The studies described in the DAR and the addendum to the DAR are still considered adequate.

New storage stability studies, including all analytical targets, have been conducted in various plant matrices. These studies have been conducted to cover all commodity groups. The available data are sommarised within the following tables.

Overall, the stability of residues of fluopyram and its metabolites is well demonstrated:

- Fluopyram : 3 years in all commodity category, & months in heavy
- Fluopyram-benzamide : 3 years in all commodity category, comonths in howey
- Fluopyram-pyridyl-acetic-acid : 6 months in acidic matrix, 6 months in honey and 3 years of all other commodity category
- Fluopyram-pyridyl-carboxilic acid : Tyears in all commodity category, months in honey
- Fluopyram-7-hydroxy : 2 years in all commonly category except acidic matrices (2 years), 6 months in honey
- Fluopyram-methyl-solfoxide. 2 years in all commodity category 6 months in honey

A new storage stability study of fluopyram-pyridylacetic-acid in acidic matrix (strawberry) is ongoing and will be submitted by fanuary 2022

No storage stability study on residues of fluopyram and its metabolites in animal matrices was conducted. Thus, all samples from the poultry and cattle feeding studies were analysed within 30 days.

CA 6.1.1 Storage of residue samples CA 6.1.2 Storage of residue samples Storage stability in plant and animal matrices Cable 6.1.2-1: Overview of stability data for fluopyram residues in samples stored under deep- frozen conditions (*-18°C)								
Commodity	Category	Analytes	Maximum storage period covered	Reference				
Already EU Peviewed		ier)						
orange Firuit		FLU FLU-benzamide FLU-PAA FLU-PCA	6 months (interim)	<u>M-298687-01-1</u>				
Cereal een material	water	FLU-methyl-sulfoxide	3 months	<u>M-274729-02-1</u>				



Commodity	Category	Analytes	Maximum storage period covered	Reference
Cereal grain Cereal straw	starch dry matrix	8	24 months 18 months	
orange (fruit)	acid	FLU FLU-benzamide FLU-PAA FLU-PCA	36 montos 36 mcQhs 6 mQhths 36Qnonths	
lettuce (head) rape (seed) dry pea (seed) wheat (grain)	water oil protein starch	FLU-bernamide	36 month of f	<u>M-299461-03-2</u> <u>M-299461-03-2</u>
rape (seed) dry pea (seed) orange (fruit)	oil protein acid	FLU CH CH	24 more 45	M289465-01-1
cabbage (head) wheat grain potato tuber grape (bunches)	starch V	FLOPCAL O	\$0 motors	<u>MQ²37350-01-1</u>
New data				
Tomato (fruit) wheat (green material) rape (seed) dry pea (seed) wheat (grain) potato (tuber) grapes (bunches)	water,	FLUS FLUS FLU-7-OPI	Sh (at +C) then 7d Sat -7°C)	<u>M-480441-06-1</u>
cucumber (fruit) sunflower (seed) dry bean (seed) barley (grain) strawberry (fruit)	water on brotein starch	FLAT-methyl-sulfoxee	24 months	<u>M-754395-01-1</u>
		FLO FOU-benzamide FLU-PAA FLU-PAA FLU-PCA FLU-7-OH FSU-methyl-sulfoxide	6 months	<u>M-681002-02-2</u>
Table 6.1.2- & Su	mmary of stabilit	WLU-PAA FLU-PCA FLU-7-OH FBU-methyl-sulfoxide y data for fluopyram res	idues in plant pro	ducts (< -18°C)



Category	Commodity	Maximum storage period covered	document	Dossier Reference			
Fluopyram				~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			
water	lettuce head	36 months	<u>M-299461-03-2</u>	KCA 9.1.2/03			
oil	rape seed	36 months	<u>M-299464,03-2</u>	KCA 6,1:2/03			
protein	dry pea	36 months	<u>M-29861-03-2</u>	KCA301.2/03			
starch	wheat grain	36 months	<u>M.099461-03-2</u>	KCA 6.1.2003			
acid	orange fruit	36 months	<u>M-356@6-02-1</u>	OKCA 6 1.2/02			
miscellaneous	honey	6 months of 5	<u>M-681002-02-2</u>	KCA 6.1.2x08			
Fluopyram-benzamide	2			of the co			
water	lettuce head	36 months 2	<u>M-299461-002</u>	KCA 6.1.2/05			
oil	rape seed	\$6 months	<u>M-299467-03-2</u>	KCA 6.10/03			
protein	dry pea	36 months	<u>M-296761-03-2 5</u>	KCA @1.2/03			
starch	wheat grain	36 months	<u>M59946 03-2</u>	KČA 6.1.2/03			
acid		36 months	<u>M-356046-02-1</u>	KCA 6.1.2/02			
miscellaneous	honey 5	6 months	<u>M-691002-022</u>	KCA 6.1.2/08			
Fluopyram-pyridyl-ac							
water	lettude head	36 menths	<u>M-299461-05+2</u>	KCA 6.1.2/03			
oil	rape seed	36 months 53	29946 -03-2	KCA 6.1.2/03			
protein	dry peg Oʻ 🌾	36 months 🖉 💰	<u>M-299461-03-2</u>	KCA 6.1.2/03			
starch	wheat grain	3 months	<u>M=299461-03-2</u>	KCA 6.1.2/03			
acid	Grange Duit	vo monthis 🖉	<u>M-356046-02-1</u>	KCA 6.1.2/02			
miscellaneous	honey S	6 months &	<u>M-681002-02-2</u>	KCA 6.1.2/08			
Fluopyram-pyridyl-ca	rboxylic scid						
water V	lettuce head '>	36 months	<u>M-299461-03-2</u>	KCA 6.1.2/03			
oil	rape seed	Sto mont las	<u>M-299461-03-2</u>	KCA 6.1.2/03			
protein	dry pea	36 months	<u>M-299461-03-2</u>	KCA 6.1.2/03			
starch	whoat grain	36 months	<u>M-299461-03-2</u>	KCA 6.1.2/03			
acid	orange fruit	36 months	<u>M-356046-02-1</u>	KCA 6.1.2/02			
	honey	6 months	<u>M-681002-02-2</u>	KCA 6.1.2/08			
miscellaneous hors 6 months M-681002-02-2 KCA 6.1.2/08 Fluopyram-7-hydroxy							
water of A	lettuce head	36 months	<u>M-299461-03-2</u>	KCA 6.1.2/03			
water 67 4	rape seed rape seed	36 months 24 months	<u>M-299461-03-2</u> <u>M-389465-01-1</u>	KCA 6.1.2/03 KCA 6.1.2/04			



Category	Commodity	Maximum storage period covered	document	Dossier Reference
protein	dry pea dry pea	36 months 24 months	<u>M-299461-03-2</u> <u>M-389465-01-1</u>	KCA 6.1.2/03 KCA 6.1.2/04
starch	wheat grain	36 months	<u>M-299461 03-2</u>	KtCA 6.1, 2903
acid	orange fruit	24 months	<u>M-38945-01-1</u>	0KCA 6 .2/04 0
miscellaneous	honey	6 months	<u>M-681002-02-2</u>	KC@ 6.1.2/08
Fluopyram-methyl-s	ulfoxide		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
water	cereal green material cucumber fruit	3 menths 24 months 2 months 2	M-274729-0201 M-54395-01-1	KCA 6.1.2/90 KCA 6.1.2/07
oil	rape seed sunflower seed	24 months 24 months 24 months	M-754395-001	KCA 67.2/04 4 ° KCA 6.1.2/04
protein	dry pea dry bean	24 months 24 morths	M-589465-01-1 M-754295-01-1	KCA 6.10704 KCA 6.1.2/07
starch	cereal grain barley grain	24 months 24 months 24 months	<u>M-204729-62-1</u> M6754395001-1	KCA 6.1.2/01 KCA 6.1.2/07
acid	orange fruit strawberry fruit	24 months 24 months	<u>M-389465-0161</u> <u>M-7\$4395-09-1</u>	KCA 6.1.2/04 KCA 6.1.2/07
miscellaneous	cereal straw	O montes O 6 montes ()	0 <u>M-274729-02-1</u> M-684002-02-2	KCA 6.1.2/01 KCA 6.1.2/08

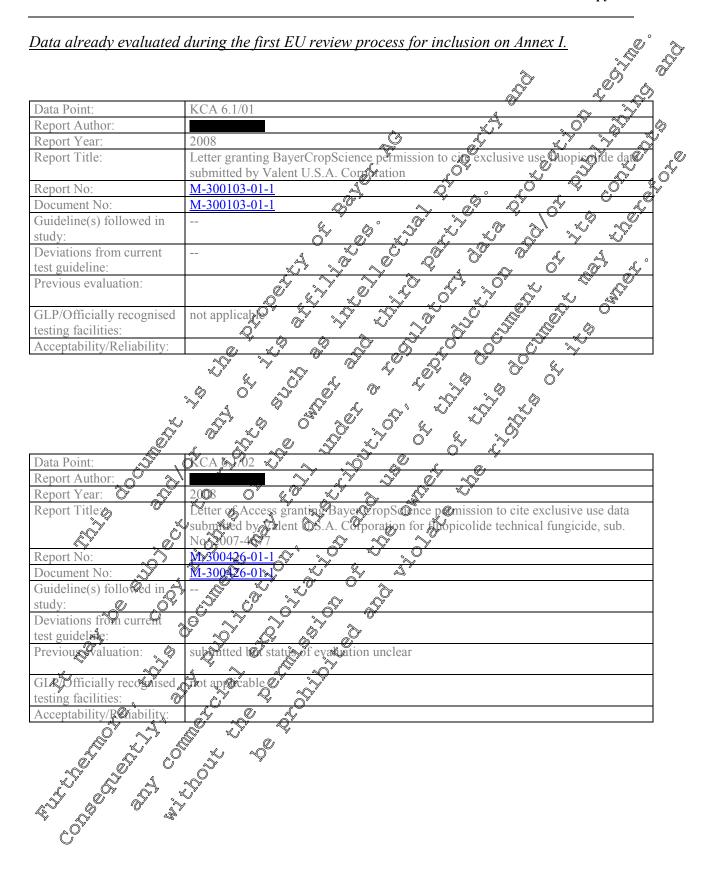
Table 6.1.2- 3 Summary of the deep-frezen storage stability periods for each commodity type, for each analytical target

Analytes C	Commodity Categories	Acceptable Maximum Storage duration
	Plant - figh water content	36 months
	Plant - high oil content	36 months
	Point - brown protein content	36 months
	Plant high starch content	36 months
	Pant - kigh acid content	36 months
	Q. High sugar content	6 months
	Plant - high water content	36 months
	Plant - high oil content	36 months
	Plant - high protein content	36 months
	Plant - high starch content	36 months
	Plant -high acid content	36 months
FLUSenzamide	High sugar content	6 months



Analytes	Commodity Categories	Acceptable Maximum Storage
	Plant - high water content	So months
	Plant - high oil content	36 months 36 months
FI II nomidul contin poid	Plant - high protein content	36 months of g
FLU-pyridyl-acetic-acid	Plant - high starch content	36 months y 0 0
	Plant -high acid@ontent	36 months 5
	High sugar content	36 months 36 months 37 months
	Plant - high water content	
	Plant - high cu content	of months
FLU-pyridyl-carboxylic-acid	Plant-high protein content	A Standard S
1 LO-pyndyr-carboxyne-acid	Bhant - thigh starch content	To months
	Plane - high acid content	5 36 months
	High Sugar content	C Months ²
	Plant, high water content	36 months
	Bant - høgh oil content	36 months
FLU-7-hydrox	Plant - krýh protein content	S Months
	Plant - high starch content	4 36 months
	Plant-high acio contene	24 months
FLU-7-hydrox	High sugar content	6 months
	Plant - high water content	2/ 18 months
	Plant - Righ starch content	24 months
FLU-methyl-styfoxide	Rant - high oil content	24 months
Q A S	Plant - bigh protein content	24 months
	Plant - high acid content	24 months
	High Sugar content	6 months







Data Point:	KCA 6.1/03
Report Author:	
Report Year:	2008
Report Title:	Phase report: 6 months stability in orange of study 07-02 - Storage stability of the residues of AE C656948 and its metabolites (AE F148815, AE C657188 and BCS AA10139) in orange during deep freeze storage for up to 4 months
Report No:	MR-08/036
Document No:	<u>M-298687-01-1</u>
Guideline(s) followed in study:	M-298687-01-1 EU Directive 91/414/EEC amended by the Composition directive 032/V595 rev (1997); US EPA Residue Chemetry Test Guidone OPPTS 8661380: Qorageo Stability Data
Deviations from current test guideline:	
Previous evaluation:	yes, evaluated and accepted rev. 1 to Vol.3 of DAR B7 Argust 2012 (references elied on)
GLP/Officially recognised testing facilities:	Yes, conducted under GEP Officially recognised Asting Beilities
Acceptability/Reliability:	$Yes \qquad \qquad$





Data Point:	KCA 6.1/04
Report Author:	
Report Year:	2007
Report Title:	Storage stability of AE C638206 and its metabolites AE C657378 (3-OH-BAM), AZ C653711 (BAM) and AE 1344122 (P1x) in/on cereals (rest of plant, graps, straw for
Report No:	MR-178/04
Document No:	
Guideline(s) followed in study:	M-2/4/29-02-1 not specified
Deviations from current test guideline:	None Y NO O O
Previous evaluation:	
GLP/Officially recognised testing facilities:	Yes, conducted utder GDP Officiely reconsed disting Scilities
Acceptability/Reliability:	$\frac{Yes}{Q^{2}} \xrightarrow{Q^{2}} Q^{$

This study was conducted in the frame of the fluopicolide (AE C638206) project. It ioconsidered to be relevant for this fluopyram EU renewal as AE 1344122 (Alias Fluopyram-methyl-suboxide) is a common metabolite between these two fungicides.

The purpose of this study was to determine the storage stability of residues of fluopicolide and its metabolites AE C655378, AEC653711 (BAM) and AE 1344122 (alias Fluopyram-methyl-sulfoxide) in fortified control samples of plant origin (wheat straw, grain, green material) during freezer storage at \leq -18 °C for 25 months?

For the purpose of this dossier, the following summary will give results only for FLU-methyl-sulfoxide (AE 1344122) which is a common metabolite of fluopicolide and fluopyram.

I^O Materials and Methods

To determine the freezer storage stability of a common metabolite of FLU-methyl-sulfoxide in cereals (wheat straw, grain, and green material), 5, g aliquots of the homogenised control materials were weighed into the bottles and were fortified with the speking solutions containing the four analytes, resulting in a fortification level of 0.40 mg/kg in all matrices. After fortification, the solvent was allowed to evaporate for about 15 min. In addition, Untreated samples of each sample material were prepared for control and recovery experiments. Subsequently, the bottles were closed and deep-frozen until analysis (at \leq -18 °C), except for the day 0 samples (five spiked samples, two control samples and two control samples for method validation recoveries).

The boxes containing the sample material for control samples were also stored in frozen conditions and were analysed at the normal storage intervals of 0, 30, 90, 180, 360, 540, and 760 days.

On day 0 (zero-time analyses) five spiked samples and two control samples were analyzed. Since these samples are recovery samples, it was not necessary to include concurrent recoveries.

Aceach campling interval at least three fortified and five control samples were removed from the deepfreezer and allowed to reach room temperature (nominal day 30 and 90 only three fortified and three control



samples were removed from the deep-freezer). Subsequently, two of the control samples of each sample material were fortified with the test items to determine the concurrent recoveries (fortification levels, were at the same magnitude as the spiked storage samples). The samples were expacted and applysed " concurrently with the third control sample and the spiked storage samples.

In order to determine residues of FLU-methyl-sulfoxide in cereals matrices the analytical method 00782/M002 was used (Schoning, R. and 01/09/2003, M-226098-02-2, see MCA section 4.1.2). Despite not being fully validated according to SANCO/3029/99 rev.4, the method is considered fit for purpose

Briefly, residues of FLU-methyl-sulfoxide were extracted with a might of acetop water adjust with sulphuric acid to pH 2. After addition of L-cysteine drochloride (250 mg/L) and filtration, the extractis filled up to volume. An aliquot is concentrated to the aqueous remainder. The solution is again adjusted to pH 2, NaCI is added and partitioned twice again MTBE. For the determination of ELU-methyl-suffexide, an aliquot is concentrated to dryness and discolved in a mixture of the ton Orile/water/amtaonium acetate. The residues are quantified by reversed phase HPLC and MS/MS-detection.

The limit of quantitation (LOQ) is 0.01 mg/kg in all tested sample materials For quantitation, the matrix-matched standards were used.

> Findings II.O

In control samples, residues of FOU-methyl-sulfoxide were below 36% LOC Summaries of concurrent reçoveries conducted as a part of this study are presented in De Table 6.1.2-4. The obtained mean concurrent recoveries per for fication level of FLAC methy sulfagide ranged between 63 % – 80 % for wheat straw, 7 $\frac{1}{2}$ – 86 % for wheat (grain) and 66 % – 1.1 % for wheat green material. Summaries of the reside behaviour of FLU-methy sulforter in stored samples are presented in the Table 6.1.2-5.

- Uncorrected mean recoveries in wheat straw show a stability period of 18 month for deep frozen • residues mean ecovories ranged between 73 % and 89 %
- Uncorrected mean recoveries in wheat grain show a stability period of 24 month for deep frozen residues (mean recoveries ranged between 70 % – 98%).
- Oncorrected mean recoveries in wheat green material show a stability period of 90 days for deep frozen resideres (mean recoveries finged between 70 % - 85 %). As the fresh concurrent recovery means in over material are quite low below 70%), the apparent instability of the residues after storage can actually be attributed to a low analytical method performance.



Residues of FLU-mchyl-sulfoxide fortified to coord samples of wheat grain at 0.1 mg/kg were stable for at least 760 days. In wheat straw, the residues were stable for at least 540 days. In wheat green material a stability of 90 days only could be demonstrated. This result can be attributed to the low performance of the analytical method as the concernment over the store over the store of the store over the store of the store over the store ove 01-1, see Co-6.1.2.7) show better result

Assessment and conclusion by applicant:

Ĉ,

Residues & LU-methyl-sulfixide in wheat grain at 0.1 mg/kg were stable for at least 760 days. In wheat straw, the residues were stable for at least 540 days. In wheat green material a stability of 90 days only could be demonstrated.



Plant naterial	Fortification Level [mg/kg]	Nominal Storage Interval (days)	FLU-methyl-sulfoxide Single Recoveries [%]*	Mean [%]	RSID ISM	"	
		0	73; 76; 83; 93; 76	80 🦨	10.0	8.6	je v
		30	75;46** 🖏	75 🛴	-		
		90	79 ; 79 📎	7 9 0°	-	\sim - \sim	
Wheat	0.10	180	68 ; ZQ	Î	-	Ø - Z	× ×
(straw)		360	69 ₄ ,Ø13	71	- 0	, Q	Å [*] «C
		540	80	Տ 80 <u>~</u> ° ՀԾՇ	4	a	
		760	Q 6 1;65 🔨	. Ø	Į.	, O [×] - <i>k</i>	a y
	Overall Mean	, RSD and st	andard deviation [%]		@10.2 💡	7.7	
		0	64; 8 2, 64; 8	74 760 01	14.2	10.3	\sim
		30	A 77 0 0	760	-0*	\$- A	, e ⁰
		90	× × × 85; 76 × ×	<u>_</u> 81	\$-		
Wheat	0.10	180	× × 88;83 ~	× 86 ×	9 - X	<u>ب</u> ج	1 C
(grain)		360 Q	<u>ر 🖓 84 کې کې د</u>	© 84 🟑		Ž	Ň
		540 ⁰ V	√ • 75 ¥71;6 8 ♥ @	710	<u>A</u>	3.5	<i>y</i>
		260	89; 64	87	, D-	Q - Q	
	Overall Mean	i, RSD and st	andard Geviation [%]	_م 0 77 _م	<u>م 11.1 گ</u>	8.6 8.6	
			⁰⁰ 74; 79, 99; 82; 78	Y 78 🕉	4.0	1. 3.3	
	*	J″ <u>3</u> 0 °	76; 78 × 07	77 2~91	O ^y	~~ -	
Wheat		Å,		<u>~91</u>	ĝ-	-	
(green	0.10 🥎	180 <i>©</i>	65.67	S 66	/	2 -	
naterial)		360	0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0	84	- A	-	
		540	Q17;11%	@17	, Ôľ	-	
		36 0	© 5 67; 6 5	66	Ċ [%] -	-	
	Overall Mean	1, RSD and st	andard deviation [%] C	82	[*] 19.2	15.7	

(10

RSD: relative standard deviation If sample size (n) S, then standard deviation is not a consideration; only the method is reported Fortification as: FLU-methyl-sulforide; determination as: FLU-methyl-sulforide; calculated as: Fluopyram

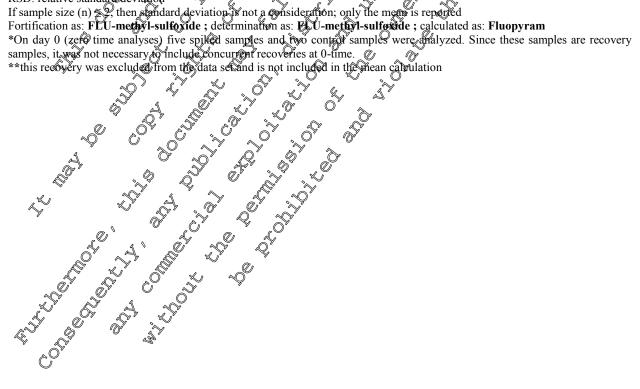


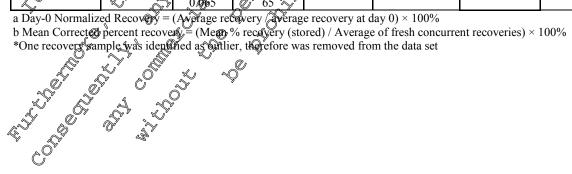


Table 6.1.2- 5:Storage stability data and concurrent recovery data for FLU-methyl-sulfoxide (fortification at 0.10 mg/kg)

	(Iortifica		0 mg/ kg/			~	<u>```</u>
C IU	FLU-methyl-sulfoxide Nomial Residue Level in Stored Samples Storage				Day 0 Normalized	Average %	
Commodity	Period (days)	mg/kg	% of nominal spiking level	Mean % recovery	%	Concurrent Recoveries	Corrected Recovery
	0	0.073 0.076 0.083 0.093 0.076	73	5 88 5 5 88 5			
	30	0.095 0.079 0.091	95 () D 76 () 91			\$ \$ 5* \$ \$	
	90	0.077 ~0.096 ~0.093&	× 77 ~ 96 ~ 95	5 ⁸⁹ (
Wheat (straw)		0.07 01074	74 74	2 173 OF		× 40 × 71	104
	\$360.	°0%082 (/	2 77 2 77		2 98 98 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	۶ 71	111
A A A A A A A A A A A A A A A A A A A	940 ×	0.0790 0.077	A 77 .			80	99
E, ^y	780	650.059 ≪ ∀ 0.0 60 05056			73	63	92
A A A		9.061 0.079 0.082 9.064 2.0.083	59 50 56 56 64 79 642 56 56 56 56 56 56 56 56 56 56	₹ 0,74 0,74	100	74	100
لمنتخب (grain)	30 5 F	C0.100	× 100×	98	133	76	129
Wheat (grain)	2 90 5 F	0.094 0.080 \$0.108	ý94	94	127	81	116
		0.061 0.077 0.071	61 77 71	70	94	86	81
	2JP						



a	Nomial Storage		-methyl-sul Level in Store		Day 0 Normalized	Average %	Mean Corrected	
Commodity	Period (days)	mg/kg	% of nominal spiking level	Mean % recoverv©	% Recovery ^a	Concurrent Recoveries	Recovery	
	360	0.080 0.090 0.089	80 90 89	A86	40 ⁷		Q 180 T	
	540	0.074 0.067	74 67					0
	760	0.074 0.077 0.082	₹44 ⁷ ⁹ 77 82 ⁴ 70 ⁹					•
	0	× 9.082	× 79 °° > 200	27 27 278 2 ⁹⁷⁸ 2 2			× 100	
	30, 30,	0.071 0.071 0.069	45 71 71 69 69 78 5 85 927	\$ ⁷⁰ ,5 ⁹	90 L		91	
~			78 ~ 85 92	\$ \$ \$ \$ 85 \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$		چ» 91	93	
Wheat (green material)		() ()		6 ⁸⁷		66	102	
4 Y '	39360 Å	0.082 0.080 Q081	\$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	\$\$1 \$	104	84	96	
		\$~0.091 0.11¥ √0.11¥			138	117	91	
Day-0 Normaliz		0.056 0.062 0.065		61	78	66	92	





Data Point:	KCA 6.1/05
Report Author:	
Report Year:	2010
Report Title:	Storage stability of residues of AE C656948 and its metabolites (AE F148815, AE
	C657188 and BCS-AA10139) in orange during deep free storage for to 3(5) months
Report No:	07-02
Document No:	<u>M-356046-02-1</u>
Guideline(s) followed in	EU Directive 91/414/EEC amended by the Continuity direction 7032/01/95 07.5
study:	
	US EPA Residue Chemistry Test Guideling, OPPT \$60.1389. Storage Stagility Dora
	OECD Test Guideline 5%, adored 16 Diober 2007
Deviations from current	Deviation to OECD 500: samples spiced at 25XLOQ orstead 51 10X. Nevertheless,
test guideline:	stability of residues still a dessable at this evel.
Previous evaluation:	yes, evaluated and accepted
GT D (0 M) + 11	rev. 2 to Vol.3 @DAR 177 Nov@nber, 2017 (references velied of)
GLP/Officially recognised	Yes, conductorunder GLP/Officially ecognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes y g g g g g g g g g g g g g g g g g g

The study was initiated to evaluate the stability of fluopyram (AE C656948) and its metabolites fluopyrambenzamide (AE F148815) fluopyram-pyridyl-carboxyle acid (AE C657188), fluopyram-pyridyl-acetic acid (BCS-AA10C9) in matrices of plant origin (orange fruits) during freezer storage period of 36 months (at \leq -18 °C).

Materials and Methods

To determine the freezer storage stability of the refevant residues of fluopyram (AE C656948) and its metabolites fluopyram-benzamide (AE F048815), fluopyram-byridyl-acetic acid (BCS-AA10139, alias FLU-PAA), and fluopyram-pyrdyl-carboxylic acid (alias AE C657188, alias FLU-PCA) in matrices of plant origin (orange fruits), 105 g aliquots specified as "spiked samples" individual samples were fortified with 100 μ L of the spiking solution at 20 mg/L, resulting in a concentration of 0.20 mg/kg of fluopyram or FLU-benzamide or FLU-PCA or FLU-PAA*. The plastic bottles were sealed and stored in frozen conditions immediately after the fortification. The baxes containing the sample material for control samples were also stored in frozen conditions (at \leq 78 °C) and were analysed at the nominal storage intervals of 0, 3 6,4Z, 18, 24, and 36 months.

Concurrent recovery experiments were performed at all storage intervals by spiking control samples with a mixture of fluopyram, FLU-benzande, FLO-PAA or FLU-PCA or at a level of 0.01 and 0.20 mg/kg. On day 0 (zero time analysis) three spiked samples per test item and one control sample were analysed. In parallel, four concurrent recoveries were conducted: one at the level of 0.01 mg/kg and three at 0.20 mg/kg. All samples were analysed according to the analytical method 00984 (**MCA**) (2007, <u>M-283301-01-1</u>, see MCA) Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.



Briefly, residues were extracted from 10 g of sample material (5g for straw) by two successive extractions's using a high speed blender with a mixture of acetonitrile:water (80:20; v:v). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

- dilution performed under acidic conditions and measured in negative electrospray ionization of the determination of FLU-PCA.
- dilution performed under basic conditions and measured in positive electrospray ion zation for the determination of fluopyram, FLU-benzamide and FKE-PAA.

*Due to its instability, the analytical standard of fluopyrand pyridyl-acetic acid (BCS-A/10139) was made available under its sodium salt form (BCS-AA10189) which was used as reference item. The limit of quantitation (LOQ) (expressed as parent fluopyram equivalents) for each single analyte is 0.01 mg/kg in all tested sample materials. The quantification was carried out using internal stable abelled standards.

II. Findings

In control samples, residues of fluopycam, HLU-bercamide, FLU-PAA and FLU-PCA were below the Limit of Quantification (< 0.01 mg/kg for each test item expressed as fluopyram). Sumparies of concurrent recoveries conducted as a part of this study are presented in the Table 6.12-6 to Table 61.2-9. The obtained individual and overall mean concurrent recoveries were satisfactory and were in the range of 70 -110 %, with the RSD < 20% for all tested analytes at two fortification levels.

- For fluopyram, uncorrected mean recoveries in orange show a stability period of 36 months for deep frozen residues (mean recoveries anged between 93 % and 100%).
- For FLU-benzanide, incorrected mean recoveries in orange show a stability period of 36 months for deep frozen residues (mean recoveries ranged between 86 % 102%).
- For FLU CA, uncorrected mean recoveries in orange show a stability period of 36 months for deep frozen resolues (mean recoveries ranget between 92% 102%).
- For FLU-PAD, uncorrected mean recoveries in orange show a stability period of 6 months for deep frozen residues (mean recoveries) anged between 78 % – 91 %).

AT. Conclusions

Residues of Ruopyram and its metabolites (flaopyram-benzamide, fluopyram-pyridyl-carboxylic-acid) fortified at 0.2 mg/kg to control complex of orange (fruit) were stable during deep-frozen storage for at least 36 months. Residues of FLU-pyridyl-acetic arid were stable in orange fruit only over 6 months of storage

Assessment and conclusion by applicant

The study is acceptables Residues FLO, FLO Denzarode, FLO-PCA in orange (fruit) at 0.2 mg/kg were shown to be stable for 36 months. Residues of FLU byridyl cetter-acid were stable in orange (fruit) only over 6 months of storage.

able 6 9.2- 6: Concurrent recovery data for fluopyram (AE C656948)



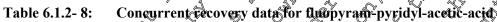
							_
Plant material	Fortification Level [mg/kg]	Storage Interval (days)	Fluopyram Single Recoveries [%]	Mean [%]	RSD	Standard deviation	
	0.01	$ \begin{array}{r} 0 \\ 3 \\ 6 \\ 12 \\ 19 \\ 24 \\ 36 \\ \end{array} $	97 85 87 86 90 95 10	97 85 87 × 86 × 90	- - - - -		
Orange (fruits)	0.2	$\begin{array}{r} 0\\ 3\\ 6\\ 12\\ 19 \end{array}$	105@02; 103 95; 95 98; 101 99@6	↓ 101 ↓ 103 ↓ 400 ↓ 98 ↓ 93 ↓ 93 ↓ 94 ↓ 107 ~	0 - 0 - 0 3.P 0 4.6 ×		
	Overall Mean	ı, RSD andşt	andard deviation [%] 🖓 🔍	^O 97,∜	6.8	6.6	
RSD: relative s	standard deviation		The share was a second and second	* <u> </u>			
If sample size ($(n) \leq 2$, then standard defined as $(n) \leq 2$.	eviation is not	a consideration; only the mean is	s reported	õ,	Š V	
Fortification as	: fluopyram; determina	ation as: fluoj	yram; calculated as: fluopyram	K ×C		, °~,	
	*				ð	s.	
			2 99 ; 93 ; 93 andare deviation [%] a consideration; only the mean is syram; alculated as: fluopyram of the			>	
COP COP							



able 6.1.2	- 7: Concurrent	trecovery	data for fluopyram-benza	amide		2°
Plant material	Fortification Level [mg/kg]	Storage Interval (days)	FLU-benzamide Single Recoveries [%]	Mean [%]	RSID ISH	
		0	104	104 🦨	Ą -	$\begin{array}{c} & & & & \\ & & & & \\ & & & & \\ & & & & $
		3	98 🖏	98 🋴	-	
	0.01	6	104 🚿	1000	-	
		12	106.	606	-	
		19	1,08/	×103	- 0	
		24	(AT A A A A A A A A A A A A A A A A A A	₩ 83 <u>~</u> ° .960	-5	
0		36	Ø 96 🥎			
Orange (fracita)		0	&102; 102; P02		@0.0 ¢	
(fruits)		3	0 [°] 92 <i>q</i> 93 «	£ ⁹³ ×		
		6		93	-67	al - al
	0.2	12	× \$6;94	.94	\sim	<u>0'- @'</u>
	19	9 3 ; 88 90 O	19 0	0 [°] 2.8 🖌	0 - 0 , (, ° <u>2.55</u> , (, ° K)	
	24	¢ [™] 91 ; 89 ; 90 ∘	© ⁷ 90 √े	1.1.	KO S	
		36,0♥	94-097 ; 100	¥ 9/(/)	3	3.0 V
	Overall Mean	n, RSD and st	tandard deviation [%] 👘 🕺	~ 96	A .3	S 6.0 Q
D: relative	standard deviation			0.0		

(1) • •

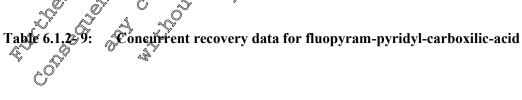
If sample size (n) ≤ 2 , then standard deviation is not a consideration only the mean is reported Fortification as: FLU-benzamide; determination as: FIQP-benzamide; calculated S. Fluopyram Ø



Ô

		y Ki		1.	. 05	
Plant material	Fortification Level	Storage Anterval (days)	Single Recoveries [%]	Mean [%]©	(*) (*) (*) (*)	Standard deviation
		P	880 20	88	-	-
	ĝ ···	© 3 .1		, © 82	-	-
		S 6 F		77	-	-
K, Y	0,00 0		\$ 79 \$ \$	79	-	-
		∞19	S ~ 78 ~	78	-	-
		\$24 ×		70	-	-
0			\$1 p	81	-	-
Orange		ð Øj	\$8; 89; \$ 91; \$	88	0.7	0.6
(fruits)		\$~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	91; 9 9	91	-	-
1		$^{\vee}6$ Q	80×79 × 9	81	-	-
1 D U	0.2	D 1255		72	-	-
	N R	19	× × × × × × × × × × × × × × × × × × ×	85	2.5	2.1
<i>L</i> ^t →		24	83 ; 86 ; 81	83	3.0	2.5
l "Y		s 36 o	78 ; 76 ; 82	79	3.9	3.1
	Overall Mea	r, RSD and st	tandard deviation [%]	82	7.2	5.9

RSD: relative standard deviation QIf sample size $Q \le 2$, then standard deviation is not a consideration; only the mean is reported Fortification is: FLU=PAA; corrination as: CU-PAA; calculated as: Fluopyram





Plant material	Fortification Level [mg/kg]	Storage Interval (days)	FLU-PCA Single Recoveries [%]	Mean	RSD	Standard	
			Single Recoveries [70]	[%]		deviation	
	0.01	0 3 6 12 19 24	96 101 95 103 84 77 77	96 101 95 x 103 y 84	- - - %	- ~~~ - ~~~~ ~_~~~~~~~~~~~~~~~~~~~~~~~~~	
Orange (fruits)	0.2	36 0 3 6 12 19 24 36	98799; 99 98; 100 92; 98 96, 4706		- 0 06 - 2 - 2 - 2 - 2 - 2 - 2 - 2 - 2 - 2 - 2		
	Overall Mear	1. RSD and	andard deviation [%]	[©] 95.∜	6.9	à c	L. C.
RSD: relative of	tandard deviation	<u>, 08</u>					Ψ
(f sample size (n < 2 then standard de	wiation is not	a consideration: only the mean is	s reported	, S		
Fortification as	• FLU-PCA: determina	tion as FLA	PCA: calculater as Fluory ran				
. or third at our ab		~(.) ^~		r di			
			A consideration; only the mean is PCA; calculated as: Fluidbyram Charter deviation [%]			ð	



Table 6.1.2- 10:	Storage s	tability da	ata for fluop	oyram (fort	ification at 0.2	200 mg/kg)	Q	°
Commodity	Storage Period	Fluopyram Residue Level in Stored Samples			Day 0 Normalized %	Agerage % of Fresh Concurrent	Nean Correctêd	\$ }
	(days)	mg/kg	% of nominal spiking level	Mean %	Decouvery	Recoveries >	Recovery	
	0	0.220 0.204 0.220	110 102 110	\$ 707		Q ¹⁰³ O ⁴		
	3	0.200 0.197 0.201	100 99 101		S S &			þ
	6	0.206 0.210 0.207	103 1054 1054 1054 1054					
Orange (fruit)	12	0.2080 0.193 0.205	× ⁴ 97 °				لم من 103	
	19	0.204 0.19 0.19 0.182	0 ²	99 A		492 7 92 7 227	104	
		0.189 0.189 04 77	91 2 95 095 5 2989			م بر 94	99	
a Day-0 Normaliz		0.204 & 0.2200 0.220				107	100	

«

a Day-0 Normalized Recovery = (Axerage recovery / average recovery at day 0) 100% b Mean Corrected percent ecovery (Mean recovery (stored) / Average of fresh concurrent recoveries) × 100%

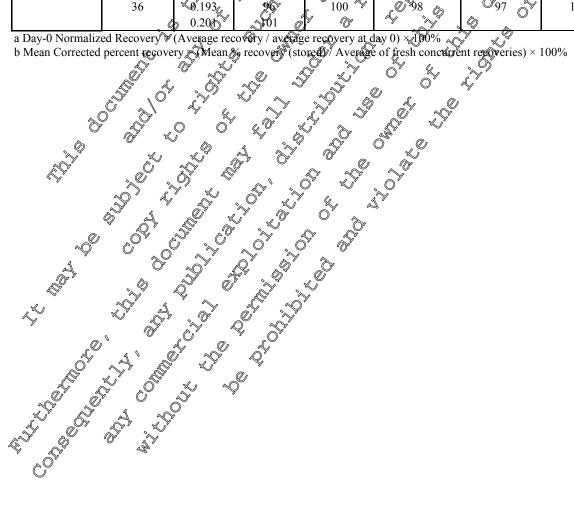
× 1

Comfodity	Storage Peciod				Day 0 Normalized %	Average % of Fresh Concurrent	Mean Corrected %
	Cays) A	,`mg∕kg	4% of nominal spiking keyel	Mean % recovery	Recovery ^a	Recoveries	Recovery ^b
Orange (fruit)		0.20 0.205 0.203	©104 © 102 101	102	100	102	100
Orange (fruit)		0.174 0.169 0.172	87 84 86	86	84	93	92

K Table 6.1.2- 11: Storage stability data for Puopyram-benzamide (fortification at 0.200 mg/kg)



Commodity	Storage Period (days)	FLU-benzamide Residue Level in Stored Samples			Day 0 Normalized %	Average % of Fresh Concurrent	Mean Corrected Becoverie
		mg/kg	% of nominal spiking level	Mean % recovery		Recoveries	
	6	0.173 0.169 0.178	86 85 89		85 Q	93	
	12	0.189 0.202 0.200	101 & 100 O				× 105~ ×
	19	0.175 0.191 0.181	~ ⁹⁶ ~				
	24	0.182 0.180 0.185	@ 92 @	25 91 25 25		2 5 90 5 5 90 5 7 90 5	0 29 ¹⁰¹
a Day-0 Normaliz	36	0.2007 0.193	103 V V 103 V V 103 V V 103 V			\$ 97 \$ \$	103





	0.200 mg	8/				<u> </u>	
			FLU-PAA			Ô ^y v	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
	Storage	Residue	Level in Store	d Samples	Day 0	Average %	Mean
Commodity	Period		% of	Č V	Normalized	of Fresh ⋟ Concurrent	Corrected
	(days)	6	nominal	Mean %	Recover	())	Recoverve
		mg/kg	spiking	recovery	A A	Recover@s	\$ 6 ^{\$} &
			level		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		Č (V
	0	0.184	92	≪ ^°			103,5
	0	0.182 0.180	91			880	× 103 F
		0.180	90 7 0	$\tilde{\mathcal{V}}$			
	3	0.166	×83 ^	83	°91∕A	91 .	\$ 91 °
		0.172	<u>86 k</u>			()* 91 * ()* *	
		0.159	D¥ 800×			5 ⁵⁶ 81,5 ⁵⁷	
	6	0.154	11 Ô-: Ô	78	86	81 S	<i>√</i> [©] 96
		0.152	× 76 2	Â,			×
Orange (fruit)	12	0.111			10 ⁶ 64 0	72 0	80
Grunge (nuit)	12	0.110	× 58	58° 2			80
	·**	0.125	62 64	A A			
	10	@0.129	64		68 K	\$ 85	73
		0.1	59 5		, ȥ	Ç, î	
	(0°1115 0.116 &	× 57~			83	69
Š		0.116 Q 0.1140	, 38% 4.97 ×			63	09
	·0· ~	0.0947			Ő "Ø		
	36°	a0957		48 O S	653	79	60

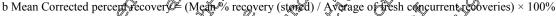
b Mean Corrected percent recovery = Mean % recovery (stored) Average of fresh concurrent recoveries) × 100% Ş

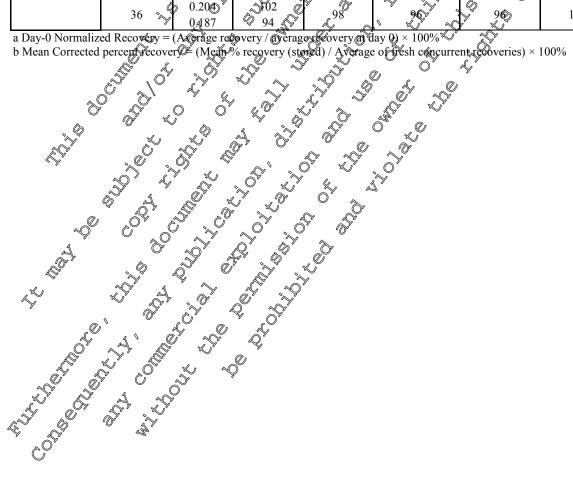
Storagestability data for fluopyram-pyridyl-carboxilic-acid (fortification at 0.200 mg/kg) Table 6.1.2- 13: à

O' adays)		ALU-PCA Qevel in Store % of nominal spiking level	d Samples Mean % recovery	Day 0 Normalized % Recovery ^a	Average % of Fresh Concurrent Recoveries	Mean Corrected % Recovery ^b
Frange Gruit)	0.208	104				
Orange Gruit)	0.205	103	102	100	99	103
	0.199	100				



Commodity	Storage Period (days)	FLU-PCA Residue Level in Stored Samples			Day 0 Normalized	Average %		
Commodity		mg/kg	% of nominal spiking level	Mean % recovery	% Recovery ^a	Concurrent	Recovery	Ĵ,
	3	0.190 0.193 0.191	95 97 95	296				
	6	0.191 0.188 0.196	96 94 O 98					
	12	0.186 0.196 0.185	98 98 98 93		() 25 ×		9467 0 0	
	19	0.185	9 07 © 93 ©	× 23	91 °	0 ³ 93 5 ⁵	s 99	
	24	0.183 0.183	→ 92 ¹ 0 ¹ 20 ²	92 J		~ ⁹⁶ &	95	
a Day 0 Normali	36 %	0.20⊕ 0.487	\$102 \$102 94	98 98		2 9 6 9	102	







Data Point:	KCA 6.1/06
Report Author:	
Report Year:	
Report Title:	Storage stability of residues of AE C656948 and its metabolites (AE F148815, AE C657188, BCS-AA10139 and BCS-AA10065) in plants during deep from the storage for up to 36 months
Report No:	
Document No:	<u>M-299461-03-2</u>
Guideline(s) followed in	EU Directive 91/414/EEC amended by the Commission direction 7032/21/95 rov.5
study:	
	EU Directive 91/414/EEC amended by the Convission direction 7032/21/95 rov.5 (1997); US EPA Residue Chemistry Test Guideline OPPT 860.1389: Storage Stavility Don; OECD Test Guideline 566, adored 16 Gotober 2007
Deviations from current	Deviation to OECD 500 : samples spiced at 26 XLOQ distead of 10X. Nevertheless,
test guideline:	stability of residues A still a dessable at this quel.
Previous evaluation:	yes, evaluated and accepted
GLP/Officially recognised	Yes
testing facilities:	
Acceptability/Reliability:	Yes y g g g g
	$\frac{\operatorname{Yes}}{\sqrt{2}} \xrightarrow{\psi} 0 \xrightarrow{\psi} $

The study was initiated to evaluate the stability of fluopyram (AE C656948) and its metabolites fluopyrambenzamide (AE F148815), fluopyram-pyrudyl-catboxylic acid (AE C671884, fluopyram-pyridyl-acetic acid (BCS-AA10139) and Puopyram-7-hydroxy (BCS AA10055) in matrices of plant origin (lettuce head, wheat grain, drypea seed, and rape seed) during freezer storage (at 2-18, C).



ß

To determine the freezer storage stability of the relevant residues of fluopyram (AE C656948) and its metabolites fluopyram-perzamide (AE F148815), fluopyram-pyridyl-carboxylic acid (AE C657188, alias FLU-PCA), fluopyram-pyridyl-acetic acid (BCS-AA10139, alias FLU-PAA) and fluopyram-7-hydroxy (BCS-AA10055) in matrices of plant origin (lettuce head, wheat grain, dry pea seed, and rape seed), individual samples (in form of tOg-aliquets specified as "spiked samples") were fortified with fluopyram or fluopyram-benzamide or fluopyram-pyridyl-carboxylic acid or fluopyram-pyridyl-acetic acid (BCS-AA10139) (sodium sait of BCS-AA10139) or fluopyram-7-hydroxy (depending on the test system) at the level of 0.20 mg/kg. After vards, the samples were stored in plastic containers at \leq -18 °C and were analysed at the nominal storage intervals of 0, 3, 6, 13, 08, 24, and 36 months.

In lettuce hear (high water content matrix) and wheat grain (high starch content matrix) the following analytes were tested: fluopyram, fluopyram-benzamide, fluopyram-pyridyl-acetic acid and fluopyram-7-hydroxy

In dry pea seed (protein content matrix) and rape seed (oil content matrix) the following analytes were tested: fluopyram FLU-benzamide, FLU-PAA and FLU-PCA.

776



To demonstrate the accuracy of the fluopyram and its metabolites determination during this study, recovery experiments were performed prior to sample storage (initial method validation) and at each storage interval by fortifying stored control samples with all the test items.

A set of three recoveries at 0.01 mg/kg and at 0.20 mg/kg for each matrix were conducted before the nominal storage interval of Day 0. For this purpose, control samples were freshly fortified with fluon tam, FLU-benzamide, FLU-PAA, FLU-PCA and FLU-7-hydroxy at 0.01 mg/kg and at 0.20 mg/kg and then analysed.

Concurrent recoveries were conducted at the nominal storage intervals of 3, 6, 13, 18, 24 and 36 months. For this purpose, stored control samples were freshly fortified with a mixture of fluopyram FLU benzamide, FLU-PAA, FLU-PCA and FLU-7-hydroxy at 0.01 and 0.20 mg/ks. The treshly fortified samples were then extracted and analysed concurrently with the control and spiked samples of these nominal storage intervals.

In order to identify any degradations into ELU-methyl-suffoxide (AE 644122), this compound was quantified during each storage interval analysis. Therefore, procedural recoveries on this analyte vere carried out in order to assure the validation of the results. No degrations into ELU-methyl-sulfoxide were observed during the study.

On day 0 (zero-time analysis) three spiked samples per test item and one control sample were analysed. In parallel, four concurrent recoveries were conducted: one at the level \$20.01 mg/kg and three at 0.20 mg/kg. The stored control samples were either analysed directly as control samples (one) or freshly fortified for recoveries (four: one at 0.01 mg/kg and three at 0.20 mg/kg). The freshly fortified samples were analysed concurrently with the remaining control samples and the stored spiked samples.

All samples were applysed according to the analytical method (0984 (19984, 05/02/2007, M-283301-01-1, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, 0whiclo comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Briefly, fesidues were extracted from 10 g of sample material (5g for straw) by two successive extractions using a high speed blender with a mixture of aceton write water (8020; v:v). After centrifugation the extract volume was adjusted. Then, the extracts were diffued to times by adding the internal standards:

- dilution performed under acidic conditions and measured in negative electrospray ionization for the determination of LU-PCA.
- dilution performed under basic conditions and measured in positive electrospray ionization for the determination of fluopyram, FLU-benzamide and FLU-PAA.

*Due to is instability the analytical standard of fluopyram-pyridyl-acetic acid (BCS-AA10139) was made available under its sodium salt form (BCS-AA10189) which was used as reference item.

No interferences greater than the LOO were observed in any of the control extracts from any matrix. Summaries of concurrent recoveries conducted as a part of this study are presented in the Table 6.1.2-14 to Table 6.1.2-19. The obtained mean concurrent recovery data were between 70 and 110% at each fortification fevel except for:

• FOU-benzamide in rape seed at 3 months : 124 % (20xLOQ level)

• QFLU-PCA in rape seed at 24 & 36 months 64 & 66 % (20xLOQ level)



This results show the accuracy of the fluopyram, FLU-benzamide, FLU-PAA, FLU-PCA and FLU-7hydroxy determination during the conduct of the study. The low method performance for FLU-PCA at 24 and 36 explains the low residue measured in stored samples at these timepoints.

Moreover, the overall mean concurrent recoveries are in the acceptable range of 76, 110%, with the RSD 20% for fluopyram, FLU-benzamide, FLU-PAA, FLU-PCA, FLU-7-hydroxy, and FLU-methol-sultoxide (AE 1344122) in all tested matrices (lettuce head, wheat grain, dry pee seed, and rape seed). Summaries of the residue behaviour in stored samples are presented in the table 6.1.2- 20 to Table 6.1.2-24.

- For fluopyram, uncorrected mean recoveries in all tested matrices show a stability period of 36 months for deep frozen residues (mean recoveries ranged between 93 106 %, 95 108 %, 95 103 %, and 95 115 % in lettuce (head), wheat (grain), dry pea (seed), and rape (seed), respectively)
- For fluopyam-benzamide, uncorrected mean recoveries in all fested tratrices shows stability period of 36 months for deep frozen residues (mean recoveries ranged between 84 96 %, 86 107 %, 83 96 %, and 85 124 %, indettuce (head) wheat (grain), dry pea (seed), and rape (seed), respectively.
- For fluopyram-pyridyl-acetic acid, the corrected mean recoveries in all tested matrices show a stability period of 36 months for deep frozen residues (not an recoveries ranged between 73 95 %, 82 95 %, 77 90 %, and 80 96 %, in lettuce (head), wheat (grain), dry pea (seed), rape (seed), respectively.
- For fluopyram-7-hydroxy uncorrected mean recoveries in lettuce (head) and wheat (grain) show a stability period of 36 months for deep frozen residuer (mean recoveries ranged between 95 104 % and 94 104 %, respectively). The stability of residues of fluopyram-7-hydroxy were not tested in dry pea (seed) and rape (seed).
- For fluopytam-PCA, uncorrected mean recoveries in ary pea seed show a stability period of 36 months for deep frozen residues (mean recoveries ranged between \$7 101 %. In rape (seed) the residues were stable over 18 months (uncorrected mean recoveries ranged between \$7 101 %). At 24 and 36 months the uncorrected mean recovery were \$7 % and 70%. As the concurrent recovery mean at 24 and 37 months is quite low (64 and 66% respectively), the low value measured in the stored sample are due to the poor efficiency of the method the day of analyses. The stability of the fluopy am-PCA residues was not tested aeither in tettuce head nor in wheat (grain).

Residues of fluopyram and us metabolites fluopyram-benzamide and fluopyram-pyridyl-acetic-acid) at 0.2 mg/kg were stable over 36 months at Te -18% in all rested matrices, i.e. in lettuce (head), wheat (grain), dry pea (seed), and rape (seed) 7 months).

Residues of fluopyram-7-hydroxy were stable in pettuce (head) and wheat grain over 36 months.

Residues of fluopyram-pyridyl-carboxylic-acid were stable in dry pea (seed) over 36 months. In rape (seed), fluopyram-pyridyl-carboxylic acid showed 18 months stability. The results at 24 and 37 months at 67% and 70% respectively can be explained by the poor efficiency of the analytical method the days of analyses as the concurrent recoveries were quite fow (64% and 66%).



Assessment and conclusion by applicant:

The study is acceptable.

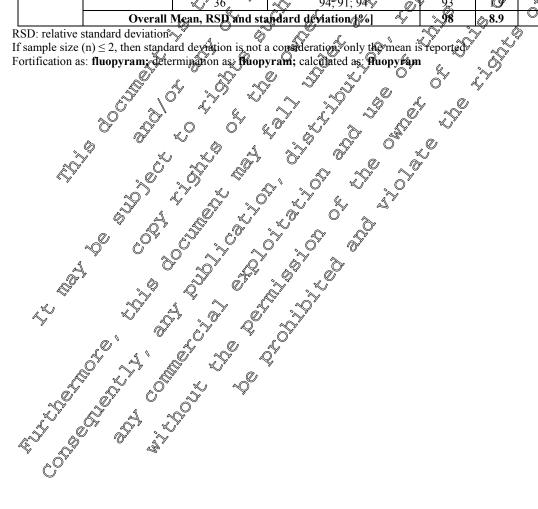
Residues FLU, FLU-benzamide, FLU-PAA in lettuce (head), wheat (grain), dry pea (seed and rape (seed at 0.2 mg/kg were shown to be stable for 36 months.

kg were	shown to be stal	ble for 36 months.	head) and wheat (grain) ove over 36 months of storage ar ata for fluopyram Single Recoveries [%)	r 26 month	- And	-	
dues of	FLU-PCA were	stable in dry nea o	over 36 months of storage ar	nd over 18	months i	in rane Reed)	Ç ^y y
sidues of	ILU-ICA wele	stable in dry pea c	over 50 months of storage at			in Tape (Seed).	
			- The second sec	"OU"			Ĩ
		<i>1</i> 4	A A	,Ô¥	*	, v , s ,	K)
le 6.1.2-	- 14: Concur	rent recovery d	ata for fluopyram	Ô.	Ő	ŏ, & `	Y (
Plant	Fortification	Storage Interval	Faropyram 🔨	Mean	RSD	Standard	Ľ
naterial	Level [mg/kg]	(days)	Single Recoveries [%]	*%	%]	deviation	, Q'
		0		98 🗶	, - C		Y
		3	A 294 0 0	94	-07	~ ~ <u>~</u>	_ 0
		0		80	<u> </u>		
	0.01	13		277 .	0'- 1	- ~~	, , ,
		18 0		O 93 K			
		24	a sy 91 sy a	910			
Lettuce		36Q*	80	3 0			
(head)				0105 107	2.4 Ĉ	283 283	
ana bh			111007; 102		400 1.5	4.5	
	0.2	<u>6</u> <u>6</u> <u>6</u> <u>6</u> <u>6</u>	2 (101; 99; 98 2 (14: 111-118		3.1	O [™] 1.5	
	0.2	Y ALO	05 05 06 0	VY NO	v	3.5	
	×,	18	95 %6; 96 v	96	0.6	0.6	
	, S	0 ³ 24 4 4		93	2.0	2.0	
3	Sugrall	Maan BOD and S	→ 95,96,96, → 95,97,90 ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓	-0 <mark>98</mark>	9.6	2.0 9.5	
	Sver all			98 88	9.0	-	
		3		103	-	-	
		\times $\overset{6}{\overset{6}}$		<i>a</i> , 94	-	-	
	0.01 ~	× 33 A		88	-	-	
<i>j</i>	Č_	13 18 21 21 21 21 21 21 21 21 21 21	84 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	84	-	_	
«Ŋ.		× 24 A		94	-	-	
1171		× 24 × 24	1 × 600 4	99	-	-	
Wheat (grain)	Q A		0 97,994; 96	96	1.6	1.5	
(grani)		N 3.00	~ LOD; 106; CNU1	104	2.5	2.6	
	Ŷ,	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0 99; 99099	99	0.1	0.0	
A A	0.2	$\begin{array}{c} & & & \\ & & & & \\ & & & \\ & & & & \\ & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ &$	\$ 99, 99, 99 113, 046, 114 109, 102; 103 \$ 97, 106; 100 100: 95: 99	114	1.4	1.5	
Ø	, Ô	10 10	100, 102; 103	104	2.0	2.1	
		× 24 36	97 ; 106; 100	101	4.5	4.6	
stor S			100, 95, 99	98	2.7	2.6	
U	Overal	Mean, R SD and sta	and rd deviation [%]	100	7.6	7.5	
			ر 103	103	-	-	
	ó ^y L ¹ .		96	96	-		
ĺ.			86	86	. =	-	
Drypen	\$ ^{30.01} C	→ <u>13</u> →	86	86	-	-	
(sted)	2 1 1	0 18	93	93	-	-	
\$.C		24	89	89		-	
	10° 47	36	104	104	-	-	
p) V	Overall 0.2	2	91; 91; 94	92	1.9	1.7	
\bigcirc		3	107; 100; 106	104	3.8	3.8	

L



Plant	Fortification	Storage Interval	Fluopyram	Mean	RSD	Standard	¢)°
material	Level [mg/kg]	(days)	Single Recoveries [%]	[%]	[%]	deviation	. 6
		6	99; 98; 97	98	1.0	1.0	5 0
		13	109; 112; 113	111	1,00	2.1	
		18	96; 101; 102	100	DŽ	3.2	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
		24	101; 96; 93	97 🗳	4 .2	4.0~~	
		36	88; 93; 93	91	3.2	29 .	
	Overall	Mean, RSD and sta	indard deviation [%	980 [°]	7.6	×7.4	
		0	94	Å.	-	0 - 2	×,
	0.01	3	299."	L 99	- ~	Y Q,	\$ 4C
		6	00	°⊱ 90 ₆₀ °	-	"- (Ŭ "O ^v
		13		<u>_</u> 87∕€°	- Qí	<u>, 0⁷ - 6</u>	â,
		18			Ø- ?		~~~
		24		85	- \$	->	Ж,
P		36	A 790 0 D	900	0	al A	
Rape	-	0	109; 104; 99	1 04	A .8	5.0	<u>n</u>
(seed)		3 🖉	113·106·108	×109 s	3.3	3,6	
		6	97; 101; 102		2.8	.Q.1 (
	0.2	13	° 14,9;98;408 ∼°	,108		\$.1 (10.5 (2.9) (10.5)	ĺ
			§ 91; 98; 91		Ô 3.1 🖉	Š 2.%	
	l	Q4	@ 93; \$ 8; 97	§ 93 §	4.9°C	4.3	
		36	~ 94, 91; 94 <i>(</i>	₹ <u>9</u> 3	ĨŎ	\$1.7	
	Overall		ndard deviation/8%]	₹93 ∿.98	<u>گ</u> 8.9	0°8.7	1





DI I		<u>.</u>			DC-A	<i>a</i> ,	Š (
Plant naterial	Fortification Level [mg/kg]	Storage Interval (days)	FLU-benzamide Single Recoveries [%]	Mean [%]	RSIO (%)	Standard deviation	
		0	91	91	Á –		
		3	102	102	· > -		
		6	105	102	_		
	0.01	13	93		-	0 - 3	×,
	0.01	18	La Qu	\$101	- 0		S i
		24	A17	ີ∳ັ 77 _{ເກ} °	~~	.r - (S a
		36	© 105	_1 65	-Qí	. 0 ⁷ - A	a s
Lettuce		0	\$101; 105; 102 S	× 103	©2.0 %	2,15	
(head)		3		√ 103 m	0.5%	0.6	Ś
		6	A 98 101; 98	970	4.2	A.0 A	
	0.2	13	112; 106; 109	109	2 .8	0 3.0	
		18	89; 92; 92	×91 %	0 <u>1.9</u> ×	1.7	A A
		24	(1) 90591; 94 ×	92 🔊	2.3	Å.	
		36	\$9,94;95, Or	95	186	@N1.5	
	Overall	Mean. RSD and sta	undard deviation [%]	_078	8	S 7.5 P	
		_00 _ ~					
				91 C 102	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		
		6	C 102 x	√ 102 ∝104	0*		
	0.01		99	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Q,		
			3 ⁵ 680 6 5	80,5		2	
	\$	24	0 899 0 k	99			
	áS.	3407		\$99	~ 		
Wheat				092	1.9	1.7	
(grain)			107, 706; 102	105	2.0	2.1	
			97; 96; 94	26 ⁷	1.6	1.5	
	0,25	$\frac{0}{\sqrt{2}}$	2 2109; 11 Q110 x	110	0.9	1.0	
~	ĝ	13 18 A	× 102,08;95	98	3.6	3.5	
	r 🔬	24	100; 95; 890	95	5.8	5.5	
R. S.		\$ 05 36 ^{\$}	\$2;91;96 X	93	2.8	2.6	
Ŷ			ndard deviation [%] x	98	7	7.2	
				98 99			
	¢ A				-	-	
	Q .Õ ^y			102	-	-	
				94	-	-	
2ñ-pea (seed)	× 0.01 &	× × × × × × × × × × × × × × × × × × ×	× ~ 88 × 0,89	88 89	-	-	
Ø	Ô	24	× × 80	89	-	-	
			99	99			
⊋ry∕pea		1 36 A	6 Y		-	-	
(seed)			90; 88; 93	90	2.8	2.5	
	a,`		0 ^v 100; 98; 97	98	1.6	1.5	
	OVeralk 0.01		95; 95; 93	94	1.5	1.2	
, k			109; 111; 104	108	3.3	3.6	
Ś	í <u>"</u> "Ó"		93; 91; 91	92	1.3	1.2	
	j C	<u>ې 24</u>	94; 89; 93	92	2.9	2.6	
K) ^y	<u> A</u>	36	97; 90; 92 andard deviation [%] 87	93	3.9	3.6	
\$.0	₩ Q¥veralk	ylean, RSD and sta	indard deviation [%]	95	7	6.6	
Rape		0	8/	87	-	-	
	0.01 ~	3	109	109	-	-	



Plant material	Fortification Level [mg/kg]	Storage Interval (days)	FLU-benzamide Single Recoveries [%]	Mean [%]	RSD [%]	Standard deviation	
		13	115	115	S	- <	
		18	113	113	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		
		24	90	90	₩		
		36	101 (3)	101	- •	<u> </u>	
-		50	86:00:08		-	<u> </u>	
		2	124: 126 123		1.7		
		5	06:00/02	024	27		\$° 10
	0.2	12	<u> </u>	$\frac{3}{2}$ 107° °	<u> </u>	3.3	
	0.2	15	112,98,109			0.0	
		18	<u> </u>	~,94/	2.98	0 2.3	
		24	88;80,83	× 84	0*4.8	4.00	
		36	0 100;090; 93	94	5.4	5.1	- [~]
	Overall	Mean, RSD and sta	ndard deviation [%]	¥ 996°	130	لي 12.9	
	Fortification as: I	FLU-benzamide ; de	stermination as: FDV-benzami	de; calculat	edcas: Flu	10pyram	A
			FLU-benzamide Single Recoveries [%]				



Plant material	Fortification Level [mg/kg]	Storage Interval	FLU-PCA Single Recoveries [%]	Mean [%]	RSIO	Standard deviation (
1114101 181	[mg/kg]	(days)	Single Kelover les [70]	[/0]	1891		\$\$
		0	71	71	Å -	-68	
		3	106 🕅	106	-	, × ×	Ŷ ×
		6	100	100	-	<u> </u>	y Ş
	0.01	13	83 🎣	Â	-	<u> </u>	×,
		18	9,60	<i>S</i> 96	-	Q.	S (
		24	603	∲ 103 ₆ °	-5	(, Ĉ
		36	85	、 8 8 /	- Qi	<u>, 0' - </u>	a s
Lettuce		0	& 90; 97 095 S	× 94	@3.8 ?	0" - 3.6%	
(head)		3	0 101; 161; 97	S 100 m	2.3	2.3	\swarrow'
		6	A 92796; 940 0	940	1.8	A.5 A	0
	0.2	13	× 94:96,99	2 96	2 .6	0,1.0	a second
		18	2, ~ 90; 10k, 101	~ 97 ·	6.5	6.4	
		24	91; 97, 104 7	97 🔊	6.7	65	
		36 10	82,97; 98, 9	95	<u>s</u>	@14.9	U Contraction of the second se
	Overall Mean	n, RSD and s	standard deviation [%]	<u>)</u>)5	~8	§ 7.2	
		@0 %			<u>Č</u>		
		3	85 L A	85 C 85			
	×		0 4 101 ~ L	√ 8,5 ∝,1091	 		
	0.01 💊 🖗	P3	N 01 07 0	≈181 ≈©¥87 °≈			
	~~	\$ 10		80,5	_~	-	
	~	24,9	0 80 0 V	.80		-	
	S C	~ <u>~</u> ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		\$87	\sim	-	
Wheat			92; 10 ⁹ , 98 <i>0</i>	0 ₉₇ /	4.7	4.6	
(grain)	$\sim 10^{\circ}$		82, 98; 92 82, 98; 92	87.0	5.8	5.0	
	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u> </u>	88,90; 88	* *	1.3	1.2	
	O A A	13	91; 90; <b>9</b> 1	91	0.6	0.6	
0	Q	13 Q18 1	92; <b>96</b> , 90	93	3.3	3.1	
		24 0	96; 91; 96 0	94	3.1	2.9	
K, Y'	, Č, Š	36	<b>S9</b> ; 87; <b>9</b> 5	90	4.6	4.2	
-	Qverall Alcan	n. RSP and a	tondard deviation [%]	90	6	5.5	
				107	-	-	
			108	107			
			0 0 108 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 109 0 10	108	-	-	
				86	-	-	
4	0.01 0 0.01 0	$9^{13}$		80	-	-	
Ø	, Ô, Â	240	80	80	_	-	
Drypea (seed)		~36	106 × 106	106	-	-	
Dry pea							
(šeed)			88; 89; 89	89	0.7	0.6	
	_@`` L		O ^v 101; 101; 99	100	1.2	1.2	
	A AN Q		85; 89; 90	88	3.1	2.6	
B.		10	[™] 86; 83; 85	85	1.8	1.5	
Ś			83; 90; 94	89	6.3	5.6	
		× 24 °	84; 88; 88	87	2.7	2.3	
,≪v ^v		DSD and a	88; 94; 89 standard deviation [%] 95	90	3.6	3.2	
×× ×	<u>y averant ylear</u>	i, KSD and s		<b>91</b> 95	9	8.4	
Rape	a at	2	95 94	95 94	-	-	
(seed)	0.01	5	107	107	-	-	



Plant material	Fortification Level [mg/kg]	Storage Interval (days)	FLU-PCA Single Recoveries [%]	Mean [%]	RSD	Standard deviation	
		13 18 24	116 101 85	116 101 85	  	- 4	
		36 0 3	78 97; 96; 103 93; 89; 94 90; 96; 90		- 3.8 2.9	- ~~ - ~~ - ~~ - ~~ - ~~ - ~~ - ~~ - ~~	
	0.2	6 13 18 24	90; 92; 90 106; 87; 97 16; 113; 87 4, 65; 61; 66 60; 40; 62; 42;	\$ 91 976° 102	98	<u>9.5</u> <u>0</u> 13.3 <u>2.6</u> <u>36</u>	
		24 36	$0^{65; 61;266}$	× 64	©~4.1 ° 5.5∢©	3.6	Ŵ,
	Overall Mear	, RSD and s	tandard deviation [%]	890	17	AJ 5.4 A	°
Fortification as	: FLU-PCA ; determin	ation as: FL	U-FCA; catenlated as Fluopyra	m	S	0. %	
			1060 87; 97 1060 113; 87 4 65; 61; 66 0 69; 60; 62 10 PC A; catcalated as Fluopyra 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4				



		Storage					j V
Plant naterial	Fortification Level [mg/kg]	Interval (days)	FLU-PAA Single Recoveries [%]	Mean [%]	RSIO LON	Standard deviation	
		0	93	93	Å -	-05	
		3	92 🖏	92 🛴	-		
		6	108 📡	108	-	$\delta$ - $\delta$	
	0.01	13	91 L	Ĵ¥	-	<u> </u>	×,
		18	<u>_</u>	97		, Q	Ô' K
		24	<u>í</u>	≶ 90 ₆ °	Ś	<u> </u>	
Lettuce		36	\$\$°90	<u>, 90</u> /°	- Q	$0^{\nu} - 46^{\nu}$	Ĩ
(head)		0	\$ 93; 90 <b>6</b> 99		@4.9 🏾 🏹	y 4,6℃	*
()		3	0 104; 94; 99	y 99 🔊	5.1~	5.0	
	0.2	6	<u>97</u> ,96;96	960	0.6	0.6	' L°
	0.2	13	107; 106; M1	<u>1</u> 08	2.4	2.6	
		18 24 Q	100; 106, 88 91, 94; 91	98 92,50	9.4	∫ 9,2 [™]	
		36	25, 86; 95 V	92	1.5°	0.5.2	$\sim$
	Overall Meet		andard deviation [%]	.06	N7	§ 6.6	
	Over all Ivical						
				<u>91</u>		-1/	
	*		2 4 108 A	> 90 \$168	ð	~ -	
	0.01	93 ×		~(~)85 ~		- -	
	0.01 ×	1 1 Q	2 A8 0 1	88,5		2 -	
	× 4	\$ 24 9	89 . O K	89	- AS	-	
		~~~~~		\$2	×-	-	
Wheat		<u>, 0</u>	84; 82, 86	0 ₈₄ *	2.4	2.0	
(grain)	Č N	× 3,	90,89;93	91	2.3	2.1	
		64	69.85.85	\$87	4.6	4.0	
	, W w	13	304; 1020103	a. ¹⁰³	1.0	1.0	
\$		218 A	94; 96; 95	95	1.1	1.0	
Ŕ	Û â	24 0°	92; 85; 84	87	5.0	4.4	
«\\	, Č, Č	36		81	4.9	4.0	
	Overall Mean	n, RSD and st	andard deviation [%]	90	8	7.5	
	δ A.		NO OSO A	80	-	-	
		30	× × 89 ×	89	-	-	
		No A	0 [°] 0 [°] 95 [°]	95	-	-	
_1	Overall Alean			88	-	-	
Ø	Ô		<u>90</u>	90 73	-	-	
		240	× × 75 × × 76		-	-	
Dry ∕pea				76	-	-	
(šeed)			83; 80; 77	80	3.8	3.0	
	0 . K		Ø [*] 88; 90; 86	88	2.3	2.0	
	O ^V O ^V eralk Mean 0.01 ^N		85; 85; 83	85 102	1.5	1.2 2.3	
<i>A</i>		18	[♥] 101; 105; 101 87; 80; 88	85	2.3 5.1	4.4	
and the		y 24	79; 74; 82	78	5.2	4.4	
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		36	85: 87: 83	85	2.4	2.0	
L' -	🔊 🖉 🖉 🖉	n, RSD and st	andard deviation [%]	86	9	7.8	
Rape (seco)	0.01	0	94	94	-	-	
(see	0.01	3	96	96	-	-	
(SKAM)		6	97	97	-	-	



Fund         Fortification         Storage laterval (days)         Single Recoveries [%]         Mean         RSD         Standard deviation           13         13         98         92         92								
Plant material         Fortification Level [mg/kg]         Interval (days)         FUU-PAA Single Recover(s [%]         Mean [%]         RSD (eviation (eviation)         Standard (eviation)         Standard (eviation) <th></th> <th></th> <th>Storage</th> <th></th> <th></th> <th></th> <th></th> <th>o s</th>			Storage					o s
Interial         Ing/sgl         (days)         Single Recoveries  %          %          %          %         deviation           13         98         98         98         42         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -         -							Standard	
Image: constraint of the second sec	material	[mg/kg]		Single Recoveries [%]	[%]	[%]	deviation	S' O'
Image: Second			13	98	08	Ś		
Image: state						<i>"0</i> "		
Image: Second					87 √	<b>.</b> -	0	S ^Y B
Image: Non-State of the second seco				92 ~ 🖏	92	-	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
0.2         3         91 91 91 92         OT         6         0.6         0.6           13         11 996 104         1039 924 295         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36         31 1         36			0	94; 92; 88	Å	3.3	03.1	
0.2         6         0.9         8/8         3         1.1         1/2           18         498         66         22         10         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24         24				91; 91; 92	Û.	0.6	0.6	
0.2         13         115967 (104         102         94         0.5         0           24         0.78         25         0.5         24         0.5         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0					6 × 89	1.1	1:2	Ô ^V &
18         36         18         28         18         21         10           36         0         80         90         90         51.0         43         10           Overall Mean, RSD and standard deviation [26]         28         28         51.0         43         51.0         43         51.0         43         51.0         43         51.0         43         51.0         43         51.0         43         51.0         43         51.0         43         51.0         43         51.0         43         51.0         43         51.0         43         51.0         43         51.0         43         51.0         43         51.0         43         51.0         43         51.0         43         51.0         43         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0         51.0		0.2	13	115,96;104	≫ 105°	94	9.5	
Image: Arrow of the second			18	<b>*8</b> \$; 86; 82 ¥	× 86/	5.90		
Fortification as: FLU-PAA; determination as: FLU			24	<u> </u>	× 80	5 3.0	$\sqrt{2}$	1 St
Forthfication as: FLU-PAA; determination as: FLU-PAA; categorial (20) (20) (20) (20) (20) (20) (20) (20)		Overall Mea	n RSD and st	$\sim$ 30, $\infty$ , 81 $\sim$	<u> </u>	9.3~ i	4.3 	_
	Fortification a	s: FLU-PAA : determin	ation as: FLU	-RAA : cabalated as Fluonvra	m «			
The solution of the solution o	1 0101100000011 0				A.	Ő ^y	,	, Q'
					Ó XÃ			St.
			Ő¥			Ű	ŝ, C	
			<u>í</u>		s, starter and the second seco	Ň		
					,0°, C	° é		
And the and the art of			~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		Ŷ Õ		, , , , , , , , , , , , , , , , , , ,	
The solution of the solution o		\$	G & .		× . Ø	. 0*	0 [×]	
And the and the providence of		. Ŷ	O ^Y ,	S O V		9	2	
		$\sim$	1				2	
And the solution of the soluti		~		Õ N .Õ k	st s	×,		
And the contract of the contra					×			
And a construction of a construction of and a construction of a co			~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	ž ^{ov} ož a	0 1	4		
the transfer of the transfer to the transfer t					$\langle 0 \rangle$			
the set of			í 👋					
The transfer of the transfer o		N N V			a.			
The man and a construction of the and the address of the addres	%		XI A		S .			
At the offer the	je S		S S.		r			
	**			$\mathcal{O}_{\lambda}$ $\mathcal{O}_{\lambda}$ $\mathcal{O}_{\lambda}$ $\mathcal{O}_{\lambda}$ $\mathcal{O}_{\lambda}$				
		6 A	L' S	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~				
			× p					
			`~~~~					
	1	, õ	$\sim$ $Q^{1}$					
	Ø	) Â						
	A CONTRACTOR	NY A		× .~~				
	¥	. 8	N Q	~~~				
				×				
		A A Q	29	Ş				
		× × ×						
	a, ^y		v v					
	,\$\$		<i>y</i>					
	Å.	OF A A						
	st of							
		L'						
	õ							



		C4.					۶Ÿ
Plant aterial	Fortification Level [mg/kg]	Storage Interval (days)	FLU-7-OH Single Recoveries [%]	Mean [%]	RSIO ISM	Standard deviation	
		0	86	86	Ą -		Â,
		3	96 💍	96	-	<u>`</u> ``	
		6	95 💱	9 <b>6</b> 0	-	<u> </u>	, Ô
	0.01	13	87	<u>Š</u>	-	<u> </u>	×.
		18 24	20 20 20 20 20	√ 92 92 ° °	- 0		0 [×] %
					- Q	, 0' / A	
ettuce		36	( ⁹ / [°]		n ⁻		
nead)		0	O 105; 1∰; 107 ≪		2.8	3.1∕∕	Ś
,		3	104,105;102	108 104	1.9	L1.5 L	<i>2</i> 0
		6	× 192; 99; 193	<b>4</b> 01	.0	0 2.1	
	0.2	13	× 108; 109: 115	<u></u>	© [*] 3.4 ≪	J 3.8	£G [°]
		18 0	100,96;96	[©] 97 √ [°]	2.4	23	
		24 ^{O v}	98997; 96 V	970	20	<u>1.0</u>	, ,
	0 11 11		96; 95; 99		2.2 	2.1	
	Overall Mean		andard deviation [%]		<u>م 7 ژ</u>	6.8	
	*		086	86 0	ð	<u> </u>	
	Č			<b>, 92</b> ⊳, 98 ∿	- Ô)	O -	
	0.01	13 V		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u>م - کر</u> آرگا -	-	
	0.01			83		-	
	Ş Û		0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0	\$ <u>90</u>	~?		
		. 036 ~		093 #	ý -	-	
Vheat		× 0 ×	<u>,</u>	99	1.2	1.2	
grain)		3	105,106,109	105	0.5	0.6	
		8	99; 101, 107 99; 101, 000	100	1.0	1.0	
La		Q13 A	, 115; <b>}</b> , <b>1</b> , <b>7</b> ; 117 ♥	<i>,</i> ©116	1.0	1.2	
Ŕ			O 97; 94; 93	<u>95</u>	2.2	2.1	
≪>°	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u>× 24</u>	<b>997</b> 101: <b>957</b>	98	3.1	3.1	
		×36	98; 97; 97	97	0.6	0.6	
		n, <b>FSD</b> and st	andard deviation [%]	<b>99</b>	9	8.4	
			89	89	-	-	
	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	No No No	0 ⁹ 0 ⁹ 100 ⁹ 2 ⁹ 2 ⁹	100 92	-	-	
21	Overall Mean 0.01 0.01 0.01 0.01 0.01	13 2	2 <u>9</u> 2	92 86	-	-	
Ø	, 0.01		× 84	84	-	-	
		≈ 24	₩ <u>90</u>	90	-	_	
\sim		. @ 36 @	× 96	96	-	-	
řy pea	. 8		94; 98; 97	96	2.2	2.1	
seed)	O`, A		111; 108; 106	108	2.2	2.5	
	A A	× %	100; 96; 100	99	2.2	2.3	
, é	× 0.2 ×	13	108; 109; 108	108	0.5	0.6	
Ĩ		18	93; 95; 90	93	2.7	2.5	
× S	ST A SO	24	92; 94; 94	93	1.2	1.2	
ς γ a		36	98; 98; 101	99	1.7	1.7	
	<u>O'Overally Mean</u>	n, RSD and st	andard deviation [%]	97	7	7.1	
Kape≪,≫	0.01	I U	103	103	-	-	

r



Plant material	Fortification Level [mg/kg]	Storage Interval (days)	FLU-7-OH Single Recoveries [%]	Mean [%]	RSD [%]	Standard deviation	
		6	97	97	- A	- 🖑	
		13	90	90	4 -		
		18	95	95 🛒	, - <i>4</i>	<u>`</u> -0 [∞]	S O
		24	84 _ 🛇	84	-		
		36	97 😵	R	-	õ - S	
		0	106; 102 102	003	2.2	0 2.3	
		3	109; 106, 103	\$106	2.8	3:0	
		6	93,95;96	🎙 95©°	1.6/	£1.5 (
	0.2	13			<i></i>	\O10.7	
		18	15(9); 99; 113 (k, 90; 88; 87 (k) 90; 90; 90; 90; 90; 90; 90; 90; 90; 90;	88	@1.7 🐐	3.Q <u>(1.5</u> <u>(1.5</u>) <u>(1.5</u>) <u>(1.5</u>) <u>(1.5</u>) <u>(1.5</u>) <u>(1.5</u>) <u>(1.5</u>) <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u> <u>(1.5)</u>	
		24	0 97; 98, 98	k 97 👗	1.0~	1.0	l≪v ^v
		36	A 105 107; 99	97 97 100 99	4.00	A.2 🗳	
	Overall Mea	n. RSD and st	andard deviation 1%	.09	<i>6</i> 8	0 8.1	* ~
Fortification a	s: FLU-7-OH : determine	nation as: FL	7-OH : valculated as: Fluenvr	ant	0 d		
						× «	and the second s
		Ő¥			Ű	S (Ĩ
		Ś		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			
		~~	$\sim \sim \sim'$	0,	Õ.	Š. S	
		_@{		\sim \sim		, °~/	
	~	, Si in		ç o	\approx	% ,	
	~	× «	i de la de	í . Ô		O^{*}	
	. Ŷ	0 ,	5 _0 ¹ ⁽ 0 ¹ ¹ ¹)		<i>?</i>	6	
	\sim	.1		$\sqrt{2}$, , , , , , , , , , , , , , , , , , ,		
	~		Ö XÜ Ö V	- W	20		
	S C			& <i>"</i>	~		
		A A		0 * 4	\$ ⁷		
	, 0 ^y	N W		ſ <i>@</i> .	v		
		~ (a.					
	ð Æ o	O¥ .	v v s s	K) ^v			
	N N	A .		<i>Q</i> 1			
%	× ×,	XI A		S .			
<i>p</i> C	_0` ^	Č "Q"		r			
			\sim \circ \circ \sim \circ				
		× ć					
		ř. Č	X & &				
		_^~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~					
4	i õř	and R					
Ĩ) (a)						
	~~~~ Q						
.«			, °°				
$\sim$							
		rj ^a "Sy	O ^y				
			4				
			\$				
a de la calencia de l	S d' d'						
Â,		ş ~Q	120; 99; 113 90; 88, 87 97; 98 105 107; 99 and and deviation 1%] 77-OH; calculated as: Fluopyr 4, , , , , , , , , , , , , , , , , , ,				
~~~	Nº , O	ŋ					
* **	8 A 18						
ST R							
Ki "R	ŭ di la constante de la consta						
»Ô¥							
U							



Dlawt	East. Cast. I.	Storage		Maria	DCD	Store 1 - 1	6 N
Plant naterial	Fortification Level [mg/kg]	Interval	FLU-methyl-sulfoxide Single Recoveries [%]	Mean [%]		Standard deviation (
materiai	[mg/kg]	(days)	Single Recoveries [70]	[/0]	1391	ueviation	
		0	82	82	Ą	-65	
		3	94 🕅	94	-	, × ×	Ø ×
		6	109 🐨	1000	-	δ - \sim	
	0.01	13	101,	601	-	0 - 7	Ś
	0.01	18	1.04	<i>√</i> 104	- Õ	Q Q	Ô ^y «
		24	203 °	≶ 10 <u>3</u> ⊱°	Ś	(Ĩ, Ĉ
		36	86	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~	\ ⁰ ′©	
Lettuce				× 100 ×		5.8	2 S
(head)		0	0 ⁹ 93; 108, 103 x			5.8%	\sim
		3	117; 111; 112 109: 108 42	110	2.8		
	0.2	6 13	109; 108, 12 103; 102, 106	10 104 s.	Ø <u>7.8</u> Ø2.0 ≪	2.1	
	0.2	18 0	108; 109	0^{104}	0.2		S V
		24	108,107,109	<u> 108 </u>	0.2 y	0.6	Ĩ
		270	104: 116: 112		×38.5	6.1.0	
	Overall Mear		andard deviation [%]	O105_ C	8 6	8.0	
		$\sim 0^{\circ}$		94 0			
	×			<u> </u>	ð		
	, Ôj		S _ € 106 [°] C	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	\$	-	
	0.01	<u> </u>		§ 92 ~	- % 1	-	
	≪ .	Q 18 Q	0 8406 0 K	106		_	
	S C	24		\$9,1	s 2	_	
		. 036 ~	× ~ 93) «.	093 4	ý -	-	
Wheat		x 0 V		/ 105@	5.3	5.5	
(grain)		3	96; 95	,95	1.6	1.5	
	O A VO	P	× 01; 10097 ×	100	2.3	2.3	
۰.	Q 0.2	Q13 A	\$ 90; \$ 94	, © 91	2.9	2.6	
			O* 108; 100; 10 6	105	4.0	4.2	
<i>K</i> [™]	, Č , Ó	24	109, 107, 194	105	1.6	1.7	
		₹36	\$ <u>\$</u> \$00; 101; 103	101	1.5	1.5	
	Overall Mean 0.01 0.01 0.01 0.01 0.01 0.01 0.01	1, R SD and st	andard deviation [%]	99	7	6.7	
			83	83	-	-	
		, ¢	0 ⁷ 0 ⁷ 94	94	-	-	
A	× × ×	$\sqrt{6}$	× <u>80</u> × <u>80</u>	80	-	-	
	, 0.01	<u>9 13 65</u>	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	107	-	-	
	× Q		× × 80	80	-	-	
.*		24	× 84	84	-	-	
Dry pea		<u>, '0' 36</u>	99 •	99	-	-	
(seed)	<i>a</i> .\ <i>'0'</i>	×` 0 کر	90; 94; 94	93	2.5	2.3	
	~ ~ ~ ~	Ľ.	100; 102; 99	100	1.5	1.5	
<u>"</u>		× ^v 6	[∞] 90; 92; 94	92	1.8	2.0	
L. C.	× × °0.2		94; 95; 77	89	11.4	10.1	
	ÔÝ Č Â	× 18 ∛	99; 100; 96 102: 100: 04	98	2.1	2.1	
N.	à a	24	103; 109; 94 106; 109; 104	102 106	7.4	7.5 2.5	
Å .@		JO RSD and at	andard deviation [%]	<u> </u>	2.4 9	2.5 8.7	
⊻ © Rane		n, rest and st	102	102	-	-	
in here	0.01	v	118	112	l		

theyl culforde (AE 1244122) hla (1) 10. 0 data fan fl



Plant material	Fortification Level [mg/kg]	Storage Interval (days)	FLU-methyl-sulfoxide Single Recoveries [%]	Mean [%]	RSD [%]	Standard deviation	
		6	78	78	Ř	- 4	
		13	94	94	4 -	- 🔊	
		18	101	101 🛒	,> -	<u> </u>	
		24	116 S	116	-	× 7 ~ 7	
		36	104	104	-	<u>َ</u>	Ŭ, Č ^y , "O
		0	99; 99; 4 01	000	1.2 📡	0 1.2	
		3	107; 106, 103	∕≫105	2.0	2:P	
		6	9 5, 9 6; 99	ັ≶ 97Շթ°	1.0	£2.1 (рт "Qʻ
	0.2	13	192; 84; 97	<u></u> ,94/°	9. 8	\ 0 ″9.3 ⊘	a y
		18	(113; 112) f08		@2.6 %	Ş. 2,9€∫ [®]	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
		24	O 110; 100; 109, 🗸	چ 110	1 0.3	0.6	×0°
		36	111;108;192	100	4.9	LA.6 🗳	
	Overall Mean	n, RSD and st	andard dèviation 🌾 🔍	103	~9	0 8.9	

* : this value was corrected by the suppression of the interferent stressent in the control sample (00028 mg/kg); the ideal value was 1328

Higher control of the second o In order to identify any degradations into FLU-methyl-sulfoxide (AF 1344122), this compound was In order to identify any degradations into FLU-methyl-sulfoxed (AF 1344122), this compound was quantified during each storage interval analysis Therefore, procedural recoveries on this analyte were carried out in order to assure the validation of the results. No degradation into FLU methyl-sulfoxide were observed during the study.



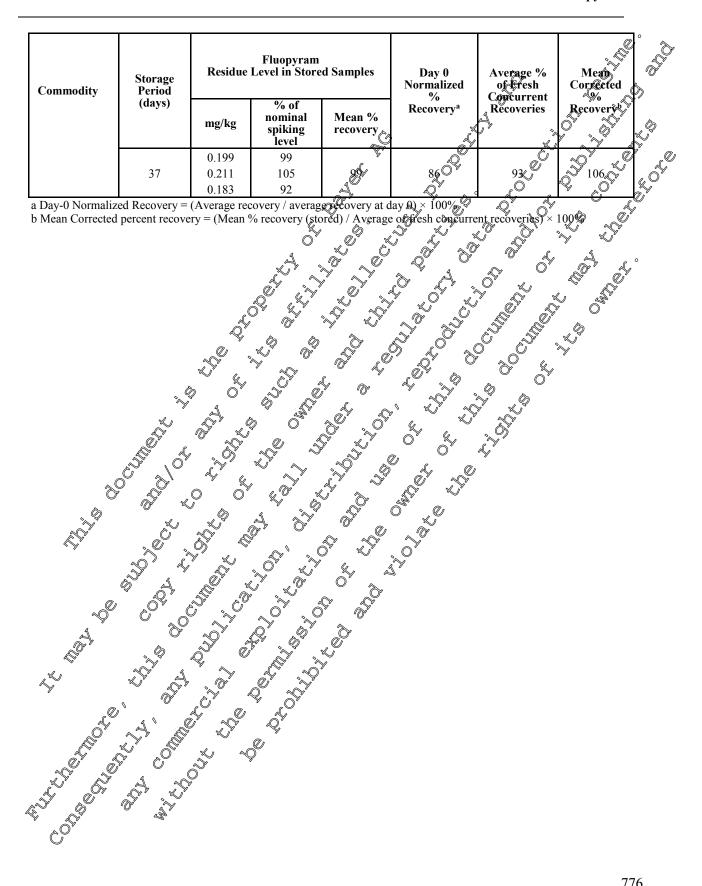
Ũ

ble 6.1.2- 20:	Storage s at 0.200 r	ng/kg)				*	
Commodity	Storage Period	Residue	Fluopyram Level in Store	ed Samples	Day 0 Normalized	Average %	Mean
č	(days)	mg/kg	% of nominal spiking level	Mean % recovery	% Recovery	Concurrent Recoveries	Corrected Recovery ^b
	0	0.208 0.193 0.207	104 97 103	9 101 4			96 0 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
	3	0.207 0.198 0.206	_\$103 \^		Q101	107 Š ⁴	
	6	0.207 0.209 0.217	104 105 109	× 106 °			197 197
Lettuce (head)	13	0.577 \$200 0.219%	× ³ 89 × 100 × 100				≫ 87
		0.21 0.21 0.203	96 2 106	201 0 201 0 201	190 J		106
. (5 ⁵ 24	0.188 04.80 0.191 (c	<u>المع</u> المع المع المع المع المع المع المع المع			93	100
n n n n n n n n n n n n n n n n n n n		0.2050 0.2097	103 107 107			98	106
K.J.			103 599 201 101 101 101 101 101 101 101		100	96	106
		0.197 0.199 0:292	99 99 101		98	104	96
Apreat (grain)		0.190 0.182	₹ ⁵ 10€0 ⁻⁴ 95 - 10€0 ⁻⁴	95 V	93	99	96
		0.206	2 103 ×	104	102	114	91
Alfreat (grain)		0.206 50.211 0.206	103 105 103 103	104	102	104	100
	0 24 Y	0.208 0.193 0.209	104 97 104	102	100	101	101



Commodity	Storage Period	Residue	Fluopyram Level in Store	d Samples	Day 0 Normalized %	Average % of Fresh Concurrent	Mean Corrected Recoverve	
	(days)	mg/kg	% of nominal spiking level	Mean % recovery	Recovery ^a	Recoveries	O' ès'	Ŝ
	36	0.211 0.215 0.221	106 108 110	Los I	106	80 90		
	0	0.185 0.194 0.187	93 97 94				× ⁹ 103	
	3	0.202 0.199 0.202	101 (101)				\$ ⁹⁶ 0	
	6	0.192 0.193 0.191	@ 96 @	\$ ^{\$\$} 96\$\$	7 101, 27 27 0 101, 27		98 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	
Dry pea (seed)	13	0.207 0.202	× 104 °		2 408 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	ði11 ×	≫ 93	
	184 45	0,205 0,206 0.198		0 ² 102 0 ⁵	×08 ×08 ×08 ×07 ×08 ×08 ×08 ×08 ×08 ×08 ×08 ×08		102	
ð		0.183	99 100 100 100 91	297 S	E 402 @	\sim	100	
	36 ×		\$99 3 98 100		2 2) 30 30 30 30 30 30 30 30 30 30 30 30 30	91	109	
\$¥		0.242 0.247 2233	0 ¹⁰⁹	\$115 0 \$	100	104	111	
~~ A		\$0.207 0.219 \$18	2 109 C		92	109	97	
	in the second	0.198 0.195 0.195 0.195		98	85	100	98	
Nape (seed)	13 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.1992 9.197 5 0.1990 0.493	\$ 9 6 \$00 \$98	99	86	108	92	
Kape (seed)		0,192 0.189 0.202	96 95 101	97	84	93	105	
	24 C	0.190 0.188 0.193	95 94 96	95	83	93	102	







	Storage	Residue	FLU-benzami Level in Store	de ed Samples	Day 0	Average %	Mean S
Commodity	Period (days)	mg/kg	% of nominal spiking level	Mean % recovery	Normalized % Recovery ^a	of Fresh Concurrent Recoveries	Corrected % Recovery ^b
	0	0.183 0.177 0.193	92 89 97	293 07	LEC CON		
	3	0.199 0.192 0.185	100 96 93	en e			× 93×5
	6	0.190 0.192	96 ×				98 (J 98 (J 98 (J
Lettuce (head)	13	0.163 0.169 0.0072	2, 94 × 85 ∞ 85 ∞ 86 %	*~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			2 2 77 77
	18	0.192 0.201		5 960 S		91 91 91	105
		0.176 0.128	88 88 88 88 88 88 88	89°-7 89°-7	96 (k) 0 96 (k)	\$92 \$	96
ð		0.184 0.184 0.180	[∞] ″ 91∼	€ ² 91 ~5	98 J	95	96
		0, f \$0 0, f \$0 0, 186 0, 0.186	90 93 93	92 Q 57 x 7		92	100
		0.205 0202			110	105	96
A A Vhore Commin		0.176 0.191 0.190	088 °C Q 96 Q F 959	° © ^y ⊘93	101	96	97
Wheat (grain)	2 ⁵ 13	0.175 0.175 0.175 0.175 0.168	2 86 86 87 86 87 87 80 87 80 80 80 80 80 80 80 80 80 80	86	94	110	78
		0.189 0.203 0.202	95 901 001 001	99	108	98	101
		0.183 0.178 0.179	91 89 90	90	98	95	95



	Storage	Residue	FLU-benzami Level in Store	de d Samples	Day 0	Average %	Mean
Commodity	Period (days)	mg/kg	% of nominal spiking level	Mean % recovery	Normalized % Recovery ^a	of Fresh Concurrent Recoveries	Corrected Recovery ^b
		0.187	94	Ċ			
	36	0.180 0.185	90 92	92 😴	100	93 🔬	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
		0.183	92		<u> </u>		
	0	0.182	91	A90	190 g		
		0.175	87				. 📣
		0.197	98 🐇				
	3	0.188	94 O [*]	× ⁹⁶ č			98
		0.192	96	<u> </u>		OF OF	
	6	0.185 0.177 0.183					976 ⁴
Dry pea (seed)	13	0.1(1	82 ⁽²⁾ 82 ⁽²⁾ 85 ⁽²⁾ 85				× 77
	18	0.179 0.180 0490	991 091	920 20		\$ 92 \$	100
		0.179 0.176 0.169	95 5 90 088 588		98 % 0 98 %	<u>92</u>	95
ð		0.177	4 88		97 2	93	93
Rape (seed)		0.120 0.174 0.168	*88 **********************************	27 85×57		94	91
		04372 0.244 0.248C	126 ×	⁰ 124 ∂	146	124	100
		04.93 29.98 20.189 ©	97 × 97	97	114	93	104
ky [™]		0.167 9.971 0.177	\$84, ~ 86, ~ 80, ~	86	101	107	81
		0.196 0.196 0.187	Ø7	96	113	91	106
	24 °S	0.168 0.175 0.171	84 87 86	86	101	84	102



	Storage	Residue	FLU-benzami Level in Store	de ed Samples	Day 0	Average %	Mean Corrected
Commodity	Period (days)	mg/kg	% of nominal spiking level	Mean % recovery	Normalized % Recovery ^a	of Kresh Concurrent Recoveries	Corrected &
	37	0.186 0.183 0.179	93 92 90	92	108	94 ×	
a Day-0 Normaliz b Mean Corrected	ed Recovery = percent recove	(Average rec ery = (Mean %	covery / averag % recovery (sto	e recovery at d pred Average	lay 0) \times 100% e of frest concurre	ent recoveries) ×	
		(
							N N N N N N N N N N N N N N N N N N N
ð							
Ø							
Ç ^a							
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~				¥			
			Q [°]				
							Mean Corrected Recoveryb 100% Out the the the the the the the the the the

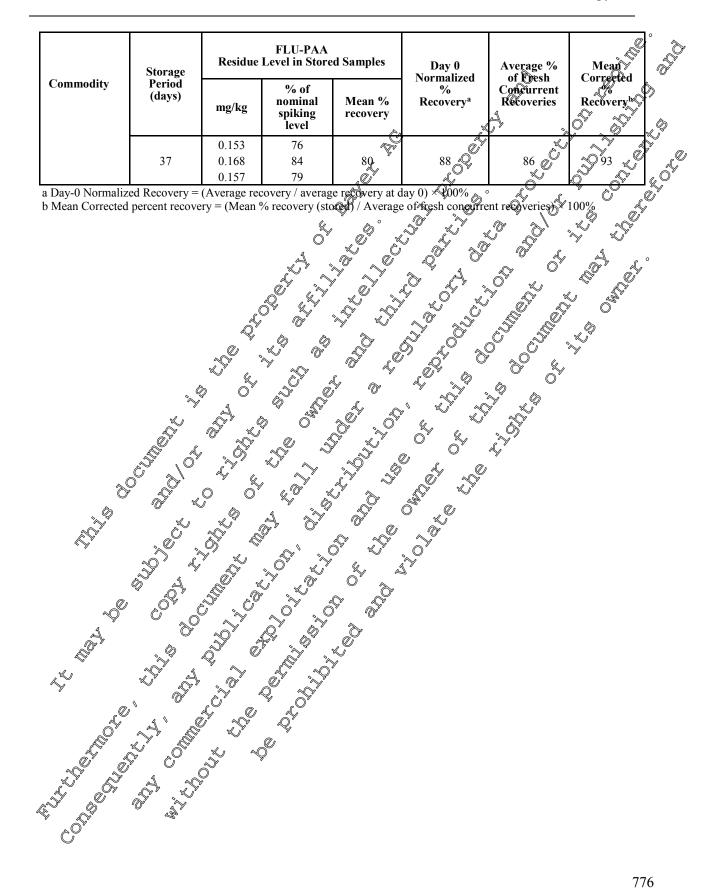


	Storage	Residue	FLU-PAA Level in Store	ed Samples	Day 0	Average %	Mean
Commodity	Period (days)	mg/kg	% of nominal spiking level	Mean %	Normalized % Recovery	of Fresh Concurrent & Recoveries	Recovery ^b
	0	0.185 0.186 0.197	92 93 99	95 95		\$94 6 ⁵	
	3	0.190 0.193 0.178					× ×
	6	0.186 0.187 0.184	94 94 94 94				
Lettuce (head)	13	×0 [°] .163	85 83 83 83 83 83 83 83 83 83 83				₩ У 77
		0.164 0.153 0.168	2 2 76 84 84 84 84 84 84 84 84 84 84	× 81		× 289	82
		0.157 0.165 0.165 0.159	79 81 79 79			م ب 92	87
ð 		0.153 % 0.140 0.444	×70 ×70 ×70 ×72 × × × ×		25 77 0 Q	92	79
Ê,		0.166 0.162 0.166 Q173	81 81 81 81 81 87 87 87 87 87 87 87 87 87 87		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	84	98
		50.176 0.170	085 C	\$ 87. \$	106	91	95
Wheat (grain)		0.173 0.172	86 86 86	86 86	105	87	99
Y Q		0.185 0.185 0.185 0.480	93 × 1 95 × 1 95 × 1 95 × 1 95 × 1	93	113	103	91
		0.192 0.197 0.173	90 96 99 86	95	116	95	100
	24, W	0.182 0.172	91 86	88	107	87	101



	Storage Period	Residue	FLU-PAA Level in Store	d Samples	Day 0 Normalized	Average %	Mean	<i>S</i>
Commodity	Period (days)	mg/kg	% of nominal spiking level	Mean % recovery	% Recovery ^a	of Oresh Concurrent Recoveries	Mean Corrected Recovery ^b	
	36	0.162 0.169 0.164	81 84 82	82 82		81	39 ¹⁰²	
	0	0.164 0.158 0.170	05 //2	\$ 82 \$ \$		Q 80 . O		Ŭ
	3	0.174 0.173 0.180	87 ^O 87 87 87 90	× 88 0	Q107 00		AT A	þ
	6	0.171 0.164 0.163		× × × × × × × × × × × × × × × × × × ×				
Dry pea (seed)	13	0.175	× 89 m	·0 4			×5 >> 85	
	18	0.17 0187 9.179	× 84 × 84 × 87 × 87 93 × 90				106	
. (	5 ⁵²⁴	100 L	77 77 77 75		2 94 2 94	× 78	98	
	\$6 ×	0.127	4 <b>08</b> √79 86 91		100	85	95	
Rap(Geed)	\$° 4	0.180 0.181 0.180 0.180			100	91	100	
		0.174 0.174 0.173	87 88 88 87 86 87 86 87 86 87 80 87 80 87		96	91	96	
	\$ 69 .		× 84 ~	85	93	89	96	
° Y É ^Y		0.167 0.167 0.192 0.192 0.190 0.183	96 96 95	96	106	105	91	
		0.183 $0.171 \ll$ 0.180 0.1(0)		89	98	85	105	
	24°	0.160 0.171 0.158	80 86 79	82	90	80	102	



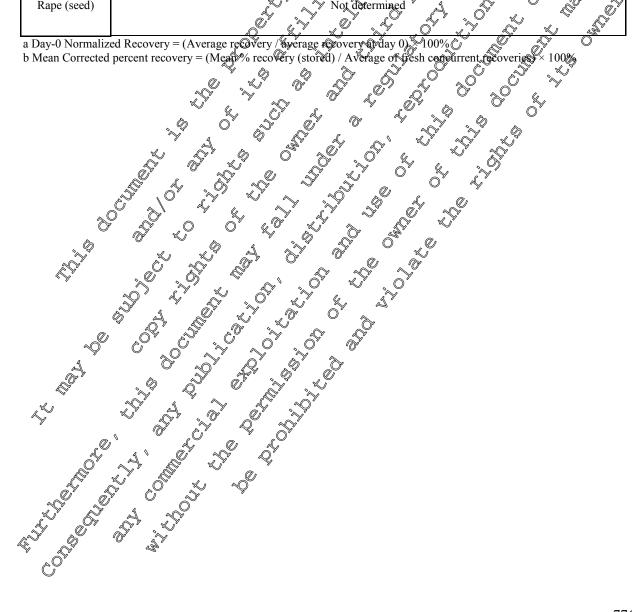




	Storage	Residue	FLU-7-OH Level in Store	ed Samples	Day 0	Average %	Mean Corrected Recovery ^b
Commodity	Period (days)	mg/kg	% of nominal spiking level	Mean %	Normalized % Recovery ^a	of Fresh Concurrent Recoveries	
	0	0.209 0.197 0.218	104 98 109	Ar04		408 Q 0	
	3	0.192 0.192 0.202	96 & 96 O 101				
	6	0.193 0.195 0.199	98 98 98 98 98				975 ⁵⁷
Lettuce (head)	13	0.195 0.200 0.93				. 0 .	× 88 > 88
	18	0.186 0.18€ 0.205	\$92 102	960°		97. 7 7 7 7	99
		9.188 0.188 0.199	94 94 97			97 4 97	98
		0.204 0.203	99,7 402 101 9	5 101 5 101	97 2 97 2 0 2	97	104
L. C.		0.209	105 102 104		~~100	99	105
		0,200 0.203 0.203 0.203 0.203	100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 × 100 ×		97	107	94
Wheat (grain)		0-1.88 20187 0.191	94 93 98 98	\$ ⁹⁴	90	100	94
a		0.219 0.204 0.208	98 105 102 102 102 102 102 102	104	100	116	90
		0.196 0.196 \$0.190 \$ 0.199	98 95 99	97	93	95	102
	24 S	0.193 0.189	96 95	97	93	98	99



	Storage Period (days)	FLU-7-OH Residue Level in Stored Samples			Day 0	Average %	Mean Corrected				
Commodity		mg/kg	% of nominal spiking level	Mean % recovery	Normalized % Recovery ^a	of Fresh Consurrent Recoveries	Corrected ⁶⁰ Recevery ^b				
	36	0.202 0.195 0.199	101 97 100	99 🖗	95	97					
Dry pea (seed)		Not determined of the state of									
Rape (seed)	12			Not determ	nined A						



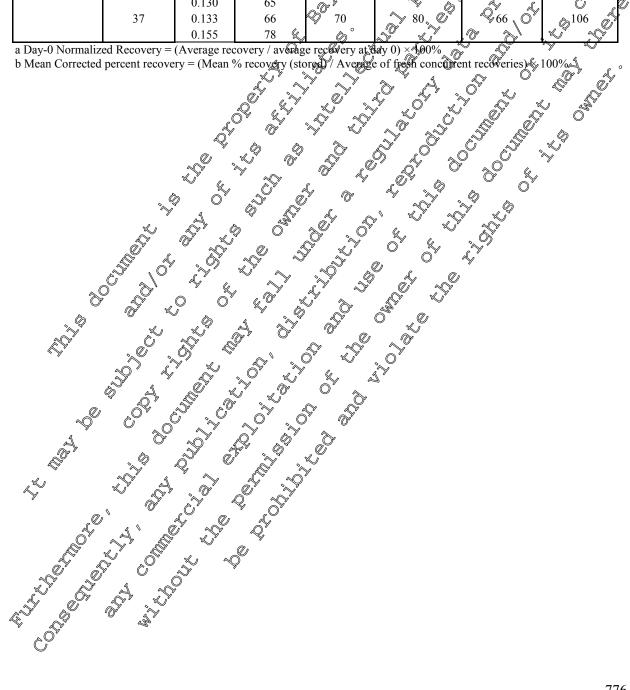


# Table 6.1.2- 24: Storage stability data and concurrent recovery data for fluopyram-pyridylcarboxilic-acid (fortification at 0.200 mg/kg)

	Carboxin	c-aciu (ioi	uncation a	t 0.200 mg/	Kg)	~	, N	, ô
	Storage	Residue	FLU-PCA Level in Store	d Samples	Day 0 Normalized	Average %	Mean Forrected Recovery ^b	Ď
Commodity	Period (days)	mg/kg	% of nominal spiking level	Mean %	%	🦉 Concurrent 🗞	Recovery ^b	
Lettuce (head)				Not determ	Recovery of			
Wheat (grain)				Not determ				o
	0	0.182 0.182 0.179	D 9 8 9 94 × ⁹ 89				\$ 103	
	3	0.209% 0.219	93 104 2106	ç 101	2 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 1111 2 11111 2 11111 2 11111 2 11111 2 111111		101	
		0,193 0.188 0.189	an a		× × × ×	5 ⁵ 88	108	
Dry pea (seed)	2 ⁵ 13	0%172 0%174 «	× 86 87	2 ⁸⁷ 5		85	102	
ð , ø	<u> </u>	0.1730° 0.1554	87 87 87 86 87			89	98	
		0.1% 0.1%	87 5 9 93 5 89 5 9	93 9	3 96 7 102	87	107	
Q		0.180 0.180 0.181	589 37 82 969 091 091	88 0 88 0 6	97	90	97	
A. Dela		0783 9.167 Q 0.178		88	100	99	89	
	3 6 F	0.172 0.172 0.172	Q 86 V	87	99	92	95	
Rape (seed)		0.187 0.184 0.186	© 92 93	93	106	91	102	
		0.187 0.193 0.186	94 97 93	95	108	97	98	
	18	0.194 0.207	97 104	101	115	102	99	



	Storage Period (days)	FLU-PCA Residue Level in Stored Samples			Day 0 Normalized	Average % of Desh	Mean
Commodity		mg/kg	% of nominal spiking level	Mean % recovery	% Recovery ^a	Concurrent Recoveries	Recovery th
	24	0.135 0.134 0.133	67 67 66	67	76 Q	64 V	3 ¹⁰⁴ 2 ⁶ 2 ⁶
	37	0.130 0.133 0.155	65 66 78 🕵	70 0 0			





Data Point:	KCA 6.1/07
Report Author:	
Report Year:	2010
Report Title:	Storage stability of residues of AE C656948 metabolites (AE 1344122 and BCS- AA10065) in dry pea, rape and orange during deep freeze storage for up to 24 months
	AA10065) in dry pea, rape and orange during deep freezestorage for up 24 2
Report No:	MR-10/045
Document No:	<u>M-389465-01-1</u>
Guideline(s) followed in	EU Directive 91/414/EEC amended by the Corporission direction 7032/QI/95 0.5
study:	
	US EPA Residue Chemistry Test Guideling OPPT \$60.1388. Storage Stability Doa
	OECD Test Guideline 5%, adopted 16 Strober 2007
Deviations from current	Deviation to OECD 500 : sanofes spin d at 25XLOQ orstead 3 10X, Nevertheless,
test guideline:	stability of residues still a gessable at this vel.
Previous evaluation:	yes, evaluated and accepted a by a b
	rev. 2 to Vol.3 @DAR 17 Nov@nber 2017 (recreases velied as)
GLP/Officially recognised	Yes Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q
testing facilities:	
Acceptability/Reliability:	Yes y & & & Y & & Y

The purpose of this study was to determine the storage stability of residues of the fluopyram metabolites fluopyram-methyl-suffixing (AE  $\sqrt{44122}$  and  $\sqrt{1000}$  and  $\sqrt{1000}$  and  $\sqrt{1000}$  and  $\sqrt{1000}$  and  $\sqrt{1000}$  and  $\sqrt{1000}$  by the storage (for 25 months), and rape (for 24 months) under reezes conditions at about  $\leq -18$  °C.



To determine the freezer storage stability of the relevant residues of fluopyram metabolites fluopyrammethyl-sulfoxide and fluopyram-7 hydroxy in dry pea (seed), rape (seed), and orange (fruit), 10- g aliquots specified as 'spiked samples'' individual samples were fortified with 100  $\mu$ L of the spiking solution at 20 mg/L, resulting in a concentration of 0.20 mg/kg of FLU-methyl-sulfoxide or FLU-7-hydroxy. The plastic bottles were sented and stored in frozen conditions inmediately after the fortification. The boxes containing the sample material for control samples were also stored in frozen conditions (at  $\leq$  -18 °C) and were analysed at the nominal storage intervals of 0, 3, 7, 12, 18 and 25 months for orange, at 0, 4, 7, 13, 19 and 25 months for dry pea and at 0, 3, 6, 12, 18 and 24 months for rape seed.

Concurrent recovery experiments were performed at all storage intervals by spiking control samples with a mixture of FLU-methyl-sulfoxice and FLU-7 hydroxy at a level of 0.01 and 0.20 mg/kg.

On day 0 (zero time analysis) three spiked samples per test item and one control sample were analysed. In parallel, four concurrent recoveries were conducted: one at the level of 0.01 mg/kg and three at 0.20 mg/kg. All samples were analysed according to the analytical method 00984 (**Marcon 1**, 05/02/2007, <u>M-283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 fev 4.

ĉ



Briefly, residues were extracted from 10 g of sample material (5g for straw) by two successive extractions using a high speed blender with a mixture of acetonitrile:water (80:20; v:v). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

- dilution performed under acidic conditions and measured in negative electrospray ionization of the determination of FLU-PCA.
- dilution performed under basic conditions and measured in positive electrospray ion zation for the determination of fluopyram, FLU-benzamide and FNU-PAA.

*Due to its instability, the analytical standard of fluopyram pyridyl-acetic acid (BCS-A 10139) was the available under its sodium salt form (BCS-AA10189) which was used as reference item.

# II. SFindings

In control samples, residues of FLU-methyl-sulfoxide and FLU-hydroxy were below LOQ. Summaries of concurrent recoveries conducted as a part of this study are presented in the Table 6.1.2-25 and Table 6.1.2-26. The overall mean concurrent recoveries of FLU-methyl-sulfoxide and FLU-hydroxy were satisfactory and were in the range of 70 110 % with the RSD < 20% for all tested analytes at two fortification levels.

Summaries of the residue behaviour of FLU methyl sulfoxide and FLU. Shydroxy in sorred samples are presented in the Table 6.1.2- 27 to Table 6.1.2- 28

- For FLU-methyl-sulfoxide, uncorrected mean recoveries in orange how a stability period of 24-25 months for deep frozen residues (mean recoveries ranged between 85 99% 91 96%, 91 103%, for dry pea (seed), rape (seed), and orange (fruit), respectively).
- For FLU-7-hydroxy, uncorrected mean recoveries in orange show a stability period of 24-25 months for deep frozen residues (mean recoveries ranged between 85 96%, 91 96%, 91 103%, for dry per (seed), rape (seed), and orange (fruit), respectively)

III Conchrsions

Residues of FLU-method-sulforide and FLU-7-hydroxy fortified at 0.2 mg/kg to control samples were stable in dry pea (seed) and orange (fruit) for 25 months and for 24 months in rape (seed) in frozen conditions (T  $\leq$  -18°C).

# Assessment and conclusion ov applicant:

The study is acceptable. Residues FLU, FLU-methyl-suffixed and FLL 7-hydroxy in dry pea (seed) and orange (fruit) at 0.2 mg/kg were shown to be stable for 25 months. Residues FLU, FLU-methyl sulfox fe and LU-2 hydroxy in rape (seed) at 0.2 mg/kg were shown to be stable for

Residues FLU, FLU*meth C sulfaxing and CU-7-bydroxy in rape (seed) at 0.2 mg/kg were shown to be stable for 24 months.

### Table 6.5.2-25 Concurrent recovery data for fluopyram-methyl-sulfoxide (AE 1344122)

l' ést	Fortification Bevel	Nominal Storage Interval (days)	FLU-methyl-sulfoxide Single Recoveries [%]	Mean [%]	RSD [%]	Standard deviation
Ċ	0.01	0	92	92		



		Nominal				~	
Plant	Fortification Level	Storage	FLU-methyl-sulfoxide	Mean	RSD	Standard	
material	[mg/kg]	Interval (days)	Single Recoveries [%]	[%]	[%]	deviation	
		(uays) 4	87	87	Ŕ	- 4	
		7	89	89	ч0 <del>г</del> а -	- 🔊	
		13	73	73 🛒	.≯ -	<u>,</u> -0 [°]	ê ^ş .
		19	83	83	-		
		25	84	ð	-		Ŭ,
Dry pea		0	82;90,400	O)Y	9.9 🕺	9.0	
(seed)		4	803 84	€ <u>99</u> €	3.4 0	2:8	
	0.20	7	99, 98 904 ; 111	[™] 99⊘° ⊾168	0.7%	0.7 ( 4.9 g	-4
		13 19	<u>\$04;111</u> & 91; <b>0</b> 2°	92	4.6 Ø 0.8 <i>°</i>	0.7	
		25	O106; 106; 100	√ 104 ~	3.3	3.3	K, Y
	Overall Mean		andard deviation [%]	930	10.9	A10.1 A	0
				94	<u>S-</u>		
		3		×107 %	<u>,                                     </u>		
		6	6 × × ×	122	-65		Ś
	0.01	12	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	. 23	Å	<u>_</u>	
		Â,	122 5	022	õ		
		_@ 24 گ		√ ⁰ 99 ∕	C	°~≫	
Rape	*		95; <b>9</b> 04; 104	100	466	×4.6	
(seed)	l l	Å.	2 x07; 10 - ~	×1,06	¢2.0	© _{2.1}	
	0.20	6 Ø	104,112	\$108 \$	5.2	5.7	
	0.20	S 120	\$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	10%	2.67	2.8	
	Ş (	, ist	Q. (102; 104)	\$103	°~9.4	1.4	
		. 624 ~	× 109; 112; 115	O ₁₁₃ 4	2.9	3.2	
	Ó Överall Mear	RSD and st	andard deviation [%]	/ 106	7.7	8.2	
		<del>*                                    </del>	100 ×	100	-	-	
		. 3	× 6 1040 5	@ ¹⁰¹	-	-	
^≈		× 7 7		91	-	-	
<u>í</u>		12	<u>~ 90</u> ~	90	-	-	
**		×18	\$* \$ <u>0</u> * 103 [*] \$0	103	-	_	
	~~ ~~ ~~ ~~ ~~ ~~ ~~ ~~ ~~ ~~ ~~	\$25 %		100	-	-	
Orange	Q A		100; 100; 100	100	0.0	0.0	
(fruit)			⁵ ⁹ 97; 105 ⁹	100	7.6	7.8	
		× 7 ~	109; 109	109	0.0	0.0	
La l	0.20	9 12	100 100 in 100	120	2.4	2.8	
		18	× ×100 100	120	1.4	1.4	
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		25	2, 100; 102 2, 2, 120; 116	120	3.7	4.5	
\sim			ands(rd deviation [%]	120	9.6	4.3 10.1	
SD: relative	standard deviation			105	9.0	10.1	l

 Overate Mean (KSD and standard deviation [%]
 105
 9.6
 10

 RSD: relative standard deviation
 Is and a deviation is not consideration; only the mean is reported
 Fortification as FLU-methyl-sulfoxide; calculated as: Fluopyram

 Fortification
 Fluopyram
 Image: Standard deviation is not consideration; only the mean is reported



		Nominal					N.
Plant	Fortification Level	Storage	FLU-7-OH	Mean	RSIO	Standard	
material	[mg/kg]	Interval	Single Recoveries [%]	[%]	1291	deviation	
		(days)			4	`	N. N
		0	90	90	Ą -	-0%	ŝ,
		4	88 💍	88	-	`~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	× .~
	0.01	7	87 🔗	8 C	-	<u> </u>	Ĩ
	0.01	13	81	Ô		<u> </u>	×,
		19	<u> 2</u> @´	<i>√</i> 5 96		, Q	Ô K
Dry pea		25	888	°√ 88⊘°	-5	(Ĩ,Œ
(seed)		0	99; 100	. 98	<u>3</u> ,3	6.4¢	a y
(3000)		4	<u>(</u> 98; 89 - 0	¥4	@-6.8 @	6.4	.~~
	0.2	7	0 ⁹³ 095	A 74 A.	1.5	1.4	
		13	96,98 U	97	1.5	<u>1.4</u>	, e ⁰
		19	× × 97; 100 ×	99	2.2	0°2.1	a. Y
		25	ý <u>ý</u> 91; 92, 95 Ör	3 33	0*2.2	<u>0</u> 2.1 0 2.1	£
	Overall Mean		andard deviation [%]	O´ 93 🏑	5.4	<u>5</u> 1	S.
		0,0*	\$95 \$	9.5 ^C	<u>s</u>	Ĵ'-	
		Q [*]	85	<u>S</u> S	~) [~] -	Ş - Q	
	0.01	6		0 ⁸⁰	<u>م</u> - ۲		
	0.01	12 %		¥ 73 ⊘	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		
	×	<u>18</u>	85 1	85	-	~~ -	
Rape	Q	- ³⁴	\$ 6, 87 m 4	~87	<u>6</u> -	<u> </u>	
(seed)	×		99; 96; 99	98 °	1.8	2 1.7	
· /	*		\$ ⁹⁵ ,95	96	167	1.4	
	0.45 0		Ø96; 90,	<u>93</u> 94	\$0.8	4.2 0.7	
			<u>94;95</u>	95	0.8	0.7	
		× 18 ×	104y96;96	95	3.0	2.9	
			andard deviation [%]	· · · · · · · · · · · · · · · · · · ·	7.6	7.0	
		i, KSD and st	Andrard deviation [%]	90	/.0 -	-	
	ĝ ^{"U} "V			2 0 90 2 0 75	-	-	
^× ∞	Ý "Š	7.00		y 99		-	
<u>k</u>	0.0	12	× × × × ×	83	_	-	
,		×18 é	102	102	_		
_	J . V	\$ 25 ×		102	_	-	
Orange	Q A		101; 99; 10	101	1.2	1.2	
(fruit)		i a	× × × 95; 94	95	0.7	0.7	
			94:94	94	0.0	0.0	
~		12 Q	90100	99	2.2	2.1	
n and a start of the start of t			× 103; 99	101	2.8	2.8	
		25	299 ; 107; 106	104	4.2	4.4	
× 1			andard deviation [%]	97	7.8	7.5	

RSD: Felative standard deviation If sample size (n) ≤ 2 ; then standard deviation is not a consideration; only the mean is reported Fortification as: FLU-7-QH; determination as: FLU-7-OH; calculated as: Fluopyram

Table 61.2- 27. Storage vability data for fluopyram-methyl-sulfoxide (AE 1344122) (fortification



	Nominal		U-methyl-sulf Level in Store		Day 0	Average %	Mean	
Commodity	Storage Period (days)	mg/kg	% of nominal spiking level	Mean % recovery	Normalized % Recovery ^a	of Gresh Concurrent Recoveries	Recoverv ⁴	
	0	0.195 0.201 0.196	98 101 98	995 40	100	91	59109 × 0	
	4	0.158 0.162 0.165	82 /	81 81	~ ⁸² , 0 ²	₹ ⁵ ² ⁸² ⁶		Ů
Dry pea (seed)	7	0.206 0.203 0.193	103 O 102	×100 Č			v	5
Dry pea (seed)	13	0.218 0.199 0.202	299 × 109 × 109 × 109 × 109 × 109 × 109 × 109 × 109 × 100 ×				955 ⁴⁷	
	19	0.186 0.178 0.081	× 91 °				*\$ [©] 99 >>	
	25	0.192 0.195 0.18		ç 96	2 ⁰⁹⁷ , Q	104 OF	92	
		0191 9:206 0.211	394 94 94 100 100 105 108	s s			100	
8		0.211 🌾	106/		2 d06	106	100	
Rape (seed)		0.2120 [*] 0.206 0.208	103 104 109	Q.Y		108	97	
		0.217 0.209 0.226	405		0 ⁵ 109	109	100	
		©196 50.211 0.1900	105 105 105 105 105 105 105 105		99	103	96	
, A	24 🛇	0496 0209 0.218		©104	104	113	92	
stor Sy − Sy −		0.199 0.292		100	100	100	100	
Orange (April)	A ³	0.216 0.206 0.209	104 113	105	105	103	102	
Orange (forit)		©.227 ~ >0.204 0.210	102 105	107	107	109	98	
		0.239 0.229 0.223	119 115 111	115	115	120	96	



	Nominal Storage Period (days)	FLU-methyl-sulfoxide Residue Level in Stored Samples			Day 0	Average %	Mean
Commodity		mg/kg	% of nominal spiking level	Mean % recovery	Normalized % Recovery ^a	of Gresh Concurrent Recoveries	Corrected Recoverve
	18	0.201 0.207 0.187	100 103 93	99 40	99	101	98 5 98 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5
a Day 0 Normaliz	25	0.221 0.225 0.225	110 113 113	© 112			

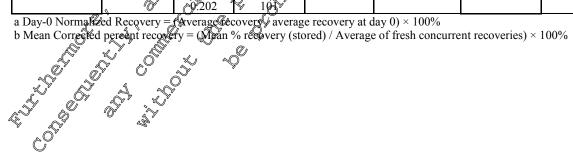
a Day-0 Normalized Recovery = (Average recovery / average recovery at day 0) × 100%b Mean Corrected percent recovery = (Mean % recovery (stored) / Average of frequencies) 100% 100%

Table 6.1.2-28: Storage stability data for thopyram-7-bydroxy (BCSAA10265) (fortification at 0.20 mg/kg)

	0.20 mg/kg		~	<u>A</u>		×,?
Commodity	Period (da0x) mg/kg	FLU 7-OH Level in Store % et nominal priking ~	Mean [®]	Day 0 Normalized	Average % of Fresh Cancurrent Recoveries	Mean Corrected % Recovery ^b
\$\$ \$	0.196 % 0.201 0.298	985 401 ×			98	101
	0.173 0.175 0.162	99 86 88 0 88 88 88	5 85 5 A	2 3 100 2 3 4 86 3 4 86	94	90
	© 0.193	95°° 297 -	₽ ⁹⁶ ₽	97	94	102
Dry pea (seed)	12 0 0 0 0 0 0 0 0 0 0 0 0 0	097 C Q 99 C 7 94 Q 7 94 Q 7 94 Q 8 2 ×	95 Ø	96	97	98
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		92 \$ 95 95 96	93	94	99	94
	0.192 25 0 0.192 0.187	&95 Ø 96 94	95	96	93	102
Rape (seed)	0.195 0.188 0.197	97 94 98	96	100	98	98



	Nominal Storage	FLU-7-OH Residue Level in Stored Samples			Day 0 Normalized	Average % of Fresh	Mean	
Commodity	Period		% of		%	Concurrent	ñ/	, .
	(days)	mg/kg	nominal	Mean %	Recovery ^a	Recoveries	Recovery	Ŵ,
		mg/ Kg	spiking	recovery		, S		
		0.100	level	×	- A			í "O
	2	0.182	91		ŝ			«O″
	3	0.175 0.189	88 94	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	ľ E	Ů
		0.189						>
	6	0.183	90 91		N 95 ×		× 97	
	-	0.181	9k	N Ô			1	o
		0.182	and a second	X X	à A	r ⊂ O`	→ 97√2 → 97√2 → 98€	
	12	0.187 0.183	2 92 4 5 7					
		0.185 0.184	905	$\sim$ $\sim$			Č.	
	18	. @	\$ ⁹²	B	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	^ل 95 گ	× 98	
		0 <b>1</b> 86		<del>r</del> ê _k ê			/	
	24	0, <b>43</b> 6 , 0.191 0.190 0,189	\$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	\$ 95 ₀	10 10 10 10 10 10 10 10 10 10 10 10 10 1		97	
		0.200 0.200	990 100 100			2 5 100	100	
ð		0.180 0.180 0.182	92 90 491	5 ⁷ 91 5	91 25 P	95	96	
Crown (fruit)		0, 199 0.189 0.193	99 95 96	97. 97. U	0 ⁹⁷	94	103	
Orange (Iruit)	5 6 12 4	0.202 201 × 20.205	• ^O 101 √ × 1000 1000		101	99	102	
		0,20¥ 40,202 -0,193			100	101	99	
	25 A	0.247 0.202 0.2092		103	103	104	99	
a Day-0 Normal	ed Recovery =	Average	overskaverag	e recovery at c	$\frac{1}{100\%}$	-		•





Data Point:	KCA 6.1/09
Report Author:	
Report Year:	2004
Report Title:	Final report - Determination of the storage stability of AE C638206 and the metabolites AE C653711 (BAM) and AE C657188 (PCA) in grape, porto, calculate, and wheat grain
Report No:	C045739
Document No:	C045739     V     V     V       M-237350-01-1     V     V     V       OPPTS 860.1380     V     V     V
Guideline(s) followed in	M-23/350-01-1         Ov
study:	
Deviations from current test guideline:	none yes, evaluated and accepted 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
Previous evaluation:	DAR (2005)
GLP/Officially	Yes, conducted upder GNP/Officially regignised testing decilities
recognised testing facilities:	Yes, conducted under GND/Officially recognised testing ficilities
Acceptability/Reliability:	Yes of the state o
	Yes y g g g g g g g g g g g g g g g g g g

Materals and Methods

This storage stability study was conducted for the Buopicolide project. As fluopyram-pyridyl-carboxylicacid (FLU-PCA alias AE C657188) is a common metabolite between fluopyram and fluopicolide this study is presented in this EU renewal dossier.

The fluopicolide renessal is currently ongoing and the present study was submitted to the RMS Austria. For a sake of clarity, only the results for fluopy cam-pyrevil-carboxylic acid are reported below.

For a sake of clarity, only the results for huopycam-pyndyl-carboxylic-acid

# Executive summary

The study investigated the stability of the picolide (AE C638206) and its metabolites, M-01 (BAM, AEC653711) and M-02 (AE C657188, and FLU-pyrdyl-carboxylic-acid) in grapes, potatoes, cabbage, and wheat grain under storage conditions at  $\leq 48$  °C for a period of 30 months and residues were considered to be sufficiently stable over this period.

Portions of untreated subgrate were for fied with the analytes. Separate batches were prepared for the fluopicol de and its metabolites The substrates were wheat grain, grapes, potato tubers and cabbage leaves (head).

The fortification level was at a forminal concentration (fresh weight basis) of 0.1 mg/kg. The fortified specimens were stored in a freezer at  $T^{\sim}$ -18  $\odot$ .

Fluopicolide and its metabolities were analysed according to the method 00782 ( $\blacksquare$  E., 13/09/2002,  $\underline{M}$  <u>217563-02</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO 3029/99 rev 4.

Residues were extracted with acidified water and acetone. After filtration and concentration, the solution is partitioned with MTBE and an aliquot of the MTBE phase is evaporated to dryness. The residues are



dissolved in methanol and methylated under acidic conditions. Then the mixture is cleaned up on a cartrigge and diluted to be injected in the LC-MS/MS system.

FLU-PCA was analysed after derivatization as methyl ester using FLU-PCA-meth@ester (AE 0898899) as reference item. However, the residue concentrations were calculated with respect to FLU-PCA

The residue concentrations of the analytes in the specimen extracts were calculated from the (peak area) of each peak by means of a second order calibration curve.

The limit of quantification was 0.01 mg/kg for each analyte.

# Findings,

At each storage interval, fluopicolide and its metabolites were determined in the stored control samples and in the stored spiked samples according to the following method:

Freshly fortified specimens with a nominal concentration of on mg/kg were analysed concurrently with each set of stored specimens. The results of these concurrent recoveries are presented in the Table 6.1.2-29 for each of the tested matrices. The concurrent recoveries meet the acceptability criteria; the mean Summaries of the residue behaviour of FLU-PCA in stored samples are presented in the office of the transfer of the residue behaviour of FLU-PCA in stored samples are presented in the office of the transfer recoveries are within the range 70 - 110% for each analyte / matrix combination and the %RSD values are <20% (where applicable). These results demonstrate acceptable method performance and support the



Table 6.1.2-30.

- For FLU-PCA, uncorrected mean recoveries in wheat (grain) and grapes show a stability period of 30 months for deep frozen residues (mean recoveries ranged between 74 97% (wheat) 9 91 (grapes), respectively)
- For FLU-PCA, uncorrected mean recoveries in potato (tuber) show a stability period of 12 months for deep frozen residues (mean recoveries ranged between 77 and 82%). The low recovery level in the stored samples at 18 months can be attributed to a poor performance of the abalytical method the day of analyses (concurrent recovery mean at 70% only). It is confirmed by the good results at the storage intervals of 24 and 30 months were the stored samples show residue level at 77 and 78%. It can be considered that fluopyram-PCA is stable 30 months in potato for the 12 months in the storage for the stored samples in the stored samples how residue level at 77 and 78%.
- For FLU-PCA, uncorrected mean recoveries in cabbage prow a stability period of 12 month for deep frozen residues (mean recoveries ranged between 73 and 90%)

# HT. CONCLUSION

Residues of FLU-pyridyl-carboxylic acid fortified at 0.1 mg/kg to control samples were stable niwheat (grain), grapes and potato for 30 months and for 12 months in cabbage) in bozen conditions (T  $\leq -18^{\circ}$ C).

### Assessment and conclusion by applicant:

The study is acceptable. Residues FLU-PCA in grape, potato, wheat grain and 1 mg/kg were shown to be stable for 50 months at  $T \le -18^{\circ}C$ . Residues FLU-PCA in cabbage 20.1 mg/kg were shown to be stable for 12 months at  $T \le -18^{\circ}C$ .

		inceder,		, in Lacos	100)
Plant I maternal	Fortification Level	Storago Intersal (months)	FLU-PCAQ Single Recoveres [%]	Mean [%]	RSD [%]
		\$0 °C	×99, 94, \$3, 85, 89	90	4.0
	6 A	3 %	9, 94, 95, 85, 85, 85, 85, 85, 85, 85, 85, 85, 8	80	-
			× (×73, 80 86, 89	77	
Wheat		°≫12 ~	0 <u>86,</u>	85	
grain 🔬	ð .	× 18 Q	\$ 10×77	76	200
A.		24 - 5 - 5 - 5 - 5 - 5 - 5 - 5 - 5 - 5 -	\$ \$ \$6,74	75	( <del></del> )
	N Q	30	78,75	77	
12	Worall Moor	, RSD and st	andarî veviation [%]	82	9.2
Y	Gwei an Zagean	$\sim 0 Q$	×(× 90, 82, 93, 96, 91	90	5.84.0
		, ×	⁰ 78, 80	79	25
4	S A S		68,77	73	0.50
Q	×0.1	₩ ¹ 2	\$ 87, 89	88	1.0
Grapes		180	75, 76	76	-
Grapes		24	75, 75	75	020
st b		30	92, 84	88	
	Over al Mean	, RSD and st	andard deviation [%]	83	9.5
Potato	0.1	0	71, 83, 87, 90, 81	83	8.8
tiller	0.1	3	72, 72	72	5 670

Table 6.1.2- 28 Concurrent recovery data for fluopyram-PCA (AEC657188)



Plant material	Fortification Level [mg/kg]	Nominal Storage Interval (months)	FLU-PCA Single Recoveries [%]	Mean [%]	RSD [%]	
		6	79, 87	83	<i>~</i> -	
		12	96, 83	90 🚄	-	
		18	71, 81	76 🕵	» -	
		24	73, 68	70	- ~	
		30	86, 80	688	Ű	Z 2
			Overall Mean, RSD and	<b>6</b> √ 81	209	Q O ^y &
		0	85, 84 93, 98, 93	× 916	6.6	
		3	<u>74,70</u>	\$2	× - \ ⁰	
Cabbaaa		6	~ 75 <b>4</b> ~	× 75 🗸		No de la companya de
leaves	0.1	12	\$U, 73 C	~ 75 <u>0</u> °	0 ² 4	A
(head)		18	× 1,73 ×	72	_∞ - 0	
. ,		24	Y 72, JY O	J75 .	P° 🔬	
		30 2	<u>6</u> 18,81 ×	Q 80≪″	<u> </u>	
	Overall Mean	n, RSD and st	andard deviation [86]	79	<b>\$10.4</b>	, Č
D: relative s	standard deviation $(x) \leq 2$ then stended deviation	· · · · · · · · ·	2 Q		Ĵ Ĵ	, W
tification as	$(n) \leq 2$ , then standard do s: <b>FLU-PCA</b> • determin	aduan as∶ikatu	<b>PCA-methylester</b> · completed	Sreponed		<b>N</b>
Â,						
2 2 2 2 2 3						
			FLU-PCA Single Recoveries [%]			
						((



Page 67 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

able 6.1.2- 30:	Storage stabili at T=-18°C	ity data for flu	opyram-PCA	A (AE C657188)	) following sto	rage	× 0 [°]	
Commodity	Nominal Storage Period (days)	Spike level (mg/kg)	mg/kg	FLU-PCA te Level in Stored	Sample® Mean %	Day 0 Normalized Recovery ^a	Average % of Fresh Concurrent Recoveries	Menter Corrected 9 Recovery ^b
	0	a Dit	0.093 0.098 0.088 0.093 0.088 0.093	85 89 89 89 89 89 89 89 80 80 80 80 80 80 80 80 80 80 80 80 80	20 993110 20 993110 2005 76205	oduction of	DE TRAY	
Wheat grain		012102 012102 012104 02	0.083 0.082 0.089 0.114	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	70 ⁵ 78 5 5	10 ¹² 87 0 ¹	≈ 80 77 85	93 101 114
	18	Liect as				2 ² 88	76	104
	24 \$		0.082 0.082 0.024 0.079	$\begin{array}{c} & & & & & & \\ & & & & & & \\ & & & & & $	0 ^{10 80} 80 ^{15 32}	89 82	75 77	107 96
J.C.		e docu	0.085 0094 0.095 0.097 0.097		91		90	101
Grape			0.085	> 82 87	84	92	79	106
n C	Car 22	Ret the	0:089 	86 88	87	96	73	119
CORPE			0.087 0.091	84 88	86	95	88	98



Page 68 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

							O.L.D.	of the allow
	Nominal		Residu	FLU-PCA ue Level in Stored		Day 0 Nør malized	Average %	A Del Mean
Commodity	Storage Period (days)	Spike level (mg/kg)	mg/kg	% of nominal spiking level	Mean %	Day 0 Normalized	Average Oof Fresh Concurrent Recoveries	Corrected %
			0.077 0.079	0 ⁰ 74	273	Part Start	j. 1	SC 99
			0.090 0.090 0.090	91 91 91*©	21 89 7 C	98 GB	0 ⁵ 75 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	119
			چ 0.080 <u>چ</u>	770	ð. 77 JØ	200 ⁵⁸⁵ 60 ⁵	1988	° 88
	0	CUMERT	0.07€ 0.084 0.086 0.090 0.090 0.094	6 ¹⁰ 81 81 8 8 90 8 90 8 7 90 8 7		6 <u>30</u> CUIR	M 22 AN 2	99
	3. G	and to	0.081		× × × × ×		72	111
Potato	T.C.	674 50 . 30	©078 © 0.081 %	75 0° 78 0°	e 77 5	<u>, 0</u> )94	83	93
			0.083 0.085	1 80 82 0 0	112 ⁶¹	§ 99	90	90
	18 90	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.058 0.062	264	570.	70	76	75
	24 C	3.0 CUIRES	0.082, 0	75 × 59 75 × 50 79	77	94	71	108
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	30			\$\$ 7Z do	78	95	88	89
≫ Cabbage	NOTE 10 3	0	0.087 0.088 0.096 0.097 0.182	85 93 93 98	90		91	99
* . DCT	C.D. S. M.	Per the P	0.080	69 77	73	81	72	101
E ^{ULL} COLGE	BLEDES COLLE	J _{IL} D _C	- Y					68



Page 69 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram

					Ċa	ara d	O ^j I ^R C°
	Nominal		Resid	FLU-PCA ue Level in Stored Samples	Day 0 Normalized	Average Sof	A Del Mean
Commodity	Storage Period (days)	Spike level (mg/kg)	mg/kg	% of nominal spiking level recovery	Recovery?	Eresh Concurrent O Recoveries	Corrected %
	6		0.080 0.084		Cont Stor	Ô. 1 , 75\$	105 IV
	12		0.079 0.080	~ 76 · 76	0 ⁴ 840 ⁵	0 ⁵ 75 5 1	101
	18		0.071 S			\$72 °C	° 96
	24		0.080 × 087		OCC OULLING TH	er dar	111
	30	ounent.	0.062 0.071		g 71,00°	<u>م</u> الله الله الله الله الله الله الله الل	80

a Day-0 Normalized Recovery = (Average recovery / average recovery at the 0) × 100% b Mean Corrected percent recovery = (Mean % recovery (stored) / Average of fresh concurrent recoveries) 100% * The analysed concentration was unrealistic. The result was considered as an anomaly and was therefore excluded from the formal stability data.



New studies

New studies Data Point:	KCA 6.1/10
	KCA 6.1/10
Report Author:	
Report Year:	
Report Title:	Amendment no. 3 to final report - 7 days freezer store stability strictly with different combinations of a total of 61 analytes (parent and the tabolite molecules) and five matrix types (high water / acidi@ starch / protect / oil)
Report No:	S13-03307
Document No:	M-480441-06-1 Commission Regulation (EU) No 544/20 of 10 June 2001 implementing
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for acrive substances (0) EPA Residue Chemistry Test - Guideline OPPTS 860.1380. Storage Stability Data OECD Test Guideline 506, adopted 16 October 2007.
Deviations from current test guideline:	adopted 16 October 2007
Previous evaluation:	No, not previously submitted Study was not found in DAR/RAR and the Addenda Yes, conducted under, GLP/Officially, recognized testing facilities
GLP/Officially recognised	Yes conducted under GLP/Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Nes C C C C C C C C C C C C C C C C C C C

Materials and methods

A study was completed to determine the stability of desidues of fluopyram (AE C656948) and its metabolites Duopyram-benzamide AE F148815% fluopyram-pyridyl Garboxylic acid (alias AE C657188, alias FLUPCA) and flue yram -hydroxy (BCS AA10065) & fortified control samples of material of plant origin (tomato (fruit); wheat (green material), grape (bunches), wheat (grain), potato (tuber), peas (dry peas) and oilseed rape (scolis) during stating for a period of & hours $at +1^{\circ}C$ followed by 7 days of storage at -7°С.

This study was conducted in order to cover frozen temperature exceedance during the sample shipment of residue trials. O

The spiking solutions were prepared in actionicale for auopyram, in acetonitrile/water (1/9) pH8+ammonia for Flue yram-benzann'de and for fluopyram-7-bydroxy and in acetonitrile/0.5% acetic acid (1/9) for fluopyram-pyridyl carboxylic acid

The sample materials were homogenized in scutter with dry ice. Individual aliquots were prepared by filling 50 mL Barstedt tubes with 50g of specimen material. Samples were fortified with 1.0 mg/kg of fluopyram and its metabolites. Some other aliquots were not spiked to be used as control sample and procedural recoveries. The storage containers were labelled with a unique sample number, the study number Sample material, storage interval and the compound analysed and then sealed and placed in a freezer at ± 1 immediately after the fortification. After 8 hours the storage containers were placed in a freezer at - TC for Tdays.

On day O (zero-time analysis) five spiked samples per test item and one control sample were analysed to confirm the fortification level and performance of the method.



At each storage interval, one stored control sample and procedural recoveries were analysed concurrently with the stored spiked samples.

Residues of fluopyram in/on plant material were determined by HPLC-MS/MS according to BCS method 01207 based on the QuEChERS multi-residue method (S., 11/12/20)3, M-424756-02-1, see section MCA 4.1.2). Extraction of residues was done with acetonitrile/water (4/1, v/v) by shaking An aliquot of the extract was taken and, when relevant, internal stable labelled standards were added. The solution was subjected to LC-MS/MS.

Quantification was performed with matrix matched calibration solutions and double injection of each sample and calibration solution. The Limit of Quantification (LOQ) of BCS Method 01207 is defined as 0.01 mg/kg as validated in the original report S10-00279.

After the day 7 analysis, a decrease of the recoveries in the stored camples was observed for tomato (thirt), wheat (green material) and peas (dry peas); this was not the case of the fresh fortifications. Following this observation, an extended extraction time was applied to the stored saffiples which led to better recoveries. Therefore, longer extraction times were applied for additional re-analysis and confirmation after 22 days storage at -7°C for wheat (green material) and after 30 days of storage at -7°C for tomato (fruit) and peas (dry peas).

Residues of the metabolites fluopyram benzamide (AE F148815) fluopyram-pytulyl-caboxylic acid (alias AE C657188, alias FLU-PCA) and fluopyram thydroxy (BCS AA00065) in/on plant material were determined by HPLC-MS/MS according to analytical method 00984(final 0.5/02/2007, M-283301-01-1, see MCA section 4.1.2). Extraction of residues was done using two successive extractions using a blender with acetonitrile / water (8/2 %/v). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards. One first dilution was done using two successive extractions for the determination of fluopyram-pyridyl carboxybe acid. Another dilution was performed under basic conditions for the determination of fluopyram-pyridyl carboxybe acid. Another dilution was performed under basic analysed by HPLCDIS/MS

Quantification was performed using calibration solutions in actionity water (1/9, v/v) pH 8 or acetonitrile/ 0.5% acetor acid (1/9, v/v) and the internal standards in the same concentration as in the sample ex-tracts (4 fg/mL).

The Limit of Quantification (LOO) of the method 00984 is defined as 0.01 mg/kg as validated in the original report.

Prior to the storage stability tests method validation was performed using BCS methods 01207 and 00984.

 \bigcirc

Results and discussions

¥-31: 8

The performance of the analytical method was good during the conduct of the whole study. Indeed, mean concurrent recoveries were deeped acceptable between 70 and 110%) and RSD was below 20%, as shown in Table 8.1.2-32.

For the untreated samples as well for the treated samples, a sufficient number of samples has been tested for each storage period. In the control samples, the apparent residues were below 30% of the LOQ. The results of the space stored samples are summarised in the Table 6.1.2-33.

Fluopyram and its metabolities were shown to be stable in all tested matrices during storage after 8 hours at $+1^{\circ}$ C followed by at lease 7 days at -7° C.

Residue relative decrease (%) compared to initial analysis.



Commodity category	Sample material	FLU	FLU- benzamide	FLU-PCA	FLU-7-OH	
High water	tomato green material	3* 10*	0 1	-5 -3		
High acid	grape	4	-6	s -1	\$ ⁷ 2 >	
High starch	wheat grain potato	19 15	2 12 12	0		
High protein	peas	-7*	CA P	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	A 4	
High oil	rape seed	7	& 0 & °	5 ⁹ - 5 ⁷	· -10	

*: The extracts were shaken for 15 minutes on day 30 compared to 2 minutes on day 7, which led to better recoveries. This longer extraction procedure was applied for all samples thereafter, sa sa

Conclusion The storage stability demonstrated that the parent Buopyram as well as its metabolite fluopyram benzamide, FLU-PCA and FLU-7-OH are stable for Puctuations of the temperature between + band -7 C for at least one week in all commodity categories. Therefore, no degradation of residues is expected when fluctuation of temperature occurs due togefrost cycles of other teasons during the storage of the sample shipment.

reserver une sample shipment.



Table 6.1.2- 32:	Concurrent	t recoveries of f	luopyram and	l its metabolites fro	medifferent m	atôjces.
Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural	Mean ±RSD 0 (%) 0	anaxes.
fluopvram (AE (C656948)		م	6 ^Q		
	1.0	0	5	93,83,95,97,96	90±6.0	
tomato (fruit)	1.0	7*	2	99.95	98 °	
tomato (fruit)	1.0	30*	2% ¢°	93 92 8 0	93	× S
	Overall Mean.	RSD and standard	deviation [%]			1
	1.0	0 5	5 5	81, 87, 82, 88, 100	88±896	
Wheat (green	1.0	7*		86.91 5	88 x	S.
material)	1.0	22* 0 4		97.93	95 ^(S)	\bigcirc
	Overall Mean.	RSD and standard	deviation [%]		89 # 3 8	
	1.0		W S	97.95.96,97.93	96±1.8 ×	
Grape (bunches)	1.0 *	¥7 <u> </u>	2		ÿ3 [™]	
	Overall Mean.	RSD and standard	d deviation [%]	n=7) ~ ~ ~ ~	95+2.3	
	1.0		<u> <u></u></u>	96.97.95.98.98	97±1.3	
Wheat (grain)	1.0			85.88 &	87	
	Overall Mean.	RSD and standard			94 ±5.6	
	1.0 °		5 ~ ~	90,9392,93.94	92 ±1.6	
Potato (tuber)	1.0 % 5	7 5		96,96	96	
	Ĉi a	RSP and standard	Adeviation [%]		93 ±2.3	
	1.0		5 5 5	88,72,80,89,81	82 ±8.4	
Peas (dry peas)		7***	2° y	\$1,85	83	
	\$0 <u>4</u>		p <u>2</u> 0'	99.92	96	
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		ŘSD and standard	deviation [%]		85 ±9.2	
Oilseed Arape	1.0 0		S ^Y O	95.93.89.86.89	90 ±4.0	
(seeds)	1.0	V df		90,86	88	
		RSD and standard	deviation [%]	(n=7)	90 ±3.7	
Fluopvram-benz		<u>8845) ~~~~</u>	¥		101.1.1	
	1.0		5	106,104,103,104,105		
tomato (fruit)			2	106.107	107	
		RSD and standard			105 ±1.3	
Wheat (green		0	5	97.95.81.79.84	87 ±9.5	
material)		7	2	78.87	83	
	ž	RSD and standard			86 ±8.8	
Ĉ	1.0	0	5	98.97.93.88.102	96±5.6	



Matrix	Spike level	Storage	Sample size	Individual	Mean	
	(mg/kg)	Interval (days)	(n)	procedural recoveries (%)	±RSD	
Crone (hunches)	1.0	7	2	98,96	97	
Grape (bunches)	Overall Mear	n. RSD and standa	rd deviation [%]		96 ±4.6 0	
	1.0	0	5	98,96,98,89,102	97 ±4,5	
Wheat (grain)	1.0	7	2	94.100	97, 0	
	Overall Mean	n, RSD and standa	rd deviation [%]		₽9±4.4 ×	
	1.0	0	5	100,1,17,94,0,7,104	106,±9.7	s á
Potato (tuber)	1.0	7	25 00	9\$2105 L	920 .	× 23
	Overall Mean	n, RSD and standa	urd deviation [%]		@04 ±9 <u>(</u> 4	A
	1.0	0	5 5 2 2	110.91.97,107.95	100 ±8.1	
Peas (dry peas)	1.0	7		9.4.90 O 2 2	20 x	
	Overall Mean	n, RSD and standa	re deviation [%]	n=7) ~ ~ ~		$\bigcirc$
0.1 1	1.0	0 %	5,000	8057.71.29.77	76.54.4	¹
Oilseed rape (seeds)	1.0		Ŷ.	\$\$3.71 \$ \$ A	d in	
(50003)	Overall Mean	n. KSD and stand	rd deviation [%]	(n=7) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) (	76 ±508	
AE C656948-pvi	ridvl carboxy	ic acid AE 6057	7188			
	1.0 🔬		<u> 6</u> 3 <u>0</u> 0	99.100.91.87.88	93± 6.6	
tomato (fruit)	1.0	7	2 5	93.008 5 2	101	
	Qoerall Moar	n, RSD and standa	urd deviation [%]	<u>(()</u>	95 ±7.9	
Wheat (gree	0.0		5 ~ ~	91.83087.89 82	86 ±4.5	
( 1)	1.0 % «	, 7 ° °		81.389	85	
material)	Overall Mean	n. RSD and standa	ur deviation [%]	(n=7) 👋	86 ±4.6	
<i>K</i> ^y ^u	1.0 .		5 5 29	100 000.100.102.95	$99 \pm 2.6$	
Grape (bunches)	1.00	<u>7, ~ , 0 , 0 , 0 , 1 , 0 , 1 , 0 , 1 , 1 , 1</u>	ŹŸ &	<u>\$</u> 6.99	98	
	Øverall-Mear	n. RSD and standa	rd deviation [%]	(n=7)	99 ±2.5	
Peas (dry peas)	1.0 0 6		557 57	93.87.84.89.90	$89 \pm 3.8$	
Peas (dry peas)	1.0			94,92	93	
<u> </u>	Overal Mean	SD and standa	rd deviation [%]	(n=7)	90 ±3.9	
AE Ç656948-7-h	vdroxv (BCS	-ĂA149065) 🔊				
4	1.0		~	104.108.106.107.94	$104 \pm 5.5$	
tomato (fruit) 🦉	1.0		$\mathbb{O}_{2}$	110.110	110	
<u></u>	Overall Mean	h, RSD and standa	rd deviation [%]	(n=7)	106 ±5.2	
	3 <u>40</u> 0		5	98.96.92.95.95	95 ±2.3	
Wheat @(green) material)	1.0	€ 7	2	94.101	98	
	Overall Mear	n, RSD and standa	rd deviation [%]	(n=7)	96 ±3.0	
Grape (Sunches)	1.0 Â	0	5	109.109.110.105.106	$108 \pm 2.0$	



Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%)	Mean ±RSD (%)				
	Overall Mean, I	RSD and standard	l deviation [%] (	n=7)	106 ±5.2				
	1.0	0	5	109.111.110.104.108	108 ±2.5 0				
Wheat (grain)	1.0	7	2	106,111	109 🔬				
	Overall Mean, I	RSD and standard	l deviation 👫 ) (	n=7) 0	108 2.4				
	1.0	0	5	109,99,005,105,107	195 ±3.6				
Potato (tuber)	1.0	7	2		110, O				
	1.0       0       5       109.111.110.104.108       108 $\pm 2.5$ 1.0       7       2       106.111       109         Overall Mean. RSD and standard deviation $\frac{1}{6}$ (n=7)       108 $\frac{9}{2.4}$ 108 $\frac{9}{2.4}$ 1.0       0       5       109.99905.105.107       108 $\pm 3.6$ 1.0       7       2       110 $\frac{10}{10}$ 110 $\frac{9}{2}$ 0       5       109.99905.105.107       105 $\pm 3.6$ 100 $\frac{9}{2}$ 1.0       7       2       110 $\frac{10}{10}$ 110 $\frac{9}{2}$ 0.0       5       109.99405.105.107       105 $\pm 3.6$ 1.0       7       2       110 $\frac{10}{10}$ 100 $\frac{9}{2}$ 0.0       5       109.99405.105.107       105 $\pm 3.6$ 100 $\frac{9}{2}$ 1.0       7       2       110 $\frac{10}{10}$ 100 $\frac{9}{2}$ 100 $\frac{9}{2}$ 0.0       7       2       100 $\frac{9}{2}$ 100 $\frac{9}{2}$ 100 $\frac{9}{2}$ 100 $\frac{9}{2}$ 1.0       10       10       10       10       10       10								
	1.0	0	5 🐇 🤅		$(A \otimes 1) + A \circ 1$	4			
Peas (dry peas)	1.0	7		106.101 1	104 0″				
	Overall Mean, I	$\frac{1.0}{1.0} \qquad 7 \qquad 2 \qquad 9 \qquad 101, 20, 101, 200 \qquad 0.2 \qquad 102 \qquad $							
	1.0	0 0 5	15 <u>\$</u>	104,96,99,109,90	98±58	$\bigcirc$			
Oilseed rape (seeds)	1.0	7 8 6	200	108.109	10,25	þ			
(30003)	Overall Mean, J	SB and standard	eviation [%]		₫01 ±6.7 ×				

*The extracts were shaken for 15 minutes on day 30 compared to 2 minutes on day 7, which led to better recoveries. This longer extraction procedure was applied for all samples thereafter.

Table 6.1.2-33: Stability of residues of fluopyram and its metabolites in different matrices

Matrix	Spike • Jevel (mg/kg)	Storage interval (dats)	Individual recovered residues (mg/kg)	Mean	Individual recoveries (%)	Mean	Relative decrease %**
• 7		fluðpyrg		) N			
Tomato	1.0	A Do	0.936, 0.832, 0.927, 0.973, 0.963	0.926	93, 83, 93, 97, 96	92	-
(fruit)	1.0 C	7*0	£791,0803,0.838,0.818,0.8475	0.819	79, 80, 84, 82, 85	82	11
	1.0	30* 8	0.871 0.920 0.933, 0 852, 0 857	0.887	87, 92, 93, 85, 86	89	3
Wheat	1.0	0,0	0,807, 0.867, 0.822, 0.877, 0.996	0.874	81, 87, 82, 88, 100	88	-
(green material)	1.0		0.661 0.708, 9.738, 0.906, 0.653	0.693	66, 71, 74, 71, 65	69	22
	1.0	22* 🔊	0.796, 0.79290.79	0.794	80, 79, 79	79	10
Grape	1.05	Q `	<b>0</b> .973, <b>0</b> .954, 0. <b>9</b> 59, 0.971, 0.925	0.956	97, 95, 96, 97, 93	96	-
(bunches)		7	0.949, 0.893 0.914, 0.941, 0.929	0.925	95, 89, 91, 94, 93	92	4
Wheat	1.0	0 0	<b>6</b> 965, 0.973, 0.946, 0.980, 0.984	0.970	96, 97, 95, 98, 98	97	-
(grain)*	1.97		0.793, 0.779, 0.768, 0.810, 0.801	0.790	79, 78, 77, 81, 80	79	19
The state	9 1.0	0 3	0.903, 0.934, 0.915, 0.926, 0.940	0.924	90, 93, 92, 93, 94	92	-



Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (mg/kg)	Mean	Individual recoveries (%)	Mean	Relative decrease
Potato (tuber	1.0	7	0.774, 0.790, 0.774, 0.774, 0.814	0.785	77, 79, 77, 81	7 <b>8</b> /	15
Peas	1.0	0	0.879, 0.723, 0.796, 0.888, 0.812	0.820	88Ç72, 80, 89, 81	82°	×, -
(dry peas)	1.0	7*	0.789, 0.798, 0.819, 0.791, 0.674	0.774	<b>3</b> , 9, 80, 82, 79 <b>6</b> 7	S N	<u>6</u>
1 /	1.0	30*	0.907, 0.817, 0.945, 0.840, 0, 595	0.881	91, 82, 94, 84, 89	88 0 2	\$~7
Oilseed	1.0	0	0.946, 0.928, 0.894, 0.858 0.887	0.903	Ø5, 93, 89, 86, 89 ⁴	80 6	S -
rape (seeds)	1.0	7	0.834, 0.814, 0.859, 0 28, 0.869	<b>0</b> .840	83, 8, 86, 80, 87	⁸ 4 2 ⁹	7
		fluopyra	m-benzamide			de la	。 1
Tomato	1.0	0	1.061, 1.044, 1.033, 1.044, 1.043	P.045 5	106,194,103,104,105	104	-
(fruit)	1.0	7	1.054, 0.910 1.04% 1.123 0.063	1.040	105, 91, 2105, 202, 206 , 5 , 6	10 <b>0</b> ©	0
Wheat	1.0	0	0.97400.955,0808,0788,0893	Ø.874	97, <b>9</b> 5, 81, <b>(9</b> , 84 ~)	87	-
(green material)	1.0	7	0.847, 0.834, 0.810, 0.867, 0.922	0.886	§5, 83, 89, 87, 87	86	1
Grape	1.0	0 %	0.978, 0.972, 0927, 0880, 1,020	0.955°	98, 97, 93, 88, 102	96	-
(bunches)	1.0	7	1,699, 1.062, 1.084, 1.009, 0.961	1.625	101, 106, 108, 101, 96	102	-6
Wheat	۾ 1.0	Ĵ, Ó	0.97,9,0.956,0.983,0,895, 1.919	0.966	98, 96, 98, 89, 102	97	-
(grain)	1.0 %	7	0-911, 0.977, 0.909, 0.879, 1.046	0,944 ×	91, 98, 91, 88, 105	95	2
Potato (tuber			1.00001.170, 0.939, 1, 70, 1, 92	À.064 @	100, 117, 94, 117, 104	106	-
	1.0	75	Q287, 0.923, 0.981, 0.990, 0.858	0029	89, 92, 98, 100, 86	93	12
Peas	1.0	) J	1.102, 0.905, 9.970, 5074, 0.954	1.001	110, 91, 97, 107, 95	100	-
(dry peas)	1.0	7	0.9873, 1.028, 0.942, 0.964, 0.989	0.959	87, 103, 94, 96, 99	96	4
Oilseed	<u></u> .0°	0 8	0.803 0.771 0.714, 0 754, 0 75	0.763	80, 77, 71, 75, 77	76	-
rape (seeds)	1.0	7.	0,009, 0.781, 0.849, 0.734, 0.738	0.756	71, 75, 85, 73, 74	76	0
(arras) ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	\$	AE COS	188 (fluopyrum-pyridyl carboxylic a	cid)			
Tomato	1.0 0 ×	0	0.989, 0.997, 0.909, 0.872, 0.881	0.929	99, 100, 91, 87, 88	93	-
(fruit)	1.0		0.967 0.955, 0.987, 0.999, 0.981	0.978	97, 95, 99, 100, 98	98	-5
Wheat	A.0	0 0	0.207, 0.833, 0.871, 0.886, 0.816	0.863	91, 83, 87, 89, 82	86	_
(green ) maternal)	1.0 1.0	A ~	9.883, 0.941, 0.871, 0.864, 0.880	0.888	88, 94, 87, 86, 88	89	-3
	Ø.0	0	1.000, 1.003, 0.998, 1.016, 0.948	0.993	100, 100, 100, 102, 95	99	-



Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (mg/kg)	Mean	Individual recoveries ())	Mean	Relative decrease
	1.0	7	0.983, 1.005, 1.038, 1.012, 0.979	1.003	98, 101, 204, 101, 98	100	-1
Peas	1.0	0	0.929, 0.872, 0.842, 0.890, 0.899	0.886	93, 87, 84, 89, 90 0	*89 🌮	
(dry peas)	1.0	7	0.927, 0.939, 0.947, 1.000, 0.932	0.949	95, 94, 95, 100, 93	95 [°]	\$~-7 ₀
		fluopyra	m-7-hydroxy	Ś			×0×
Tomato (fruit)	1.0	0	1.037, 1.083, 1.056, 1.070, 0938	1.037	104, 108, 106, 407,	10\$ \$	\$ -
	1.0	7	1.054, 1.071, 1.063, 1076, 1.01	Л.075 Қ Ф.	105 107, 496, 1087	107	<b>-3</b>
Wheat	1.0	0	0.976, 0.964, 0.222, 0.949, 0.949	<b>6</b> 952	98, 96 ⁹ 92, 95, 95	995 O	-
(green material)	1.0	7	0.923, 0.943 0.924, 1,003, 0.924	0.943	9 <b>3</b> , 94, 92, ¥00, 9 <b>2</b> ,	94	1
Grape (bunches)	1.0	0	1.091, 1.093, 1,101, 1.054, 1.061	1,080	10,60 0 5	Ĵ <b>P</b> 08	-
	1.0	7	1.609, 1.057, 1.065, 1.085, 1.042	1.056	103, 100, 106, 109, 104 0	106	2
Wheat (grain)	1.0	0	1.092 1.115, F.101, \$044, 1\$85	٦.087	109, 111 410, 104, 108	108	-
	1.0		1.038, 6095, 1, 11, 1.000, 1.083	1.083	104,4009, 111, 109, 108	108	0
Potato (tuber	1.0		1,089, 0,988, 1,047, 1.05,1, 1.066	1.048 *	009, 99, 105, 105, 107	105	-
I.	Ĵ.0	7	1.084, 1.067, 1.065, Q.099, 1.049	1.075	108, 107, 107, 110, 105	107	-2
Peas (dry	1.0		1.012 7.003, 0073, 0972, 1460	¥.024	101, 100, 107, 97, 106	102	-
peas)	1.0	7,09	£032,1063,1.029,1.085,1.085	1.060	103, 106, 103, 109, 108	106	-4
	A.0	0	1.091, 0.959, 0.98521.029, 0.895	0.982	104, 96, 99, 103, 90	98	-
rape (seeds)	1.0		1.057, 1.090, 1.081, 1.095, 1.079	1.080	106, 109, 108, 109, 108	108	-10

*The extracts were shaken for 15 minutes of day 30 compared to 2 minutes on day 7, which led to better recoveries. This longer extraction procedure was applied for all samples thereafter. **: (1 - final recovery mean / initial recovery mean) x100



Data Point:	KCA 6.1/11
Report Author:	
Report Year:	
Report Title:	Storage stability of fluopicolide metabolites AE C657378 and AE C656948-method
	sulfoxide (AE 1344122) in/on sunflower, dry bean, cucimber, strawber@ and barley
	and AE C643890 in/on barley during Greezer storage for up to 24 months - Final
	report v v v v v v v v v v v v v v v v v v v
Report No:	<u>M-754395-01-1</u>
Document No:	<u>M-754395-01-1</u>
Guideline(s) followed in	OECD Guideline for the Testing of Chemicals. Stability of Posticide Residues in
study:	Stored Commodities 506, 2007-10-16;
	US EPA OPPTS 860.1280, Storage Stability Data, $\chi_{j}^{\infty} = \sqrt{2}$
	Coordenação Geral de Acreditação do Inmetro NIT-DOCLA 035.
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised	Yes, conducted under GLP/Officially recognised resting facilities
testing facilities:	
Acceptability/Reliability:	Yes v v v v v v v v v v v v v v v v v v v

This study was conducted in the frame of the fluopicolide (XE C638206) project. It is considered to be relevant for this fluopyram EU reneval as AE 1340/22 (A) as Fluopyram methyl-sulfoxide) is a common metabolite between these two fungioides.

The purpose of this study was to determine the storage stability of residues of fluopicolide metabolites AE C657378, AE O44122 (alias O luop o am-methyl-subfoxice) and AE C643890 in fortified control samples of plant origin (Sunflower (seed), Dry bean, Cucumber (four), Soawberry (fruit) and Barley (grain)) during freezer storage at  $\leq$ -18 % for 25 months.

For the purpose of this dossied the following summary will give results only for FLU-methyl-sulfoxide (AE 1344122).

# Material and Methods

For the purpose of this dessier, the following summary will give results only for FLU-methyl-sulfoxide (AE 1344)22) which is a common mertbolite of fluopicolide and fluopyram.

Samples of sunflower seed (high oil matrix), dry boans seed (high protein matrix), cucumbers (high water matrix), strawberry (high acid matrix), barley stain (high starch matrix) were fortified with fluopicolide M05 (alias Fluopyram-methyl-orifoxide, AE 344122) at the level of 0.1 mg/kg and stored deep frozen ( $\leq$  -18°C) for a period of 24 months.

Portions of antreated substrate were fortified with individual analytes The fortification level was at a nominal concentration (fresh weight basis) of 0.1 mg/kg. The fortified specimens were stored in a freezer at < -18 °C. After (nominal 30, 90, 180, 360 and 540 days, three fortified per analyte and one control samples of each tested plant material were removed from the deep-freezer and analysed using the HPLC-MS/MS method 00782 M006 (1997), 2017, M-610859-01-1, see section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.



Residues are extracted with a mixture of acetone/water adjusted with sulfuric acid to pH 2. After addition of L-cysteine hydrochloride (250 mg/L), the extract is made to volume and an aliquot is concentrated to the aqueous remainder. The solution is again adjusted to pH 2. NaCl is added and partitioned twice with of TBE. An aliquot is concentrated to dryness and dissolved in methanol/water before LC-MS/MS analysts.

The limit of quantification (LOQ) for FLU-methyl-sulfoxide was 0.01 mg/kg for all matrices. The metabolite was not calculated as parent equivalents but the concentration is expressed as FLU-methyle, sulfoxide itself. The limit of detection (LOD) was estimated to be  $\leq 30\%$  g/2 the LOQ.

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established with at least 5 concentration levels. Correlation coefficients were above 0.99.

The quantification was done by external standardization using matrix matched standards

Analysis was performed within 24 hours after extraction \$\overline{2}^{\circ}\$

# Findings

In order to assess the accuracy of the residue analyses, recoveries were determined by analysing freshly fortified samples alongside the stored for field samples. At all storage intervals except for day  $0^{\circ}$  two concurrent recoveries were determined at level of 0, 0 mg/kg. No additional considerent recoveries were determined on day 0, since there were five the shly fortified storage samples. The procedural recoveries meet the acceptability criteria; the mean recoveries are within the range  $0^{\circ} - 110^{\circ}$  for each analyte / matrix combination and the %RSD values are 20% (where applicable). These procedural results demonstrate acceptable method performance and support the analytical results obtained for the forthied deep-frozen samples. Summaries of the residue behaviour of FgU-methyl-sulfoxide in stored samples are presented in the Table 6.1.2-35.

For FLU-methyl-sulfoxide, uncorrected mean recoveries in orange shows stability period of 24-25 months foldeep frozen fesidues (mean recoveries ranged between \$7 - 97%, 87 - 101%, 96 - 109%, 90 \$103% 84 - 404%, for sunflower seed, dry pea (seed), cucumber (fruit), strawberry (fruit) and barley (grain)? respectively)

Representative plant commodities (surflower seed, dry bean seed, cacumber, strawberry, and barley grain) were fortified at 0.1 mg/kg with -methyl-suffoxide. The fortified camples were stored at low temperatures at -18°C and analysed at set intervals. The recoveries show that residues of FLU-methyl-sulfoxide are stable for up to 24 months in the tested commodities.

Conclusion

Assessment and conclusion by applicant?

The study is acceptable Q Residues FLU-methy sulfoxide in stufflower seed. By bean seed, cucumber, strawberry, and barley grain at 0.1 mg/kg were shown to be studie for 4 months at T -18°C.

Table 6.72- 34: Summary & concurrent recoveries of FLU-methyl-sulfoxide from various plant matrices



Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%)	Mean	
	Fh	opyram-methyl-	sulfoxide	<i>u</i> ₀	5 ⁵	
		0	1	88	88	
		30	2	83, 75	79 🕺	
		97		80, 85	\$3 [©]	
Sunflower seed	0.1	183	æ 2	×85, 86 °	x 86	
		387 🔬		79,88	× 84 0	
		568 Ô		~81, 84~~~	83	
		756	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Q 76, 19	77 0	
				× 581 ~	<b>%</b> 1	
		<u></u>		× 840	Ø84 (	Ç [®] Ö
		~~ 96 <u>6</u>		y _997 č~	85	
Dry bean seed	0.1	× 182 0	ST O	2 ⁹ 81 0 ⁹	83 081	*¥
	n n n n n n n n n n n n n n n n n n n			K 75,97	76 O	2
		5923		£ 82, 82	×\$2	
		× 761		× 79.82 °	\$ 81	
	\$ . 6 ×			<u> </u>	96	
		🔬 30 🥎 🖉	2 1 5 ²	0 880 C	88	
O'	5° 50	0 ⁻ 93%		96, 95 89, 83	96	
Cucumber		78 8	02	\$\$9,83	86	
A A		385		97, 94	96	
		\$ 501 0	× ×2 á [×]	87, 85	86	
		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		84, 74	79	
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~				104	104	
<u></u>		÷ 30 Q	<u> </u>	84, 83	84	
N.		~ 98 ~	× 2	100, 101	101	
Strawberry			2	88, 80	84	
		386	2	77, 76	77	
		⁽¹⁾ 567	2	88, 86	87	
		^{~©} 755	2	99, 98	99	
	A 39	0	2	82, 92	87	
Barleygrain	D ³ DA	31	2	93, 92	93	
Strawberry Strawberry Barley grain		91	2	83, 85	84	



Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%)	Mean	
		183	2	83, 83	83	
		360	1	77	77	
		540	2 🖓	88, 93	91	
		758	<u>Å</u>	80, 83	83 ⁰⁰	
					Ŷ,ő	

 Table 6.1.2- 35:
 Stability of fluopicolide M-05 (FLU-methyl-sulfoxide) residues in various matrices following storage at -18°C

			B	<u> </u>	QŬ d	<u>0                                    </u>		$\approx$ $\cdot$
Sample	Actual Storage	Resi	due Level in S Qof	tored Samp Average		Day-0 O	TICSU ,	Average Corrected
Material	Period [days]	mg/kg	nominal spiking level	recovery {	RSD [%]	Recovery	Concurrent Recoveries	( ))
	AE C656	5948-methy	· ()	<u>v</u>				
		0.0931	83	100	~~			
	0	0.0957	\$ 96 C	ê, v	~		0	100
	0	0.0957 0.0960	~ 96 ~ 96	\$ ⁹⁶	1.9		\$ 88	109
		0.0960	\$90 Õ				Ş	
	Ű	0,0878	88	5 5 860 7 860 7	× 0	× ,×	/	
	30	<b>0</b> .0833	83° ~	<u>860</u>	<u>\$</u> 93	90 °	79	109
		0.0876	<u> </u>					
	97 ⁰	0.0 <b>©</b> #1 0.0833	O 8460	6 85 2	20	© 89	83	102
	9/-	0.0833 ©0.0875			20	© 89	63	102
Sunflower (seed)		0.0946	92 92 92 7 92 7 92 7 92 7 92 7 92 7 92 7 92 7 92 7 92 7 92 7 92 7 92 7 92 92 92 92 92 92 92 92 92 92		$\sim$			
(seed)	183	0,0921	در 92¢ [°]	° ⁰ 92 [∞]	0.6 ⁰	96	86	107
		0.0930			Ĩ			
		0.10992		a@a7 a@	<b>6</b> .1	101	84	115
$\sim$	Ø 387 Ô	0.191	× 90	\$ ⁹⁷ \$	0.1	101	04	115
		9.08830	188 s	p ₍ )				
	568 🖉		Ø ⁹ 99	्≪96	7.7	100	83	116
<i>v</i> [€]		0.102	0 ⁷ 99					
<i>S</i> ∽ [™]	₩ ⁹ 756	0.0891 0.0884		<b>9</b> 0	3.6	94	77	117
	, 756 , Ø	0.0944	\$88 © 94 \$	90	5.0	24	//	11/
Ő		<b>0</b> 0934 -	<i>»</i> 93≫					
Į,	20	S.0921	<b>\$</b> 2	93	2.8	100	81	115
Dry bean	Ó C	0.0953	·~~91		2.0	100	01	110
Dry beam (seed)		0.097/4 x0.0935	97 93					
	$\widehat{\mathcal{G}}_2$	×0.0933 ×0.0899	93 90	91	1.9	98	84	108
	1 4	0.0904	90	<i>.</i>	1.7	20	01	100
Ċ,	-			-	-			



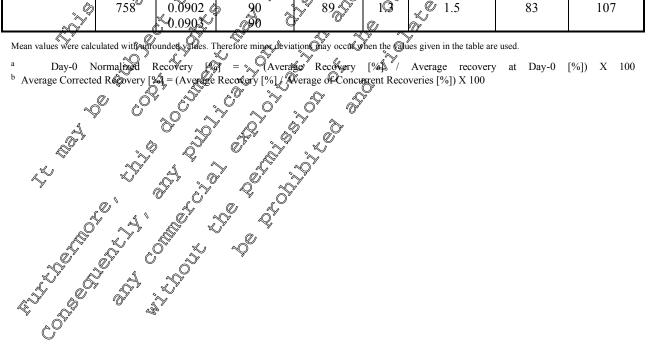
Page 86 of 789 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

$ \begin{array}{c c c c c c c c c c c c c c c c c c c $							-		<u> </u>	
0.0851         85         0         0         0         0         0           392         0.105         105         101         4.5         106         70         1337           0.0964         96         11.3         94         80         109         94         80         109           0.0951         96         11.3         94         80         109         94         80         109           0.0961         86         87         94         80         109         94         81         107           0.0861         86         87         94         81         107         96         3103           0.0887         89         99         96         108         96         96         109         96         3103           0.0993         914         99         96         109         96         100         96         103           0.0993         916         108         99         96         109         96         104           0.0997         97         96         100         1.7         101         96         114           0.0995         99         97 <t< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>ر م</td><td>&gt;</td></t<>									ر م	>
0.0851         85         0         0         0         0         0           392         0.105         105         101         4.5         106         70         1337           0.0964         96         11.3         94         80         109         94         80         109           0.0951         96         11.3         94         80         109         94         80         109           0.0961         86         87         94         80         109         94         81         107           0.0861         86         87         94         81         107         96         3103           0.0887         89         99         96         108         96         96         109         96         3103           0.0993         914         99         96         109         96         100         96         103           0.0993         916         108         99         96         109         96         104           0.0997         97         96         100         1.7         101         96         114           0.0995         99         97 <t< td=""><td></td><td>96</td><td>0.0948</td><td>95</td><td>95</td><td>0.0</td><td>102</td><td>87</td><td>1.69</td><td>¥.</td></t<>		96	0.0948	95	95	0.0	102	87	1.69	¥.
0.0851         85         0         0         0         0         0           392         0.105         105         101         4.5         106         70         1337           0.0964         96         11.3         94         80         109         94         80         109           0.0951         96         11.3         94         80         109         94         80         109           0.0961         86         87         94         80         109         94         81         107           0.0861         86         87         94         81         107         96         3103           0.0887         89         99         96         108         96         96         109         96         3103           0.0993         914         99         96         109         96         100         96         103           0.0993         916         108         99         96         109         96         104           0.0997         97         96         100         1.7         101         96         114           0.0995         99         97 <t< td=""><td></td><td></td><td>0.0948</td><td></td><td></td><td></td><td></td><td>$\sim$</td><td>S T</td><td><i>,</i></td></t<>			0.0948					$\sim$	S T	<i>,</i>
0.0851         85         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0         0<			0.0922	92				Ç,	S. O	
0.0851         85         0         0         0         0         0           392         0.105         105         101         V4.5         106         70         1337           0.0964         96         11.3         94         80         109         1337           573         0.0901         90         96         11.3         94         80         109           0.0761         76         0.0861         86         87         20         947         81         107           0.0861         86         87         20         947         81         107           0.0887         89         98         99         947         81         107           0.0913         914         99         94         96         108         96           0.0992         98         99         96         106         96         106         96         104           0.0993         99         109         17         101         96         104           0.0995         99         99         109         107         96         104           0.0995         99         97         109		182			88	4.1	95 🖉	81	109	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $				85			4	Ś		
$\begin{array}{c ccc} Cucumber (fruit) & \hline 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 &$						ĈA		$\sim$		
$\begin{array}{c ccc} Cucumber (fruit) & \hline 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 &$		392	0.102		101	₹45	100	76	133	
Cucumber (fruit) $0.00887$ $89$ $67$ $67$ $67$ $67$ $66$ $99$ $59$ $106$ $96$ $50$ $96$ $50$ $96$ $50$ $96$ $50$ $96$ $50$ $96$ $50$ $96$ $50$ $96$ $50$ $96$ $50$ $96$ $50$ $96$ $50$ $96$ $50$ $96$ $50$ $96$ $50$ $96$ $100$ $17$ $50$ $96$ $104$ $96$ $104$ $96$ $104$ Cucumber (fruit) $0.0976$ $99$ $50$ $96$ $100$ $1.7$ $7101$ $96$ $104$ $0.0995$ $95$ $56$ $106$ $50$ $106$ $106$ $97$ $86$ $112$ $0.0955$ $95$ $596$ $106$ $97$ $16$ $98$ $86$ $1114$ $0.0974$ $997$ $16$ $98$ $86$ $1114$ $96$ $96$		372			101	1.0		l l l l l l l l l l l l l l l l l l l		Ċ
Cucumber (fruit) $0.0987$ $89$ $60$ $99$ $53$ $100$ $596$ $506$ 93 $0.0928$ $98$ $53$ $995$ $53$ $100$ $588$ $113$ $0.0928$ $98$ $53$ $995$ $53$ $100$ $88$ $113$ $0.0970$ $975$ $53$ $995$ $53$ $100$ $88$ $113$ $0.0970$ $975$ $96$ $100$ $1.7$ $7101$ $96$ $104$ $0.0975$ $995$ $596$ $100$ $1.7$ $7101$ $96$ $104$ $0.0955$ $95$ $596$ $100$ $97$ $86$ $112$ $0.0955$ $96$ $106$ $109$ $097$ $16$ $98$ $86$ $1114$ $0.0958$ $96$ $97$ $1.6$ $98$ $86$ $113$ $0.0974$ $997$ $1.6$ $988$ $86$ $113$ $0.$					, Č		~			V
Cucumber (fruit) $0.0987$ $89$ $4$ $6$ $6$ $99$ $5$ $100$ $96$ $103$ $0$ $0.0982$ $98$ $99$ $53$ $100$ $96$ $103$ $0.0928$ $98$ $99$ $53$ $990$ $63$ $100$ $58$ $113$ $0.0970$ $97$ $63$ $990$ $63$ $100$ $88$ $113$ $0.0970$ $97$ $66$ $10$ $17$ $96$ $104$ $0.0975$ $995$ $96$ $100$ $1.7$ $710$ $96$ $104$ $0.0955$ $95$ $96$ $100$ $97$ $86$ $112$ $0.0955$ $95$ $96$ $109$ $0.97$ $86$ $112$ $0.0955$ $96$ $109$ $0.97$ $1.6$ $98$ $86$ $114$ $0.0974$ $997$ $1.6$ $98$ $86$ $113$ $96$ $96$		573			sa l	113	°√° gata °	~~ 80r ×	© 109 m	
Cucumber (fruit) $0.0987$ $89$ $4$ $6$ $6$ $99$ $5$ $100$ $96$ $103$ $0$ $0.0982$ $98$ $99$ $53$ $100$ $96$ $103$ $0.0928$ $98$ $99$ $53$ $990$ $63$ $100$ $58$ $113$ $0.0970$ $97$ $63$ $990$ $63$ $100$ $88$ $113$ $0.0970$ $97$ $66$ $10$ $17$ $96$ $104$ $0.0975$ $995$ $96$ $100$ $1.7$ $710$ $96$ $104$ $0.0955$ $95$ $96$ $100$ $97$ $86$ $112$ $0.0955$ $96$ $109$ $0.97$ $16$ $98$ $86$ $114$ $0.0955$ $96$ $109$ $0.97$ $1.6$ $98$ $86$ $114$ $0.0974$ $997$ $1.6$ $98$ $86$ $113$ $92$		575				11.5				
Cucumber (fruit) $0.0987$ $89$ $4$ $6$ $6$ $99$ $5$ $100$ $96$ $103$ $0$ $0.0982$ $98$ $99$ $53$ $100$ $96$ $103$ $0.0928$ $98$ $99$ $53$ $990$ $63$ $100$ $58$ $113$ $0.0970$ $97$ $63$ $990$ $63$ $100$ $88$ $113$ $0.0970$ $97$ $66$ $10$ $17$ $96$ $104$ $0.0975$ $995$ $96$ $100$ $1.7$ $710$ $96$ $104$ $0.0955$ $95$ $96$ $100$ $97$ $86$ $112$ $0.0955$ $96$ $109$ $0.97$ $16$ $98$ $86$ $114$ $0.0955$ $96$ $109$ $0.97$ $1.6$ $98$ $86$ $114$ $0.0974$ $997$ $1.6$ $98$ $86$ $113$ $92$										
Cucumber (fruit) $0.0987$ $89$ $4$ $6$ $6$ $99$ $5$ $100$ $96$ $103$ $0$ $0.0982$ $98$ $99$ $53$ $100$ $96$ $103$ $0.0928$ $98$ $99$ $53$ $990$ $63$ $100$ $58$ $113$ $0.0970$ $97$ $63$ $990$ $63$ $100$ $88$ $113$ $0.0970$ $97$ $66$ $10$ $17$ $96$ $104$ $0.0975$ $995$ $96$ $100$ $1.7$ $710$ $96$ $104$ $0.0955$ $95$ $96$ $100$ $97$ $86$ $112$ $0.0955$ $96$ $109$ $0.97$ $16$ $98$ $86$ $114$ $0.0955$ $96$ $109$ $0.97$ $1.6$ $98$ $86$ $114$ $0.0974$ $997$ $1.6$ $98$ $86$ $113$ $92$		761			0 [×] 070 [×]	× n	~ 01~~	Q 01 Y	× 107	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		/01				G.0			107	
30 $0.0970$ $97$ $99$ $33$ $100$ $88$ $113$ $93$ $0.0995$ $99$ $100$ $1.7$ $100$ $88$ $113$ $93$ $0.0995$ $99$ $100$ $1.7$ $101$ $96$ $104$ $0.0969$ $995$ $95$ $96$ $100$ $1.7$ $101$ $96$ $104$ $0.0969$ $995$ $95$ $95$ $96$ $100$ $97$ $96$ $104$ $0.0969$ $995$ $95$ $95$ $97$ $96$ $112$ $0.0969$ $97$ $96$ $1.0$ $97$ $86$ $112$ $0.0958$ $996$ $97$ $1.6$ $98$ $86$ $113$ $0.0974$ $97$ $97$ $1.6$ $98$ $86$ $113$ $0.0974$ $99$ $97$ $1.6$ $98$ $86$ $113$ $0.0937$ $94$ $92$ <td< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>(</td><td></td><td></td></td<>								(		
30 $0.0970$ $97$ $99$ $7.3$ $100$ $88$ $113$ $93$ $0.9995$ $99$ $70$ $100$ $1.7$ $700$ $96$ $104$ $93$ $0.0995$ $99$ $700$ $1.7$ $700$ $96$ $104$ $0.0969$ $995$ $95$ $96$ $100$ $1.7$ $700$ $96$ $104$ $0.0969$ $995$ $95$ $96$ $100$ $1.7$ $966$ $104$ $0.0969$ $995$ $95$ $95$ $966$ $100$ $97$ $866$ $112$ $0.0958$ $966$ $100$ $0.99$ $97$ $1.6$ $98$ $866$ $114$ $0.0938$ $99$ $97$ $1.6$ $98$ $866$ $113$ $0.0938$ $99$ $97$ $1.6$ $98$ $866$ $113$ $0.0937$ $93$ $92$ $2.9$ $93$ $99$ $97$				91		, Or				
30 $0.0970$ $97$ $99$ $33$ $100$ $88$ $113$ $93$ $0.0995$ $99$ $100$ $1.7$ $100$ $88$ $113$ $93$ $0.0995$ $99$ $100$ $1.7$ $101$ $96$ $104$ $0.0969$ $995$ $95$ $96$ $100$ $1.7$ $101$ $96$ $104$ $0.0969$ $995$ $95$ $95$ $96$ $100$ $97$ $96$ $104$ $0.0969$ $995$ $95$ $95$ $97$ $96$ $112$ $0.0969$ $97$ $96$ $1.0$ $97$ $86$ $112$ $0.0958$ $996$ $97$ $1.6$ $98$ $86$ $113$ $0.0974$ $97$ $97$ $1.6$ $98$ $86$ $113$ $0.0974$ $99$ $97$ $1.6$ $98$ $86$ $113$ $0.0937$ $94$ $92$ <td< td=""><td></td><td>0</td><td></td><td></td><td>995</td><td>°~5.9</td><td></td><td>S 96 🖉</td><td>×103</td><td></td></td<>		0			995	°~5.9		S 96 🖉	×103	
30 $0.0970$ $97$ $99$ $33$ $100$ $88$ $113$ $93$ $0.0995$ $99$ $0.09$ $99$ $0.09$ $99$ $0.0995$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $99$ $0.09$ $0.09$ $114$ $0.09$ $0.99$ $0.09$ $114$ $0.09$ $0.09$ $0.99$ $0.00$ $114$ $0.009$ $0.99$ $0.009$ $0.99$ $0.009$ $0.99$ $0.009$ $0.99$ $0.009$ $0.99$ $0.009$ $0.99$ $0.009$ $0.009$ $0.009$						S.			0	
Cucumber (fruit)         0.0995 0.0995 0.0905         99. 99. 0.02         100 1.7         1.7         96. 97. 97. 96.         104           Cucumber (fruit)         1.72         0.0925 0.0955         95. 95. 96.         96. 1.0         1.0         97. 97.         86.         112           0.0955         95. 90.0958         96. 96.         1.0         97. 96.         97. 86.         96.         114           0.108         108. 0.0974         97. 97.         96. 97.         110. 96.         96. 114         114           567. 0.0958         0.997. 93.         97. 93.         97. 93.         98. 96.         86.         113           567. 0.0958         99. 93.         92. 92.         2.9         93. 79.         79.         116.           567. 0.0957         0.0957         94. 94.         92. 92.         2.9         93. 79.         79.         116.           0.104         0.0957         94. 94.         400. 96. 94.         87. 96.         104. 96.         96.         114.           0.104         0.0957         94. 94.         400. 96.         8.7         100. 104.         104. 96.           0.105         0.0957         94. 97.         103. 2.2         103. 84.         123.				A* 70 -					<b>ò</b>	
Cucumber (fruit)         0.0995 0.0995 0.0905         99. 99. 0.02         100 1.7         1.7         96. 97. 97. 96.         104           Cucumber (fruit)         1.72         0.0925 0.0955         95. 95. 96.         96. 1.0         1.0         97. 97.         86.         112           0.0955         95. 90.0958         96. 96.         1.0         97. 96.         97. 86.         96.         114           0.108         108. 0.0974         97. 97.         96. 97.         110. 96.         96. 114         114           567. 0.0958         0.997. 93.         97. 93.         97. 93.         98. 96.         86.         113           567. 0.0958         99. 93.         92. 92.         2.9         93. 79.         79.         116.           567. 0.0957         0.0957         94. 94.         92. 92.         2.9         93. 79.         79.         116.           0.104         0.0957         94. 94.         400. 96. 94.         87. 96.         104. 96.         96.         114.           0.104         0.0957         94. 94.         400. 96.         8.7         100. 104.         104. 96.           0.105         0.0957         94. 97.         103. 2.2         103. 84.         123.		20	0.0970	* 9 <i>1</i> 0		ja karala kar			112	
Cucumber (fruit)         0.0995 0.0995 0.0905         99. 99. 0.02         100 1.7         1.7         96. 97. 97. 96.         104           Cucumber (fruit)         1.72         0.0925 0.0955         95. 95. 96.         96. 1.0         1.0         97. 97.         86.         112           0.0955         95. 90.0958         96. 96.         1.0         97. 96.         97. 86.         96.         114           0.108         108. 0.0974         97. 97.         96. 97.         110. 96.         96. 114         114           567. 0.0958         0.997. 93.         97. 93.         97. 93.         98. 96.         86.         113           567. 0.0958         99. 93.         92. 92.         2.9         93. 79.         79.         116.           567. 0.0957         0.0957         94. 94.         92. 92.         2.9         93. 79.         79.         116.           0.104         0.0957         94. 94.         400. 96. 94.         87. 96.         104. 96.         96.         114.           0.104         0.0957         94. 94.         400. 96.         8.7         100. 104.         104. 96.           0.105         0.0957         94. 97.         103. 2.2         103. 84.         123.		30	0.0928	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	99	@.3		0 88 1	113	
Cucumber (fruit) $0.0969$ $95$ $96$ $10$ $97$ $86$ $112$ $0.0958$ $96$ $10$ $97$ $86$ $112$ $0.0958$ $96$ $10$ $97$ $86$ $112$ $0.0958$ $96$ $100$ $97$ $86$ $112$ $0.0958$ $96$ $109$ $0.98$ $110$ $96$ $114$ $0.109$ $0.99$ $97$ $1.6$ $98$ $86$ $113$ $0.0974$ $97$ $97$ $1.6$ $98$ $86$ $113$ $752$ $0.0938$ $96$ $97$ $1.6$ $98$ $86$ $113$ $752$ $0.0937$ $93$ $92$ $2.9$ $93$ $79$ $116$ $0.102$ $0.0937$ $95$ $400$ $8.7$ $100$ $104$ $96$ $0.09376$ $88$ $102$ $103$ $2.2$ $103$ $84$ $123$						<u>اي ۲۷</u>				
Cucumber (fruit) $0.0969$ $95$ $96$ $10$ $97$ $86$ $112$ $0.0958$ $96$ $10$ $97$ $86$ $112$ $0.0958$ $96$ $10$ $97$ $86$ $112$ $0.0958$ $96$ $100$ $97$ $86$ $112$ $0.0958$ $96$ $109$ $0.98$ $110$ $96$ $114$ $0.109$ $0.99$ $97$ $1.6$ $98$ $86$ $113$ $0.0974$ $97$ $97$ $1.6$ $98$ $86$ $113$ $752$ $0.0938$ $96$ $97$ $1.6$ $98$ $86$ $113$ $752$ $0.0937$ $93$ $92$ $2.9$ $93$ $79$ $116$ $0.102$ $0.0937$ $95$ $400$ $8.7$ $100$ $104$ $96$ $0.09376$ $88$ $102$ $103$ $2.2$ $103$ $84$ $123$			0.0995	O [*] 99	O ^Y O	•>		la cr	10.4	
Cucumber (fruit) $0.0969$ $95$ $96$ $10$ $97$ $86$ $112$ $0.0958$ $96$ $10$ $97$ $86$ $112$ $0.0958$ $96$ $10$ $97$ $86$ $112$ $0.0958$ $96$ $100$ $97$ $86$ $112$ $0.0958$ $96$ $109$ $0.98$ $110$ $96$ $114$ $0.109$ $0.99$ $97$ $1.6$ $98$ $86$ $113$ $0.0974$ $97$ $97$ $1.6$ $98$ $86$ $113$ $752$ $0.0938$ $96$ $97$ $1.6$ $98$ $86$ $113$ $752$ $0.0937$ $93$ $92$ $2.9$ $93$ $79$ $116$ $0.102$ $0.0937$ $95$ $400$ $8.7$ $100$ $104$ $96$ $0.09376$ $88$ $102$ $103$ $2.2$ $103$ $84$ $123$		93	0,0990	990	C> 100-		× 101 ×	× 96	104	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	<b>a</b> 1	\$	0.102			Ŏ ^Ŷ		Ç.		
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		i - Ô	0.0969	× 97	\$ . xi					
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	(fruit)	178	0,0955		ి 96 స్థా	1.0	O 97 🍫	86	112	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		- ĉ ^v	Q.0958	, <b>396</b> ~	× ,>>	, Ô	s o			
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$			» 0.108 »	×108 ×	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~					
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		[©] 385,5°	0,140	0 1106	×109 >>	0.2	110	96	114	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	, Q		0.109 @	109		0	*			
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		(	0.0974	<b>097</b> C			0°			
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	K~y ^v	567 <b>. </b> Ø	0,0938	s 99 s	6 ⁹⁷ x	× 1.6	98	86	113	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$			0:0958	<u> </u>	N U	~~~				
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		AN A	_م 0.0889	ν γοσ		Â				
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		952 <u></u>	0.092	<u></u> 93	.92	<b>∂</b> 2.9	93	79	116	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	~ (		0.0937	0°94	Ô ^y Â	7				
Strawberry $30$ $0.100$ $102$ $103$ $2.2$ $103$ $84$ $123$			<b>0</b> .110 ∧	× 110						
Strawberry $30$ $0.100$ $102$ $103$ $2.2$ $103$ $84$ $123$	A		0.104	A104 6						
Strawberry $30$ $0.100$ $102$ $103$ $2.2$ $103$ $84$ $123$		0	0.0947	©"95 Š	<u></u> ,≪¥00	8.7	100	104	96	
Strawberry $30$ $0.100$ $102$ $103$ $2.2$ $103$ $84$ $123$	× ,	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Q.104 A	104	$\sim 0^{\times}$					
Strawberry $30$ $0.100$ $102$ $103$ $2.2$ $103$ $84$ $123$	~~	К ^у	0876	× 88 .	N ³					
Strawberry (fruit)       30       0.492       102       103       2.2       103       84       123         (fruit)       0.102       0.109       69       103       4.8       103       101       102         98       0.101       101       103       4.8       103       101       102         98       0.101       101       103       4.8       103       101       102         98       0.101       101       103       4.8       103       101       102         98       0.101       101       103       4.8       103       101       102         98       0.0955       96       92       5.8       92       84       110		<pre> 4</pre>	0.106	106						
(fruit) 07102 07102 09 0.109 09 0.109 09 0.109 101 103 4.8 103 101 102 0.00955 96 182 0.0943 94 92 5.8 92 84 110 0.0863 86	Strawberry	@ 30	0,102	L 102	103	2.2	103	84	123	
No.109         O.109         O.99         O.101         101         103         4.8         103         101         102           No.900         100         100         100         103         4.8         103         101         102           No.900         100         100         100         100         100         100         100         100           No.900         100         100         103         4.8         103         101         102           No.900         No.955         96         92         5.8         92         84         110           No.9063         86         No.9063         86         No.906         No.906         No.906         No.906         No.906         No.906	(fruit)		_&®≊102 ≪	¥ 102¥						
101     103     4.8     103     101     102       101     100     100     100     101     102       101     100     100     100     101     102       101     100     100     100     101     102       101     100     100     100     100     100       102     100     100     100     100       102     100     100     100       103     101     102       104     100     100       105     100     100       100     100     100       100     100     100       100     100     100       100     100     100       100     100     100       100     100     100       100     100     100       100     100     100       100     100     100       100     100     100       100     100     100       100     100     100       100     100     100       100     100     100       100     100     100       100     100     100       100 <td></td> <td></td> <td>0.109</td> <td>a <b>6</b>9</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>			0.109	a <b>6</b> 9						
A         Q 00         100         Image: Constraint of the state of the	Ű	\$ ⁹⁸ 0	0.1401	101	103	4.8	103	101	102	
Image: Weight		× .4	00QQ							
Image: Weight of the second	, C		×0.0955							
0.0863 86		¥82 .	×0.0943		92	5.8	92	84	110	
	× Si		0.0863			2.0				
	<del>- Ô</del>	ļ			1	1	1	1		



Page 86 of 789 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram

		0.105	105					125° (7 7) 1935° (7
	386	0.106	106	95	19.8	95	77	129
		0.0728	73				~	S ^Y O ^Y
		0.0869	87				Ç.	
	567	0.0928	93	90	3.4	90 🖉	87	103
		0.0914	91			2		
		0.089	89		© ₹8.9	L.		
	755	0.0918	92	95	8.9	JEI"	98°	× 96 ×
		0.1045	105	85 ×		ŐŸ		
		0.0844	84	4				
		0.0854	85	OO, Y				C Q
	0	0.0877	88	85	1.9		§ 82	
		0.0854	85					
		0.0844	84	× 85 × 0° × 86 × 86 × 86	õ			.4
		0.0916	92	~			ŎŸ,	
	31	0.0805	80	^م ⁸⁶ م	7.05		<u>,</u> 90 ¢	× 96
		0.0847	84 92 80, 80, 102 108, 108, 108, 108, 108, 108, 108, 108,	× 86 ×		× × × × × × × × × × × × × ×	<u> </u>	
		0.102	QV2	· \$. ;	S.			$\bigcirc$
	91	0.102	Q 102 '0'	°1⁄04 *	3.3	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		124
		0.108			3.3 5.1		$-\hat{c}$	
Barley (grain)	102	0.0960 0.08 <b>83</b>	∕~ <u>9</u> 6 `		Ø .			110
	183	0.0883	88	91	√5.1 √		5 838	110
		0.0878	96 88 88 88 86 86 86 81 0 85 106				Ô	
	391 🐒	0,0856 0.0816 0.0805	860 810		6 ^{3.1}	× ~ ~	× 77	109
	391	0.0810		( 8 <b>4</b> /	0 ^{9.1} &	<b>9%</b> 0 ĉ		109
	<u> </u>	0.08005	× 83	S V	<u> </u>		/	
	- A	0,0966 0.0735		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	1Ø2	a 106	91	99
		0.0965	6 96		<b>4</b> 6.3		91	99
		0.0903	× 85 106 43 × 96 × 96 × 96 × 96 × 96 × 90 × 9	284 -57 -57 -57 -57 -57 -57 -57 -57		r ky		
(Å)	758	0.0902	- 00× - 00 <	89.00	10	<i>©</i> 1.5	83	107
	750	~0.0902 ~0.0903	án 8			© 1.5	05	107
					<u> </u>	<u>rar</u>		





	· · · · · · · · · · · · · · · · · · ·
Data Point:	KCA 6.1/12
Report Author:	
Report Year:	
Report Title:	Report amendment no. 1 to final report - Residue analytical method 01594 and short term storage stability of fluopyram (AE C656948) and its metabolites AE F148815 AE C657188, BCS-AA10189, BCS.AA10065 and AE 1344122 inon honey by
	term storage stability of fluopyram (AE C656948) and its metabolites AE F148815
	AE C657188, BCS-AA10189, BCS.AA10065 and SE 1344122 in on honey by
Report No:	<u>M-681002-02-2</u>
Document No:	<u>M-681002-02-2</u>
Guideline(s) followed in	Regulation (EC) No 1102/2009 of the European Parliament and the Council of 21
study:	October 2009 concerning the placing of plant protection products on the market and
	repealing Council Directives 79/117/FEC and 91/41 FEC
	A A A A A A A A A A A A A A A A A A A
	Guidance document on residue analytica methods, SANCO/823/00/rev. 8.1,
	European Commission, Directorate General Health and Consumer Protection
	Guidance document on residue analytical methods, SANCO/823/00/rev. 8.1, European Commission, Directorate General Health and Consumer Protection
	European Commission Fuidance Document for Generating and Reporting Methods
	of Anarysis in Support of Pre Registration Data Requirements for Againex II (Part A,
	Section 4) and Annex III (Part A, Section 5) of Directive 91/414, SONCO/3029/99
	reg. 4, 11007/00 2 0 2 2 2
×	OECD 306, 2007; OCCD Gudeline for the Testing of Chenge als – Stability of
- Starten - Star	Pesticide Residues in Stored Commodities
	SANTE/11956/2016 Tev.9 2 2 2
Deviations from current	none y wy wy wy wy
test guideline	
Previous evaluation:	No, not previously submitted
Č Č	
GLP/Officially recognised	Yes conducted under GLB Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	$Yes \sqrt{2} \sqrt{2} \sqrt{2} \sqrt{2}$
	$\frac{\sqrt{2}}{\sqrt{2}} \frac{\sqrt{2}}{\sqrt{2}} $
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
A Î	$\mathcal{F} = \mathcal{F} = $
Report 2	Residue analytical method 01594 and short-term storage stability of
Report of the second se	fluopyram (AP C656948) and its metabolites AE F148815, AE C657188,
	\Rightarrow BCSCAA10789, BCS AA10065 and AE 1344122 in/on honey by HPLC-
le la	[*] M [©] /MS [*] 2020: report No. S10,00000, document No. M 681002
, C	10071015, 10001002 , 2020, report No. 519-00990, document No. 1002002
Ó A	
Guideline Gr.	Yes Q
	Regulation (EC) No 1107/2009
	SANCO/825/00/rev. 8.1, 16/11/2010
	SANCO/3029/99 rev. 4, 11/07/00
and the second	OECD Test Guideline 506, adopted 16 October 2007
Guideline St. J. J. S.	SANTE/11956/2016 rev.9
õ	



Deviations:	No
GLP:	Yes
Acceptability:	Yes

Materials and methods

The storage stability of residues of fluopyram (AE C656948) and its metabolites fluopyram-benzamide. AE F148815, FLU-benzamide), fluopyram-pyridyl-carbox ac-acid (AE C657188, FLU-PCA), fluopyram-pyridyl-acetic-acid (BCS-AA 10139, FLU-PAA), fluopyram-7-hydroxy (BCS-AA10065, FLU-7-OH), fluopyram-methyl-sulfoxide (AE 1344122, FLU-methyl-sulfoxide) was investigated in honey. The conduct of this study was integrated in the analytical method 01594 (M-681003402-2, see section 04) and reported in the same document.

Honey control samples (1 g) were separately fortified with each analyte at 0.1 mg/kg (10 \times COQ) and stored frozen at T \leq -18°C for 1 month (28 days) 3 months (89 days) and 6 months (181 days). Five fortified samples and two control samples were analysed on the day of storage initiation (day zero) Subsequently, three fortified samples per analyte and one control sample, were analysed after storage aceach time point, with two freshly fortified concurrent ecovery samples. Recovery samples were fortified with a mixture of the analytes, each at 0.1 mg/kg.

Samples were analysed using the validated analytical method 01594 (1594 (1681002-02-2, see MCA section 4.1.2). Honey samples were extracted by full dilution with the extraction solvent, shaking with acetonitrile/water (1.1, v/y).

- An aliquot was diluted with water adjusted to pt 8 with ammonia) and analysed for fluopyram, FLU-benzamide, PLU-PAA and FLU-7-OH by HPLC MS/MS in positive ion mode.
- A separate aligned was diluted with 0.5% acetic acid and analysed for FLU-PCA and FLUmethylsulfoxed by UPLC-MS/MS in negative iop mode.

The Limit of Quantification (LOQ) in honey was 0.01 mg/kg for fluopyram and its metabolites, expressed as fluopyram.

The quantification is done against matrix matched standards.

The linearity was demonstrated of each analytical batch with a 1/x weighting calibration curve established with at least 5 concentration levels. Girelation coefficients were above 0.99.

The extracts were analysed within 2 days after extraction. The storage stability of honey final extract was demonstrated in this study for & days at to 10°C in the dark.

Results and discussions

No residues of fluopyram of its metabolites were detected in the honey control samples used for the storage stability study.

In order to assess the accuracy of the residue analyses, recoveries were determined by analysing freshly fortified samples alongside the stored fortified samples. At all storage intervals except for day 0, two concurrent recoveries were determined at a level of 0.10 mg/kg as presented in Table 6.1.2- 36. No additional concurrent recoveries were determined on day 0, since there were five freshly fortified storage samples. The concurrent recoveries meet the acceptability criteria; the mean recoveries are within the range 70 10% for each analyte / matrix combination and the %RSD values are <20% (where applicable). These procedural results demonstrate acceptable method performance and support the analytical results obtained



A CONTRACT ON A CONTRACT OF THE OWNER OW as metabolik as metabolik as metabolik as metabolik as metabolik as a statistic a



Table 6.1.2-37.

- For fluopyram, uncorrected mean recoveries in honey show a stability period of 6 months for deep frozen residues (mean recoveries ranged between 103 % and 110 %).
- For FLU-benzamide, uncorrected mean recoveries in honey show a stability period of 6 months for deep frozen residues (mean recoveries ranged between 89 % - 108 %).
- For FLU-PCA, uncorrected mean recoveries in honey show a stability period of 6 months for deep frozen residues (mean recoveries ranged between 76% - 98%).
- For FLU-PAA, uncorrected mean recoveries in hopey show a stability period of months for dec frozen residues (mean recoveries ranged between 84% - 92%).
- For FLU-70H, uncorrected mean recoveries for honey show a stability period of for nonths for dee frozen residues (mean recoveries ranged between 99 % - 10 %)
- For FLU-methylsulfoxide, uncorrected mean recoveries in honey show a stability period of 6 months for deep frozen residues (mean recoveries ranged between 85% - 100 %),

The data indicate that fluopyram and its metabolites are 6 months when stored frozen at -18°C or below.

Conclusion

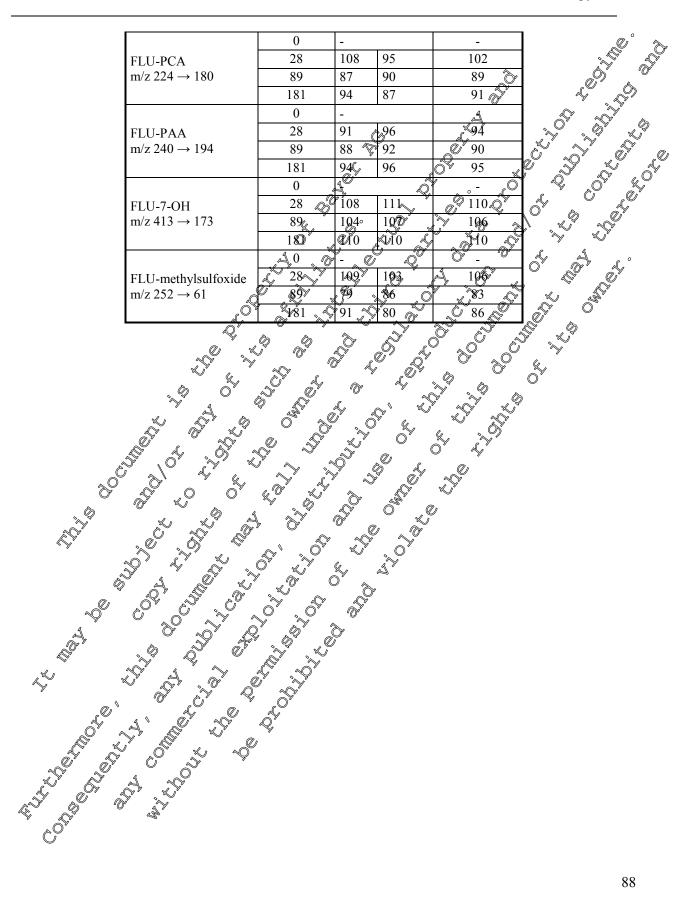
The storage stability study demonstrated that residues of parent fluopyram (AE C656948) and its metabolites fluopyram-benzamide (* F198815 FLU-benzamide), fluopyram-pyridyl-carboxylic-acid (AE C657188, FLU-PCA), fluopyram-pyridyl-acetic-acid (BCS-AA 70132 FLU-PAA), fluopyram-7hydroxy (BCS-AA10065, FLU-FOH) fluopy fm-me oyl-suffixide (AE 1344122, CLU-methyl-sulfoxide) are stable in honey for & months when stored frozen at

Assessment and conclusion by applicant:

The study is acceptable. residues of Garent fluopyram (AEGC656948) and is metholites fluopyram-benzamide (AE F148815, FLUbenzamidey, fluopyram-pyridyl-carboxylio acid (AE C657188, FeU-PCA), fluopyram-pyridyl-acetic-acid (BCS-AA 10139, FLU-PAA (fluop) am-7-hydroxy (BCS A10065, FLU-7-OH), fluopyram-methyl-sulfoxide (AE 1344122, FLU-methyl-sulfoxide) are stable in florely for 6 months when stored frozen at \leq -18°C

Table 6.1.2-00:	Concurrent recoverie	es in honey fo	or Huc	opyram and	its metaboli	
A A		*actual	Conc	urrent Recov	veries [%]	
	Analyte		0.10	mg/kg*		
store and the second se	V A . O	interxal [d]	Sing	le Values	Mean	
		JO ^v 0	-			
Å.	Bluopyra	Q 28	108	112	110	
	$\sum_{n=1}^{\infty} \frac{1}{2} \frac{3}{2} \frac{1}{2} \rightarrow 173$	89	108	111	110	
		181	105	110	108	
	AN	0	-		1775)	
	FLU-benzamide	28	102	106	104	
	$m/z \pm 90 \rightarrow 170$	89	107	104	106	
		181	108	107	108	







Commodity	Fortification level (mg/kg)	Storage period (davs)	stored residue (mg/kg)	Mean stored residue (mg/kg)	stored recovery (%) &	Mean stored vecovery (%)	Mean concerent recovery	Day-0 normalized recovery ^a (%)	Mean corrected stored recovery b
Fluopyram (AE C656948)	((8/8/	.1			TO GAR	A C A C
	0.1	0	0.109, 0.110, 0.105, 0.115, 0.113	0.110	109, *(17, 105, 115, 113	^م 110 ک			Jr FOF
Honey	0.1	28 89	0.109, 0.107, 0.111 0.0996, 0.105, 0.103	0.109	009, 107, 11 100, 005, 103	109 103			99 94
Fluopyram-l	0.1 benzamide (AE	181 F148815)	0.110, 0.108, 0.107	0,108 ***	<u>110</u> , 108, 1075	108	KO <u>× 208</u>	05 98 V	101
r,	0.1	0	0.105, 0.108, 0.112	0,808	105, 108, 112 A. 107, 107	1080	au- mer	V 100 AD	-
Hanna	0.1	28	0.0984, 0.0977,	A 0.0983 S	98,08,99	⁵ 98		ALL BI	94
Honey	0.1	89	0.0880	0.0888	0 90, 87 5	89	106	£ 82	84
	0.1	181	0.0950 0.0100, C	0.0077	93, 100, 98 S			91	91
Fluopyram-j	pyridyl-carboxi	kic-secid (AE	<u></u> .	O'Y COY		<u>e é</u>	<u> </u>		
	0.1	0	0.0889, 0.0779, 209877, 0.0894, 0.0927	00 ⁰ 0873	93 93	ND BF + D	¢ -	100	-
Honey	0.1	28	0.0927, 0.0955	00929	\$93, 96, 96	e e e e e e e e e e e e e e e e e e e	102	106	91
	0.1	89 0	0 0.0732,000758, 00784 0	0.0758	73, 76, 78	76	89	87	85
Flionvram- 1	0.1 ovridy -acetic-a	181 cid (BCS:A	0.@34, 0.100, 9.101 @10189) 20	0.0981	93, 100, 101	98	91	112	108
<u> </u>	0.1	J. V. J. Law	0.0883, 0.0955 0.0916, 0.0918, 0.0942	0.0923	88, 96, 92, 92, 94	92	-	100	-
Honey	0.100	~2 ¹⁸	0.0907, 0.0933	0.0907	91, 93, 88	91	94	98	97
		Real Real Provide Action of the second secon	0.085900.0849, 3 0.0811	0.0840	86, 85, 81	84	90	91	93



								9.J.P.O.	1) ¹ 0
							Ĉ.	0	
	Fortification	Storage	stored residue	Mean stored	stored	Mean stored	Mean concurrent	Bay-0 normalized	Mean corrected stored recovery ^b
Commodity	level	period	(mg/kg)	residue	recovery		recovery (%)_©	recovery a (%)	» stored recovery ^b
	(mg/kg)	(days)	0.0939, 0.0933,	(mg/kg)	(%)	9 94			
	0.1	181	0.0939	0.0937	94, 93, 94		~0 ⁹⁵	L LOC	1 ² . 29
Fluopyram-7	7-hydroxy (BCS	5 AA10065)			4 O ¥	, Q.Q. °		-10 - 10 ¹⁰	
	0.1	0	0.374 ^c , 0.111, 0.109, 0.110, 0.111	0.110	374°, 411, 109,	^{مر} 110 م		, ² , 0 ¹⁹⁰ , C	
Honey	0.1	28	0.114, 0.102, 0.103	0.106	QT4, 102, 103	1196	~Q ^{~1} 14Q~	0° 96 ₂	96
	0.1	89	0.0996, 0.0951, 0.102	0.0989	100,93,102	<u> </u>	106	90	94
	0.1	181	0.100, 0.0994, 0.100	0.0998	100, 99, 100 \$	100	× 110 ~	a 00 🔪	° 91
Fluopyram-1	nethyl-sulfoxid	e (AE 1344	· · · · · · · · · · · · · · · · · · ·	<u> </u>				X AN	e o
	0.1	0	0.0972, 0.0811, 0.102, 0.102, 0.0992	0.0963	97, 8 7, 102,	0- 96 Ju	11000 1000 1000 1110 1000 1000 1000 10	90 5 90 5 100 104 5 33	-
	0.1	28	0.117, 0.091 0.0914	1 0.100 A	117, 92, 91	~ 90 90 0 0	106	1040	94
Honey	0.1	89	0.0808, 0.0850, 0.103	0.0896	81, 83, 103	90 0,5	<u>)</u> 83 č	93	109
Normalized Corrected p Result excl	0.1 d Recovery = (<i>A</i> percent recover uded as an out	181 Average % y = (Agera	0.0920, 0.0845, 0.0855 recover Average age % ecovery Aver	% recovery at rage % of fres	0 92, 85 86 day 0 X 100% h concurrent re	88 00 188 20 188 10 10 10 10 10 10 10 10 10 10	1 86 00 0% 10 10 10 10 10 10 10 10 10 10 10 10 10 1	91 91	103
Normalized Corrected J Result excl	0.1 1 Recovery = (1) percent recover uded as an out $1 \text{ the } 100^{\circ}$	181 Average % y = Aspera	0.102, 0.102, 0.0992 0.117, 0.09 0.0914 0.0808 00850, 0.105 0.0020, 0.0845, 0.0835 recovers Average age % ecovery Average 10 1 C 1 0 C 1		O 92, 85 86 day 09 X 100% h concurrent re b t t i b at a t t t o t t t t t o t t t t t	Coveries X 10		91 91	103



CA 6.1.3 Storage stability in sample extracts

In most of the studies, the time between the beginning of the sample preparation and the sample analysis did not exceed 24 hours. If not the case, the maximum storage period of extractor is covered by stability experiments conducted in the course of the analytical methods validations presented in section CA

- 00984/M003 (M-467323-03-1) for plant materials •
- 01594 (M-681002-02-2) for honey. •

Fluopyram and fluopyram-benzamide were found to be stable in extracts of matrices of plant origin for least four weeks at 4 ± 3 °C which was tested within the validation of method 00984/M069.

For honey samples, the extracts were analysed within 2 days after extraction. The storage stability of honey final extract was demonstrated in this study for 8 days of 1 to 19°C in the days Ś . P

. Õ

Ð.

A.

Data Point:	KCA 4.1.2/25
Report Author:	
Report Year:	
Report Title:	Modification M003 of the residue analytical method 00984 for the determination of
	AE C656948, its metabolite AFT 1488 and tebuconacele in/out orange (fruit),
	wheat (grain) wheat (straw) bean (seed), letwice (head), rape (seed) and hop (dry
	cone) by IPLC-MSMS and a cross validation of the analytical methods 00984 and
	009984/M903 ~~ ~~ ~~ ~~ ~~ ~~
Report No:	009844M003
Document No:	<u>M-467323-03-1</u>
Guideline(s) followed	Regulation (EC) No 1107 2009 of the European Parliament and of the Council of 21
study:	October 2009 concerning the placing of plant protection products on the market and repeating Council Directives 39/117/GEC and 91/41/GEC
	repeating Council Directives 79/117/19EC and 91/41/4EEC
ð d	
l lo	Buropean Commission Gaidance Document for Generating and Reporting Methods of Analysis in Support of Pre-Registration data Requirements for Annex II (part A,
	of Analysis in Support of Pre-Registration data Requirements for Annex II (part A,
	Section 4) and Annex III (part A, section 5) of directive 91/414, SANCO/3029/99
	r_{2} , $4, 11/07/00$, 3 , 0 , 3 , 0 , 0 , $1/07/00$, 3 , 0 , 0 , 0 , 0 , 0 , 0 , 0 , 0
Q A	Guidabce document corresiduo analytical methods, SANCO/825/00/rev. 8.1,
Q OY	European Commission, Directorate General Health and Consumer Protection
4	USEDA Partica Charietry Part Guideline OCSPB 860 1340: Pesidue Analytical
	European Commission, Directorate General Health and Consumer Protection 16/11/2010 US EPA Residue Chemistry Øest Guideline OCSPP 860.1340: Residue Analytical Method
Deviations from current	
test guideline:	
Previous evaluation:	
GLP/Officially recognised	Stes, conducted under GLP/Officially recognised testing facilities
testing taguities. \sim	φ
Acceptability/Rehability.	
× × A	
Acceptability/Renability.	
⊳O×	
\bigcirc	

0 P



This residue analytical method is fully summarized in section MCA 4.1.2 but additionally the part dealing with the stability of residues in sample extracts is presented here.

The stability of residues of fluopyram and fluopyram-benzamide in plant final extracts was checked for the tested sample materials over a period of 4 weeks. The following tables show the recoveries comparing initial day of analysis and analysis after storage of the final samples at 4 ± 3 °C under dark conditions over the given periods.

All analytes were found to be stable in plant final extracts for at least 4 weeks (with the exception of Rop cone dried).

In hops extracts, the results show that fluopyram-benzamide were stable after 4 weeks. Only the results for fluopyram show a deviation of 24% compared to the Day 0 values. It is suggested to analyse samples of hops within 24h after extraction and so will be recommended using modification M009 of method 00984.

			\sim	"¥ .		.»	a.y	A.	
Sample Material	FL* [mg/kg]			Recove	ery Ra	~0~		Mean	Mean deviation [%] **
Lettuce head	0.10 🐇	initial analysis 4 week reanalysis	۶ ک 96	چ 98 97	\$95 94 ¢	96 ≥93)94 92		n.a. 1%
Orange fruit	0.1°×	initial analysis	90 %88%	90´ _©91	89, ⁷ 793	91 91	88 88	90 90	n.a. 1%
Wheat grain	9 .10	ipital analysis 4 week reanalysis	87 89	0 [°] 95 % ≫ 920	/ 94 95	96 96	⊘9́3 ⊁92	93 93	n.a. 0%
Wheat Straw	0.10	☆ initial analysis	84 89	87	89 %89 ~	88 [°] 89	88 89	87 89	n.a. 2%
Rape seed	0.10 √0	ioitial analysis 🗸 🖌	ж о	, ⊂ 92 Ø	90 ~ 92	َ ⁷ 92 91	92 91	92 91	n.a. 0%
Bean dro seed	000	≪ initiat)analysis ∕4 week reanalysis⊜	093 94		×95 95	93 96	95 94	94 94	n.a. 0%
Hop oppo dried	2 0 10 V	, initial malysis	63 (75	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	69 (81ª)	64 (76ª)	66 (78ª)	66	n.a.
Hop cone dried		4 week reanalysis initial analysis 4 week reanalysis	^ງ ໌ 87 (120	⊘ 64	`88´ (121 ª)	`89´ (122 ª)	`80 ́)(113 ª)	82	24% (46%)

Table 6.1.3- 1:	Storage of fluopyra	môm plant ext	ræts (Mass	Transition 397	′ > 208) 🧹

FL = Fortification Level

а

b

Mean deviation [%] between initial analysis and days of reanalysis. For the calculation of the mean deviation as it appears if the table above, unrounded values were used. Therefore, minor deviations may occur between the mean deviation shown above and when the values given for the mean values is the table arguised for calculation.

Values before correction. The control sample used yielded residue levels of more than 30% (0.0030 mg/kg) of the LOO and therefore the recovery was background-corrected for this signal Therecovery values are deviating by 24% compared to the day 0 values, therefore it is suggested to analyse samples of hops within 24h after extraction.



Sample Material	FL* [mg/kg]		R	ecov	very Rat	es [%	ĴÔ,	Mean 《	Mean deviation
Lettuce head	0.10	initial analysis 4 week reanalysis	97 92	97 91	96 96	94	98 91	96 93	₩.a. 3%
Orange fruit	0.10	initial analysis 4 week reanalysis	96 98	96 92	97 () 960,	97 94	95 × 91	ປ໌96 9¢Q	n.a. 2%
Wheat grain	0.10	4 week reanalysis	Ø85 95	96 102	~95 ~94	94 ∘97	94 2,99	93 97	€n.a. € 5%
Wheat straw	0.10	initial analysis	92 101	90 95	98	93 ⁽	99	98	n~a. ∼√%
Rape seed	0.10	initial analyse	93	94 910	×89 95 0	93 90	~90 88 ~	91 91	[∞] n.a. 0%
Bean dry seed	0.10	initial analysis 🗡 4 week manalysis	98 ⊘95_√	,93 ,98	93 95	96 92	94 \$%	94 95	€. 1%
lop cone dried	0.10	initiat analysis 4 week readalysis	93 95	82 × 830	ັ 95 ຊູສັງ	92 93	0 ⁹ 91 92	91 (94	n.a. 3%

Table 6.1.3- 2: Stability of fluopyram-benzamide in plant extracts (Mass Transition 190 > 170)

Fortification Level

the states with the state of the states of t Mean deviation [%] between initial analysis and days Preandysis. For the calculation of the ** mean deviation as it appears in the table above, unrounder values were used. Therefore, minor deviations may occur between the the an deviation shown above and when the values given for



Data Point:	KCA 6.1/13
Report Author:	
Report Year:	
Report Title:	Determination of the standard stability for prothioconazole, 1900 6476-desthio,
	fluopyram, fluopyram-benzamide, JAU 6476-alpha-hydroxy-desthio, JAU 6476-3-
	hydroxy-desthio, JAU 6476-4-hydroxy-desthio, JAU 6476-5-hydroxy-desthio, 🕸 🛛 👔
	6476-6-hydroxy-desthio, 1,2,4-triazole triazole alanine, triazole acetic acid and
	triazole lactic acid
Report No:	P602176032
Document No:	<u>M-654837-01-1</u>
Guideline(s) followed in	European Commission Guidance Document for Generating and Reporting Methods
study:	of Analysis inSupport of Pro-Registration data Reguirements for Annex II spart A
	Section 4) and Annex IIK(part A@section \$) of directive 99/414 \$ANCO 3029/99
	Guidance document on residue analytical methods; SANCO/\$25/00 rev. 8.1,
	European Commission, Directorate General Dealth and Consumer Protection, 2010, •
	$11-16 \qquad \qquad$
	US EPA Residue Chemistry Test Guideline OS PP 869.1340 Residue Analytical Method
	Guideline OC\$PP 860.1340 Residue Analytical Method
	OECD (2607). Gundance Document on Resticide Residue Snalytical Methods,
	Enviroment No. 72 and Series on Pesticides No. 39 0 5 5
Deviations from current	none $\begin{pmatrix} & & & & & & \\ & & & & & & & \\ & & & & $
test guideline:	
Previous evaluation:	No, not previously Cubmitted
	Study was not found in DAR/RAR and the Addenda
GLP/Officially recognised	Yes, conducted under OLP/Officially recognised testing facilities
testing facilities:	$\frac{Y \text{ es}}{\sqrt{y}} = \frac{y}{\sqrt{y}} = \frac{y}{\sqrt{y}$
Acceptability/Reliability:	Yes a grad a g

The stability of fluopyram (AE C656948), fluopyramobenzamide (AE C656948-benzamide), and other compoutes in standard solutions was analyzed over a storage period of 184 to 404 days. For sake of clarity only the results concerning fluopyram and duopyram ben zamide are reported here.

Table 6.1.3- 3: Stability in standard solution

active substan	nce	investigated storage period at < 6 °C [days]	devation [%]
fluopyram	fluop@am	205	3.9
	Wuopyam-benzamide	205	4.3

deviation [%] = 100_{\odot} ((courts per µg/L)_{aged} / (coupe per µg/L)_{aged} x100) Different secondary standard solutions were stored for 184 to 404 days at T< 6 °C until analysis. The standards were difuted and analyzed by HPLC-MS/MS for fluopyram and fluopyram-benzamide (transitions m/z \$97>208 for FLU and 190>170 for FLU-benzamide). The standards solutions were found to be stable for the investigated storage period.

For the determination of the standard stability, primary standard solutions at 500 mg/L in acetonitrile were difuted and secondary standard solutions in acetonitrile/water (1/9) were generated. Internal standard was adde to the secondary standard solutions, as this is the general procedure for the analysis in the laboratory.



Since the internal standard is not part of the analysis of the standard stability in this study and the result of f the internal standards were not reported, information regarding the internal standard solutions is not given in this report.

The secondary standard solutions were stored at < 6 °C for 184 to 404 days. For the determination of standard stability the aged secondary standards were compared to freshly prepared secondary standards diluted from fresh primary standards.

		22		Ĩ Qı ^v .
Analyte	date of prepara-tion	storage time [days]	tourian Otocon Or Contest [%] analyte	Çounts per µg/L
	2017-06-26	205	1161107 1141698 1221849 1161107 1141698 1221849 1141658 1140029 1120941 1259884 9202839 1097841 1259884 9202839 1097841 1259884 9202839 1097841 1259884 9202839 1097841 1259884 9202839 1097841 1259884 9202839 1097841 11499109 6.0 10.000 1135793 1284982 1135793	A15395
fluopyram	2018-01-17	205	1259884 \$202839 1097841 1199109 6.0 10000 1289982 1135793 5 6.0 10000	119911
		*		3.9
	2017-06-26	\$ \$ \$ 205 0	221488 21942 218482 4.7716 221023 219562 22505	46294
fluopyram- benzamide	2018-01-15	Kn [*]	236044 234430 223066 230205 2.8 4.7691 226914 237235 223640 4.7691	48270
		\$* <u>,</u> 0	O «deviation» /%]	4.3
deviation [r µgµ = mean 20 = 100 - ((co dard solution	punts per u	nd to be soble for the investigated storage period.	
The stud Standard	ent and concl y is acceptable prolutions are	usion by a	pplicant:	
- A	J ^y	S.		

Table 6.1.3- 4: Stability of fluopyram and fluopyram ben	zamide in standard solution	d
--	-----------------------------	---

tabolism, distribution and expression of residues CA 6.2 Metabolism, distribution and expression of residues in plants

Data to address this point were presented in the dossier submitted for first inclusion in Annex and were deemed acceptable following evaluation and peer review at EU level (2013).



Additionally metabolism studies using [phenyl-UL-¹⁴C]- and [2,6-pyridinyl-¹⁴C]-labelled fluopyram were conducted in seed treatment (wheat) and rice.

For details of data submitted previously please refer also to the Baseline dossier CA. 9.2. For completeness a summary of these previously submitted studies are included below.

Data already evaluated during the first EU review process for inclusion on Annex studies)

Metabolism in grape (foliar spray application)

	KCA 62 1/01 A & U O O O A A
Data Point:	KCA 6.2.1/01
Report Author:	
Report Year:	
Report Title:	Metabolism @pherky UL14 AE 655694 % grapes after @ray appricatio@ MEF-06/08
Report No:	MEF-06/08
Document No:	M-282177201-16 6 2 N ~ V N
Guideline(s) followed in	US ER OPPLY 860.1900; C Sadian MRA SACO S; EU S1/414/EEC amended
study:	
Deviations from current	
test guideline:	
Previous evaluation:	ves avaluated and agented and a start with the start of t
	revoi to VSV.3 of DAR B7 sugust \$012 (references relied of)
GLP/Officially recognised testing facilities: Acceptability/Re@bility@	Les, condicted order GD/Officially recognise Desting facilities
testing facilities:	
Acceptability/Redibility	Yes & A A S O S
, ^O	Yes & Y X X X
Executive Summary 🖒	

The metabolism of [phenyl-UL C]fluopyrame form@ated_as a SC 500 (Suspension Concentrate), was investigated in grape vines following three foliar spray applications corresponding to a total application rate of 500 g a.s. And. The applications were performed at growth stages BBCH 17, 71 and 81. Approximately 100 g a.s./ha were applied for the first reatment, 200 g a.s./ha for the second, and again 200 g a.s./ha for the last application.

Leaves of the summer cut (BBCH 71) were analysed as an intermediate sample on the same day of the second application. Furthermore, grape and leaves were harvested at maturity of grape berries with a preharvest interval (PHI) of 18 and 19 days, respectively.

The TRR of the chible RAC (grapes) was 1.86 mg eq/kg and was considerably lower than those of summer cut leaves and reaves at harvest (28.55 mg eq/kg and 48.06 mg eq/kg, respectively). The major amount of radioactivity 93.9, 98.1% of the TRR) was effectively extracted with acetonitrile/water from all RACs leaving only minor amounts < 6.1% remaining in the solids (PES). Parent compound and metabolites in the extracts were quantified by HPLC.



A total of 98.2% (28.03 mg eq/kg) of the TRR was identified in summer cut leaves, 98.7% (1.83 mg eq/kg) of the TRR) in grapes, and 93.9% (45.10 mg eq/kg) in the leaves at harvest. The unchanged fluopyram was the major compound (>90% TRR) detected in all matrices. Apart from parent, the residues consisted of fluopyram-benzamide (M25) and fluopyram 7-hydroxy in grape (both @ <.1% TRR). In the leaves at harvest, the 7- and 8-hydroxy metabolites, and the glucoside conjugate of the 7-hydroxy were also detected (all <1% TRR). The metabolic reactions involved: 8 Frydrox metabolites Hydroxylation of the ethyl linking group of the a.s. forming Conjugation of the fluopyram-7-hydroxy with glucose • Hydrolytic cleavage and a subsequent oxidation read to Huopyrum-benzamide br. aterials and Met A. Materials 1. Test Material: Chemical structure position of the Ô radiolabel Compound AE C656948 N- \$2-[3-efforo-5-(rrifluoromethyl)pyridin-2-yl]ethyl}-2-IUPAC^mame Trifluoromethyl)benzamide Benzomide, @-[2-[3-chloro-5-(trifluoromethyl)-2-CAS name pyridinyl]ethyl]-2 @rifluoromethyl)-(9Cl) @\$8066-@\$-4 CAS # Ø Phen@-UL-1% Radiolabel position Specific radioactivity 3.85 MBα (104.2 μCi/mg) Purity 99% (HALC) > 992% (TLC)

2. Soil: "Monheim 2" (sandy loam from Germany), pH (CaCl₂) = 6.4, 60.0% sand, 28.2% silt and 11.8% clay, k_{2} % organic carbon, carbon exchange capacity (CEC) of 10 meq/100 g

99% (HPLC)

3. Plant, Grapevine (*Vilis vinifera*), variety: "Mueller Thurgau"

Chemical Purity



B. Study Design

1. Experimental conditions:

The grapevine plant was grown in the vegetation area (building 6682) of Bayer CropScience AG, Metabolism / Environmental Fate, Monheim, Germany, which allows plant growth under natural sanlight and temperatures, with a glass roof that can automatically close at the beginning of a rainfall. The plant was cultivated in a 35 L bucket with a surface area of 0.125 m², filled with a sandy loam soft. The plants were sprayed with [phenyl-UL-¹⁴C]fluopyram formulated as a SC 500 (Suspension concentrate) and the spraying was performed using a graphic spray pistol.

The metabolism study simulated the envisaged use pattern and was based on a targeted application rate of 500 g a.s./ha as three sprayings. To compensate losses during applications, up to 20% excess of a.s. was applied. Three applications were performed at growth stage BBCH 17–19 BBCH 71 and BBCH 81, at application rates of approximately 100 g a.s./ha and 200 g a.s./ha and 200 g a.s./ha fespectively. This resulted in a total application rate of about 504 g a 6/ha after subtraction of the bases in the rinkes. The time interval between the first and the second application was 42 days and 49 days between the second and third application.

2. Sampling

Summer cut: Directly after drying of the spray of the second application at growth stage fruit set (BBCH 71), the grapevine plant was pruned according to agricultural practice. The teaves and stalks of this summer prune were cut into small pieces, and were homogenised with liquid nitrogen using an Ultra-Turrax homogeniser. The complete homogenised plant material was used for extraction.

<u>Grapes:</u> At maturity β BCH code 89 and β MI of β S days) whole bunches of grapes were cut from vines, and the single grapes were cut from the stems. A representative aliquot of the grapes was surface washed and used for extraction. The remaining grapes were stored in aliquot at *ca.* -20°C.

Leaves at harvests One day after the grapes had been sampled the leaves (at BBCH 89, PHI of 19 days) were cut from the vines. A topresentative aliquot of these leaves was cut into small pieces, and was homogenised with liquid ninogen using an Oltra-Durrax homogeniser and was used for extraction. The rest of the leaves were stored at *ca.* 20°C.

C. Analytical Procedures

The grape RAGs were extracted and the extracts were analysed by reversed phase HPLC and TLC. The identification of parent compound and metabolites was based on co-chromatography experiments.

1. Extraction

In general, Camples of the grape RACs were extracted 3 times with a mixture of acetonitrile/water (8/2, v/v) using an officer Turrax. The extracts were separated from the solids by centrifugation. The radioactivity of



the extracts was determined by volume measurement and LSC. The solids (PES) were air-dried, homogenised and weighed. Aliquots thereof were combusted and measured for radioactivity by LSC.

Grape berries were additionally surface washed prior to homogenization. After extraction, due to high sugar content, a phase separation acetonitrile : water occurred. Hence, the phases forganic and aqueous sugar phase) were separated using a separation funnel resulting in the combined acetonitrile phases and the combined water phases after all three extraction steps. Prior to HPLC analysis, an alique of the combined acetonitrile phases was concentrated using a rotary evaporator.

The ¹⁴C-radioactivity of liquid samples was determined ^oby liquid scintillation counting (LSC) osing Quicksafe A containing 5% of water. The radioactivity is solid samples was measured by combustion. The released ¹⁴CO₂ was absorbed in an alkaline scintillation cockail and radio assayed by LSC.

The total radioactive residues (TRR) on the RACs of grapes were determined by submation of the radioactivity in the combined acetonitrile/water extracts and in the PES. The residue levels are expressed as parent compound equivalents per weight. The combined extracts were analysed by HPLC for quantification of metabolites.

2. Identification and characterisation:

Identification of metabolites was done by co-chromatography using HPLC and TLC methods. Each metabolite was co-chromatographed either with its authentic reference compound and/or radiolabelled metabolites, which were obtained in the plant study applying byridyt-2,6-14©]fluopyram to beans.

3. Storage stability:

The RACs were extracted and analysed within a few days after sampling. All samples were stored at temperatures ≤ -18 C. A few days after extraction, the earliest metabolite profiles of the combined extracts were obtained using a preliminary HPLC method until the final profiling method for the use in all plant metabolism studies was available. The extracts were analysed again using HPLC approximately eight to ten months after the initial analysis. The profiles from the initial and the late analysis showed no significant differences in the compound pattern. Therefore, it was concluded that the results of this study were not negatively influenced by storage effects.

Q. Results and Discussion

The metabolism of pheny UL-¹⁴C]fluogyram, formulated as a SC 500, was investigated in grape following three foliar applications at application rates of approximately 100 g a.s./ha, 200 g a.s./ha and 200 g a.s./ha, respectively.



nyram and the second se The TRR amounted to 28.55 mg eq/kg in summer cut leaves, 1.86 mg eq/kg in grapes and 48.06 mg eq/kg in leaves at harvest (Table 6.2.1-1). The TRR of the edible RAC (grapes) was significantly lower than those of the leaves cut in summer or at harvest.

	A
Table 6.2.1-1:	TRR values in grape matrices after application of [phenyl-JL- ¹⁴ C]fluopyram

Matrix	Timing and Applic. No.	PHI (days)	TRR (pom, mg a.s. equiv./kg)	
Summer cut	Two applications:	N		, O S
leaves	at growth stages BBCH 17-19 and 71		28.55	8
	1 x 100 g a.s./ha and 1 x 200 g a.s./ha	a di		
Grapes	Three applications:	V X		
	at growth stages BBCH 17-19, 71 and 8			0
	$1 \ge 100$ g a.s./ha and $2 \ge 200$ g a.s./ha,			1
	total 504 g/ha	Ň, Ň		
Leaves at	Three applications:			
harvest	at growth stages BBCF97-19 71 and 81			
	1 x 100 g a.s./ha and 2 x 200 g a.s./ha,		1 5 5 48.06 5 V	
	total 504 g/ha			
	× × ~			
		v» _0		

Nearly the complete adioactive residues in summer cut baves 98.2% (28.03 mg eq/kg) of the TRR, was extracted by acetomitric vater (The grape matrices were extracted with accountrife water $(8/2; \sqrt{v})$, the extracts were analysed by HPLC



A CONTRACT ON A CONTRACT OF THE OWNER OWNER OF THE OWNER Table 6.2.1-2), whereas 1.8% (0.52 mg eq/kg) of the TRR remained in the solids (PES). For grapes, 800% (1.49 mg eq/kg) of the TRR, was found in the surface wash, while 18.6% (0.34 mg eq/kg) of the TRR, was extracted by accontrile/water (



en and a second an A star water and a star water a star and a star water a star and a star and a star and a star and a star a



A Second and a second and a second a se Table 6.2.1-2), whereas 6.1% (2.96 mg eq/kg) of the TRR remained in the solids (PES). Due to the low radioactive residue, the solids (PES) from all matrices were not further investigated.



Table 6.2.1-2:	Distribution of radioactivity in the extracts of the grape matrices after	application	^
	Distribution of radioactivity in the extracts of the grape matrices after [phenyl-UL- ¹⁴ C]fluopyram	. S	

	, ,,					A S
	Sumn	ner cut	Gra	apes	Leaves at har	est 🖒
TRR [mg eq/kg] =	28	.55	1.	86 .1	48,06	
	% of TRR	mg eq/kg	% of TRR	mg eq/kg	% of TRR mg.e	a/kg
Surface wash	n.a.	n.a.	80.0	Q1.49	H.a.	<u>n</u> @.
Acetonitrile/water extract	98.2	28.03	18.6	0.34	93.9	∂\$5.10 \$ ^O [™]
Solids (PES)	1.8	0.52	y∛ 1.4∾	0.03		2.96
Total extracted	98.2	28:03	\$° 989	1.83	∂°93.9	A\$.10
Accountability	100.0	28.55		D 86	0 ⁵ 1000 A	48.05 _°
n.a. not applicable			\sim \sim	× A ć		<u></u>

For the elucidation of metabolites, the solvent extracts (acetonit the water) were analysed by MPLC or by TLC with radiodetection. Metabolites were either identified by co-chiomatography (HPLC, TLC) with authentic reference compounds of with metabolites is pated and identified from beaps.

O

Summer cut: In the extracts of summer cut leaves, only parent compound 198.2% of the TRR, 28.03 mg eq/kg) was detected frable 62.1-3).

<u>Grapes:</u> In the surface wash of grapes, only parent compound (80.0% of the TRR, 1.49 mg eq/kg) was detected. Due to the viscosity (high sugar content), the acconitrile water extracts separated into two phases: The acetonitrile phase of the grapes (18.2% of the TRR, 0.32 mg eq/kg), contained parent compound (contributing to 17.3% of the TRR, 0.32 mg eq/kg). Hence, other than parent, metabolites detected in grapes were very minor. fluopyram benzamide amounted to 0.7% (0.012 mg eq/kg) of the TRR. In addition, fluopyram-7-hydroxy (0.3% of the VRR, 6005 mg eq/kg) was detected (Table 6.2.1-3).

The aqueous phase contained only 0.4% (0.01 rig eq/kg) of the TRR in total, and again fluopyram was the major compound (0.3% 0.008 mg eq/kg of the TRR). Overall, parent compound accounted for 97.6% (1.82 mg eq/kg) of the TRR in gapes (Table 6% 1-3). A very polar minor metabolite (0.1%, 0.002 mg eq/kg of the TRR) remained unassigned, but was characterised by its extraction and chromatographic behaviour.

<u>Leaves at harvest</u>: In the expracts of leaves at harvest, parent compound (91.8% of the TRR, 44.11 mg eq/kg) was again detected as the predominant part of the residues (.

Table 6.24-3). A mino metabolite in the extracts of leaves was the fluopyram-7-hydroxy-glc (0.7%, 0.35 mg eq/kg of the TRR) Furthermore, the metabolites fluopyram-7-hydroxy (0.7% of the TRR, 0.35 mg eq/kg) and fluopyram-8-hydroxy (0.6% of the TRR, 0.28 mg eq/kg) were identified.



Table 6.2.1-3:	Summary of characterisation and identification of radioactive residues in grape	matrices°	~
	after spray application of [phenyl-UL- ¹⁴ C]fluopyram		Ô

	-		~		Ś.		- Or
	Summ	ner cut	Gra	apes	Leaves a	t harvest	5
TRR $[mg eq/kg] =$	28	.55	1.	86	V 48	.06 🔧 🐧	,)
Compound	% of the TRR	mg eq/kg	% of the	mg eq/kg	% of the TRR [%]	Ong eq/kg	Ŝ
AE C656948, a.s., fluopyram	98.2	28.03	1 97.6	1.82	91.8	444,11	
fluopyram-8-hydroxy (M18)	-		· -	<u> </u>	0.6		_ ~
fluopyram-7-hydroxy (M08)	-	- 40	0.3	0.01 کې ا	\$7	Q 0.35	
fluopyram-7-hydroxy-glc (M11)	-		-	°⊗- ~	L0.7	0.35	Ŭ
fluopyram-benzamide (M25)	-	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.7 🥎		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u>a</u> - av	1
Total identified	98.2	\$ 8.03 <i>(</i>	° 98,6	× 1.83 . C	r 93.8	×45.09	
Unknown 1 (GR0)	-	0'@	ØN	~~~ 0.0	Ċ,	∽ <u>-</u> ∾	
Total characterised	- *	~	. 0.1 .	0.01	· ~		0
Solids (non-extractable residue)	1.8	Q.32 ~	<u> </u>	A .03	§ 6.1	\$.96 Ø	
Accountability	1000	_^°¥8.55_©	100,0	×1.86 ×	109.0	48.05	
	R (

, of III. Concluctions

After foliar spray application of *ca*. 500 g/ha [phenol²UL¹⁴O]fluopyram, most of the recovered radioactivity was detected in leaves at harvest (48.06 mg eq. kg) and summer cut leaves (28.55 mg eq/kg), whereas significantly less residues were detected in grapes (186 mg O/kg).

The radioactivity was easily extracted (minimum 393% of the TRR) and identification of metabolites was performed by co-chromatography using HPLC and TLO methods.

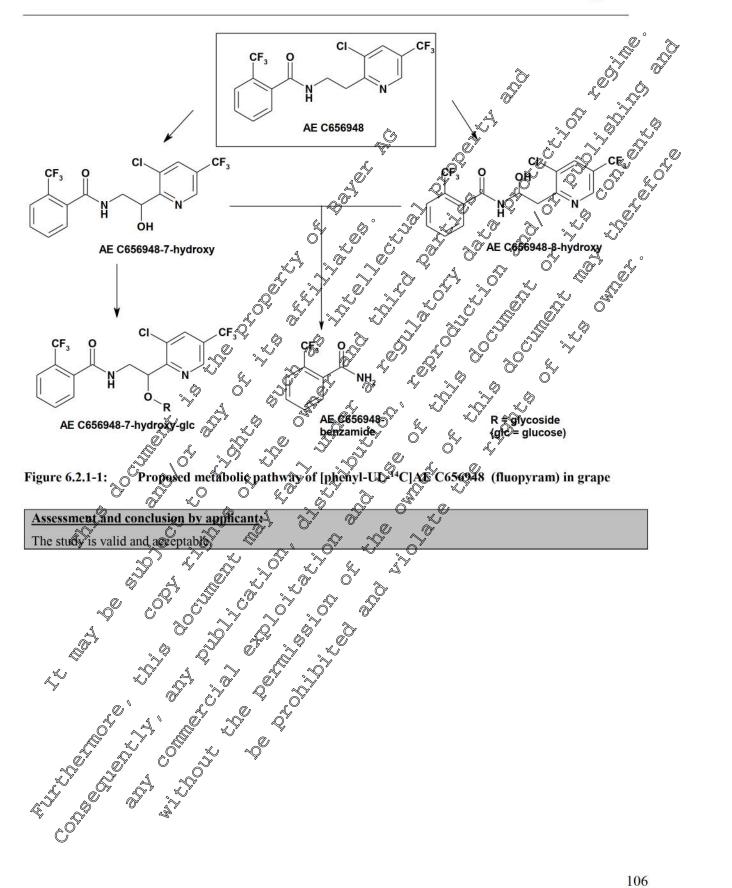
Unchanged patent compound was the predationant portion of the TRR in all matrices, accounting for more than 90% of the TRR Metabelism of fluopyram was rather limited in grapevine and none of the metabolites was detected in portions higher than 1.0% of the TRR. The label spectric compound fluopyram-benzamide was detected in grapes only, and amounted to 0.7% of the TRR. Turther metabolic reactions involved in the degradation of fluopyram were the hydroxylations of parent compound forming the fluopyram-7-hydroxy and 8-hydroxy. The latter as well as the glucovide conjugate of fluopyram-7-hydroxy were only detected in leaves.

Hence major metabolic reaction involved in the degradation of fluopyram were:

- Hydroxylation of the ethyllinking group of the a.s. forming 7- or 8- hydroxy metabolites
- Conjugation of the flugpyram-7-hydroxy with glucose
- Hydrolytic cleavage and ox dation Deading to fluopyram-benzamide

From the results of this study, the metabolic pathway of [phenyl-UL- 14 C]fluopyram in grapevines is proposed in Figure 6.2.1-k







Metabolism studies in grap	pe were conducted with [pyridyl-2,6- ¹⁴ C] fluopyram:
	pe were conducted with [pyridyl-2,6- ¹⁴ C] fluopyram:
Data Point:	KCA 6.2.1/02
Report Author:	
Report Year:	2006
Report Title:	Metabolism of [pyridyl-2,6-14C]AE C656948 in other spra application 0
Report No:	MEF-06/086
Document No:	2006 Metabolism of [pyridyl-2,6-14C]AE C656948 in ones after spra Capplication MEF-06/086 M-282460-01-1 US EPA OPPTS 860.1300; Cinadian PMRA DACC 3.3; ELO 1/41; EEC amended by 96/68/EC
Guideline(s) followed in	US EPA OPPTS 860.1300 Ginadian PMRA DACG 3.3; El 91/414 EEC amended
study:	by 96/68/EC
Deviations from current	
test guideline:	
Previous evaluation:	ves evaluated and accepted a very second and accepted and
	rev. 1 to Vol.3 of DAR B August 2012 of ferences relie on the second sec
GLP/Officially recognised	Yes, conducted under GLP/Orbitally recognis Of testing facilities
testing facilities:	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
Acceptability/Reliability:	Yes Q ^y Y Y Y Y Y
	$\frac{Y \text{ es}}{Y \text{ es}} \begin{pmatrix} y & y & y & y & y \\ y & y & y & y & y \\ y & y &$
, C	Executive Summary &
	The security summary of the security summary of the security summary of the security

The metabolism of [pyridyl-2,6¹⁴C]fluopyram, formulated as a SC 500 (Suspension Concentrate), was investigated in grape ones following three foliar spray applications. The applications were performed at growth stages BBCH 17, 71 and 81. Approximately 100 g a S ha were applied for the first treatment, 200 g a.s. ha for the second, and again 200 g a.s. ha for the last application and the total application rate was approximately 500 g a.s./ba

Leaves of the summer cut (BBCIA 71) were analysed as an intermediate sample on the same day of the second application. Grapes and leaves were barvested at maturity with a pre-harvest interval (PHI) of 18 and 19 days, respectively.

The TRR of the edible RAC (grapes) was 1.70 mg eq.kg and was considerably lower than those of summer cut leaves and leaves at harvest (64,18 mg eq/kg and 42.66 mg eq/kg, respectively). The major amount of radioactivity (94.7–97.9% of the TRR) was effectively extracted with acetonitrile/water from all RACs leaving only minor amounts < 60% with the olids (PES). Parent compound and metabolites in the extracts were quantified by HPLC.

Parent compound and metabolites in the extracts were quantified by radio-HPLC. A total of 97.0% of the TRR was dentified in grapes and 94.7% in leaves.

The inchanged fluopyram was the major compound detected in all extracts, comprising more than 95% of the TRR in both minner cut leaves and grapes, and approximately 91% of the TRR in leaves at harvest. Apart from parent, the residues consisted of fluopyram-pyridyl-carboxylic acid (PCA, M43), the 7- and 8-hydroxy metabolites, and the conjugate 7-hydroxy-glucoside. A total of 96.7% (62.05 mg eq/kg) of the



TRR was identified in summer cut leaves, 97.0% (1.65 mg eq/kg of the TRR) in grapes, and 94.7% (40.43 mg eq/kg) in the leaves at harvest.
On the basis of the nature and amount of metabolites found in the extracts of grapes and leaves the metabolic pathway of [pyridyl-2,6-14C]fluopyram in grapes was proposed and consisted of O Hydroxylation of the ethyl linking group of the a.s. forbing 7- or 8- hydroxyl metabolites (Conjugation of the AE C656948-7-hydroxy with glucose) • Hydrolytic cleavage and oxidation lead to fluopyram-pyridyl-carboxylic acid (Conjugation of the AE C656948-7-hydroxy with glucose) • Hydrolytic cleavage and oxidation lead to fluopyram-pyridyl-carboxylic acid (Conjugation of the AE C656948-7-hydroxy with glucose) • Hydrolytic cleavage and oxidation lead to fluopyram-pyridyl-carboxylic acid (Conjugation of the AE C656948-7-hydroxy with glucose) • Hydrolytic cleavage and oxidation lead to fluopyram-pyridyl-carboxylic acid (Conjugation of the AE C656948-7-hydroxy with glucose) • Hydrolytic cleavage and oxidation lead to fluopyram-pyridyl-carboxylic acid (Conjugation of the AE C656948-7-hydroxy) (Co
A. Materials
1. Test Material:
$\begin{array}{ c c c c c c c c c c c c c c c c c c c$
A. Materials 1. Test Material: Chemical structure CF O CF O
N # N &
$\langle Q \rangle = \langle Q $
A A A A A A A A A A A A A A A A A A A
Compound AEC656848 O' & S
IUPAC name
CAS name CAS na name CAS name CAS name CAS name CAS name CAS name
CAS # 2 4 658066-35-4
Radio abel position Pyridyl-26-14C
Specific radioactivity 3.85 MBq/mg (104.2 Ci/mg)
Purity $2 = 28\%$ (HPCC)
$\mathcal{O}_{\mathcal{A}}$ $\mathcal{O}_{\mathcal{A}}$ $\mathcal{O}_{\mathcal{A}}$ $\mathcal{O}_{\mathcal{A}}$ $\mathcal{O}_{\mathcal{A}}$ $\mathcal{O}_{\mathcal{A}}$ $\mathcal{O}_{\mathcal{A}}$
Chemical Parity C S S C PIPLCS
2 C C C C C C C C C C

2. Soil: Monheim 22 (sandy loam from Germany), pH (CaCl₂) = 6.4, 60.0% sand, 28.2% silt and 11.8% clay, 1.3% organic earbor cation exchange capacity (CEC) of 10 meq/100 g

3. Plant: Gropevine (*Vitis Onifera*), variety? "Mueller Thurgau"



B. Study Design

1. Experimental conditions:

The grapevine plant was grown in the vegetation area (building 6682) of Bayer CropScience A@ Metabolism / Environmental Fate, Monheim, Germany, which allowes plant growth under natural survert and temperatures, with a glass roof that can automatically close at the beginning of rainfall. The plant was cultivated in a 35 L bucket with a surface area of 0.125 m² filed with a sandy loam soil. The phant was sprayed with [pyridyl-2,6-14C] fluopyram formulated as a SC 300 (Suspension Concentrate) using a graphic spray pistol.

The metabolism study simulated the envisaged use pattern and was based on a targeted application rate 500 g a.s./ha as three sprayings. To compensate losses during applications, up to 20% excess of a.s. was applied. Three applications were performed at growth stage BPCH 17-19, BBCH 27 and BBCH 31, at actual application rates of approximately 100 g a.s./ha/200 g a.s./ha/and 200 g a.s/ha, respectively. This resulted in a total application rate of 498 gas. /ha after subtraction of the losses in the rinses. The three 2. Sampling

Summer cut leaves: Directly after drying of the spray of the second application at growth stage fruit set (BBCH 71), the grapevine plant was prune Daccording to agricultural practice. The leaves and stalks of this summer prune were cut into small pieces, and were homogenised with liquid thronogen using an Ultra-Turrax homogeniser. The complete homogenised plant matchal was used for extraction.

Grapes: At maturity (BBCH code 89 and PH) of 18 days), whole bunches of grapes were cut from vines, and the single grapes were cuo from the steries. A representative abquot of the grapes was surface washed and used for extraction. The remaining grapes were stored in allouots acca. -20°C.

Leaves at harvest: and day after the grapes had been sampled the leaves (at BBCH 89, PHI of 19 days) were cut from the vines. A representative aliquot of these feaves was cut into small pieces, and was homogenised with liquid nitrogen using an Ultra-Turrax homogeniser and was used for extraction. The rest of the leaves were stored at @. -20°C

C. Analytical Procedures

The grape RACs were extracted and the extracts were analysed by HPLC and TLC. The identification of parent compound and metabolites was based of co-chormatography experiments.

1. Extraction

In general, samples of the grape RACs were extracted 3 times with a mixture of acetonitrile/water (8/2, v/v) using an Ultra-Turtax. The extracts were separated from the solids by centrifugation. The radioactivity of the extracts was determined by volume measurement and LSC. The solids (PES) were air-dried, homogenesed and weighed. Aliquots thereof were combusted and measured for radioactivity by LSC.



Grape berries were additionally surface washed prior to homogenization. After extraction, due to high sugar of content, a phase separation acetonitrile : water occurred. Hence, the phases (organic and aqueors sugar phase) were separated using a separation funnel resulting in the combined acetonitrile phases and the combined water phases after all three extraction steps. An aliquot of the combined acetonitrile phases was concentrated prior to HPLC analysis using a rotary evaporator.

The ¹⁴C-radioactivity of liquid samples was determined by liquid scintillation counting LSC using Quicksafe A containing 5% of water. The radioactivit in solid samples was measured by combustion. The released ¹⁴CO₂ was absorbed in an alkaline scintillation cocktail and radio assayed by LSC.

The total radioactive residues (TRR) in the RACS of grapes were determined by commation of the radioactivity in the combined acetonitrile pater extracts and in the PES. The residue levels are expressed as parent compound equivalents per weight. The combined extracts were analysed by HPEC for quantification of metabolites.

2. Identification and characterisation?

Identification of metabolites was done by co-chromatography using IPLC and TLC methods. Each metabolite was co-chromatographed either with its authentic reference convoluted and/or radiolabelled metabolites, which had been isotated and identified in a support and cell culture study and/or metabolism studies in beans and inerat.

3. Storage stability:

The RACs were extracted and analysed within a few days after sampling. All samples were stored at temperatures \leq -18 °C. A few days after extraction, the earlied metabolite profiles of the combined extracts were obtained using a preliminary HPLC method ontil the final profiling method for the use in all plant metabolism studies was available. The extracts were analysed again using HPLC approximately eight to ten months after the initial analysis. The profiles from the initial and the late analysis showed no significant differences in the compound pattern. Therefore, it was concluded that the results of this study were not negatively influenced by storage effects.

II. Results and Discussion

The metabolism of [pyridy] 2,6-¹⁴C fluop ram, formulated as a SC 500, was investigated in grape following there foliar applications at single application rates of approximately 100 g a.s./ha, 200 g a.s./ha and 200 g a.s./ha respectively.

The TRR amounted to 64,18 mg eq/kg in summer cut leaves, 1.70 mg eq/kg in grapes and 42.66 mg eq/kg in teaves at harvest (Table 6.2.1-1). The TRR of the edible RAC (grapes) was significantly lower than those of the Paves cut in summer or leaves at harvest.



Matrix	Timing and Applic. No.	PHI (days)	a.s.TRR (ppm, mg a.s. opuiv./kg)	
Summer cut leaves	two applications: at growth stages BBCH 17-19 and 71 1 x 100 g a.s./ha and 1 X 200 g a.s./ha	& 0	64.18	
Grapes	three applications: at growth stages BBCH 17-19, 71 and 84 1 x 100 g a.s./ha and 2 X 200 g a.s./ha	18 2		
Leaves at harvest	three applications: at growth stages BBCH 17-19, 7 Pand 81 1 x 100 g a.s./ha and 2 X 200 a.s./ha		7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	

The grape matrices were extracted with acetoritrile/water (80, v/v), the extracts were analysed by HPLC and, where necessary, TLC, and parent compound and metabolites were identified. L G in the second se

Ì

Nearly the complete radioactive residue (97.3% of the TRR, 62,49 mg eg/kg) in summer cut leaves was extracted by acetonitrile/water (), Deaving only 2.7% (1975 mg eq/kg) in the solids (PES). Nearly the complete radioactive residues (97.1% of the TRR (1.65 ing eq.4xg)) on or in grapes, were in the acetonitrile surface wash or extracted by acetonitrike/water (Table 6.2,1%), leaving only 2.1% (0.04 mg eq/kg) in the solids (PES). The majority of the radioactive residues in leaves at harvest (94.7% of the TRR (40.43 mg eq/kg)) was extracted by aceronitrile/water (Table @2.1-5), whereas 5.2% (2.23 mg eq/kg) of the TRR remained in the solids (PES) Due to the low radioactive residue, the solids (PES) from all matrices were not further investigated.O

Jpyridyl-	2,6- ¹⁴ €JAE 65	948 🔬	& A'			
	Summer		Gra	npes	Leaves a	t harvest
TRR [mg eq/kg] =	64) *8 ** *	1.	70	42.66	
	Sof TRA	₩8 mg@q/kg	% of TRR	mg eq/kg	% of TRR	mg eq/kg
Surface wash	n.a.	Ç ^a on.a.	76.9	1.31	n.a.	n.a.
Acetonitrile/water extract	» بې 97£	62.43	20.2	0.34	94.7	40.43
Solids (PES)	2.7	1.75	2.1	0.04	5.2	2.23
Total extracted	97 .	♦ 62.43	97.1	1.65	94.7	40.43
Accountrility	⇒ 100°0	64.18	100.0	1.70	100.0	42.66
n.a. net applicable	*					
A. Q. O AY						

Table 6.2.1-5: Distribution of radioactivity in the extracts of the grape matrices after application of



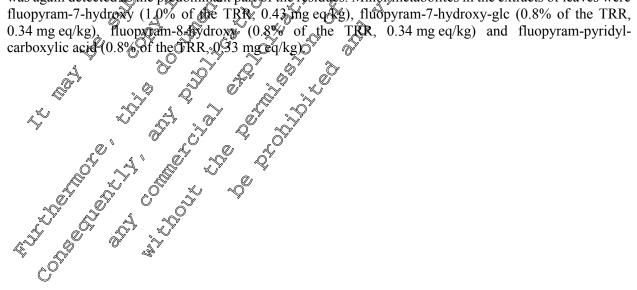
For the elucidation of metabolites, the solvent extracts (acetonitrile/water) were analysed by HPLC or by TLC with radiodetection. Metabolites were either identified by co-chromatography (HPLC, TLC) with authentic reference compounds or with isolated metabolites in the course of other metabolism studies.

Summer cut leaves: Parent compound (95.7% of the TRR, 61.39 mg eq/kg) was detected as the predominant part of the residues in the extracts of summer cut leaves (Table 6.2.1-3) Several minor metabolites were detected in the extracts of the summer cut leaves. fluopycam-pyridyl-carboxylic acid @.3% of the KRR, 0.21 mg eq/kg) was identified in the acetonitrile/water extract. The minor metabolites Quopyram-7% hydroxy (0.3% of the TRR, 0.20 mg eq/kg), fluopyrame 8-hydroxy (0.2% of the TRR, 0.13 mg eq/kg), and fluopyram-7-hydroxy-glc (0.2% of the TRR, 0.12 mg eq/kg), were also assigned (Table 6.2, 123). Additionally, one unknown compound (0.6% of the TRR 0.39 mg eq kg) was characterised by extraction and chromatographic behaviour.

Grapes: Parent compound (76.9% of the TRR, 1.31 rug eq/kg) was the only component detected in the surface wash of grapes. Due to the viscosity (bigh sugar content), the acetonitrile water extracts separated into two phases. The acetonitrile phase of the grapes contained 19.5% (0.03 mg eq/kg) of the TKR of which parent compound (contributing 1823% of the TRB, 0.3 kmg eq. Rg) was the prodominant residue.

Hence, metabolites detected in grapes were minor fluopyram-pytydyl-carboxylic acid, amounted to 0.9% (0.015 mg eq/kg) of the TRR. In additional luoperam-7-hydroxy (0.3% of the TRR, @005 mg eq/kg) was assigned (Table 6.2.1-3). The aqueous phase containe conly (19% (0.01 mg/kg) of the TRR in total, and again fluopyram was the mator compound (0.6% of the TRR 0.008 mg eq Rg). Overall, the parent compound accounted in total for 950% (163 mg cq/kg) of the TRR in gapes (Table 6.2.1-3). A very polar minor metabolite (0.1% of the TRR, 0.002 mg q/kg) remained unassigned, but was characterised by its extraction and Pomat@raphic behaviour.

Leaves at harvest: In the extracts of leaves at harvest parent compound (91.3% of the TRR, 39.0 mg eq/kg) was again detected as the predominant part of the residues. Minor metabolites in the extracts of leaves were fluopyram-7-hydroxy (1.0% of the TRR, 0.43 mg eq. g), fluopyram-7-hydroxy-glc (0.8% of the TRR,



L



Table 6.2.1-6:	Summary of characterisation and identification of radioactive residues in grap	e matrizes	۵.
	after application of [pyridyl-2,6- ¹⁴ C]fluopyram	be matrices	~C*

			10			<u> </u>	- N
	Summer cut leaves		Gra	Grapes		Deaves at harvest	
TRR $[mg eq/kg] =$	64	4.18	1.	70	42	.66	
Compound	% of the TRR	mg eq/kg	% of the TRR	mg eq.	% of the TRR	Oʻ Vmg.eqi/kg	
AE C656948, a.s., fluopyram	95.7	61.39	Ø ^{95.8}	1.63	91x3	£39.00	کې ا
fluopyram-8-hydroxy (M18)	0.2	0.13	n.d.	n.d.©°	á ^{9.8} "	0.34	, O
fluopyram-7-hydroxy (M08)	0.3	0,20	° 0.3 ℃	< 0 01		Ø.43	
fluopyram-7-hydroxy-glc (M11)	0.2	0.12	n a	n.d.	0 .8	0.34	
fluopyram-pyridyl-carboxylic acid (M43)	0.3	0.21	~ ^{0.9}		0.8 OF	Q.33 0	e o
Total identified	965	¢62.05	27,0	× 1.65 ×	ØÅ.7 K	× 40.∰	
Unknown 1 (GR0)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	^ب ر الم		<001		- - -	
Unknown 2 (SC5)	0.6 ^{%)}	Ø.39		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		`~~_	
Total characterised	%0 .6	0.3%	0.1	¢ <0\$01	× - 0	-	
Losses (phase separation)	0 [°] - ĝ		0.8	× 9.01		-	
Solids (non-extractable residue)	2,9	01.75°	<u></u>	0,04	\$ 5.2	2.23	
Accountability	\$00.0	64.98	⇒100. <u>0</u>	D.70 4	100.0	42.66	
	≫´ \ \`	\sim		L, (),			

III. Conclusions 🖉

After follar spray application of [pyridy] 2,6-14 Ofluopytam, most of the recovered radioactivity was detected in summer cut leaves (64.19 mg eq/kg) and leaves at harvest (42.66 mg eq/kg), whereas significantly less residues were referred in grapes (1.70 mg eq/kg).

The radioactively was easily extracted (minimum 594% of the TRR) and identification of metabolites was done by co_xchromatography using HPLG and TLC methods.

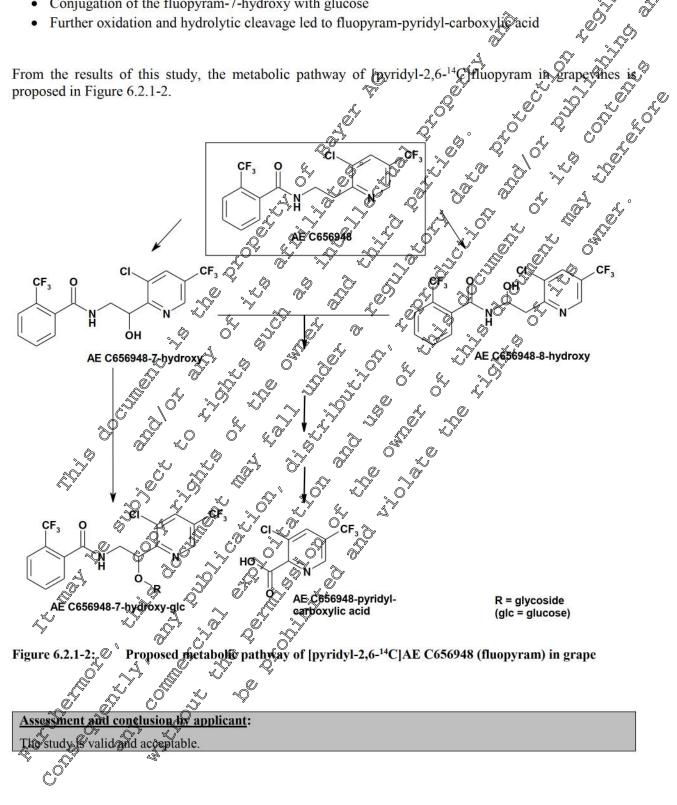
Unchanged parent compound of as the predominant portion of the TRR in all matrices, accounting for more than 90% of the TRR. Metabolism of fluopyram was rather limited in grapevine and none of the metabolites were detected in portions of more than 10% of the TRR. The label specific compound fluopyram-pyridyl-carboxylic acid (RCA, M43) amounted to up 00.9% of the TRR. Further metabolic reactions involved in the degradation of fluopyram were the hydroxylation of parent compound forming the fluopyram-7-hydroxy and 8-hydroxy metabolites. The latter as well as the glucoside conjugate of fluopyram-7-hydroxy were only detected in leaves.

Hence mailer metabolic reactions involved in the degradation of fluopyram were:



- Hydroxylation of the ethyl linking group of the a.s. forming 7- or 8- hydroxy metabolites •
- Conjugation of the fluopyram-7-hydroxy with glucose .
- Further oxidation and hydrolytic cleavage led to fluopyram-pyridyl-carboxylic acid .

CHluopyram in gra From the results of this study, the metabolic pathway of pyridyl-2,6-14 proposed in Figure 6.2.1-2.





Metabolism in potato (foliar spray application)

Data Point:	KCA 6.2.1/03
Report Author:	
Report Year:	
Report Title:	Metabolism of [phenyl-UL-14C]AE C656948 in postoes
Report No:	Metabolism of [phenyl-UL-14C]AE C656948 in positoes
Document No:	M-286400-01-1
Guideline(s) followed in	US EPA OPPTS 860.1300 Anadian PMRA Ref.: PACO 60, EU \$414/EEC amended by 96/68/EC
study:	amended by 96/68/EC
Deviations from current	
test guideline:	
Previous evaluation:	yes, evaluated and accepted 2012 Orderences reliemon
	rev. 1 to Vol.3 of DAR BY August 2012, Deferences relied on)
GLP/Officially recognised	yes, evaluated and accepted rev. 1 to Vol.3 of DAR BY August 2012 Deferences relicoon)
testing facilities:	
Acceptability/Reliability:	Yes Q X X X X

A metabolism study in potato were conducted with othenyl QL-14 & fluopyram;

Executive Summary

The metabolism of [phonyl-UL C]fluopyrand formulated as a SC 500 (Suspension Concentrate), was investigated in potato following three foliar spray applications. The applications were performed at growth stages BBCH 16, 55 and 74. Approximately 167 g a.s./ha were applied for each treatment and the total application rate way about 500 go s./ha

Tubers and leaves were havested at matority with a pre-harvest interval (PHI) of 51 days.

The TRR of the edible RAC (tubers) was 0.008 mg eq/kg and was considerably lower than that of leaves (47.64 mg eq/kg). The major portion of adjustivity (96.7–99.4% of the TRR) was effectively extracted with acetonitril water from all RAC leaving only minor amounts $\leq 3.3\%$ with the solids (PES). Parent compound and metabolites in the extracts were quantified by HPLC.

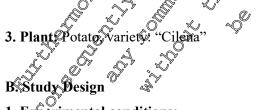
Unchanged fluopyram was the major compound detected in all extracts, comprising between 68.8% (0.006 mg cq/kg) of the TRR in tubers and 98.0% (46.69 mg cq/kg) of the TRR in leaves. fluopyrambenzamid was identified in the extract of tubers (0.001 mg cq/kg, 7.1% of the TRR) and also assigned in



1.	Test	Mate	rial

the extract of leaves (0.23 mg eq/kg, 0.5% of the TRR). fluopyram-7-hydroxy was detected in low amounts in the extract of tubers and leaves.
A total of 77.1% (0.006 mg eq/kg) of the TRR was identified in tubers and 99.2% (2.28 mg eq/kg) of the TRR in leaves.
The metabolic reactions in potato involved were:
 the extract of leaves (0.23 mg eq/kg, 0.5% of the TRR). fluopyram-7-hydroxy was detected in low amounts in the extract of tubers and leaves. A total of 77.1% (0.006 mg eq/kg) of the TRR was identified in tubers and 99.2% (47.28 mg eq/kg) of the TRR in leaves. The metabolic reactions in potato involved were: Hydroxylation of parent compound leading to fluopyram-7-hydroxy. Hydrolysis of fluopyram-7-hydroxy forming fluopyram-bezamide I. Materials and Methods A. Materials
I. Materials and Methods
1. Test Material:
Compound AE C656948 University of the compound AE C656948 University of the compound AE C656948 Compound AE C65694 Compound AE
IUPAC name V V IUPAC name V V IUPAC name V IUPAC name V IUPAC name IUPAC nam IUPAC nam IUPAC name <
CAS name Benzapiide, %[2-[3-Chloro-& (trifluoromethyl)-2- pyrieinyl]ethyl]-2@trifluoromethyl)-(9Cl)
CAS # 658066-58-4 5 0
Radiolabel position Phenel-UL-&C
Specific radioactivity 3.85 MBg/mg (104.2 μCi/mg)
Purity 99% (TLC) Chemical Purity 99% (HPLC)

2. Soil: "Monheim 3" (sandy loam from Germany), pH (CaCl₂) = 6.4, 60.7% sand, 26.3% silt and 13.0% gation elehange capacity (CEC) of 5.9 meq/100 g. clay, 1.36% organic carbon



1. Experimental conditions:



A total of six potato plants were grown in the vegetation area (building 6682) of Bayer CropScience Acc. Metabolism / Environmental Fate, Monheim, Germany, which allows plant growth under natural surflight and temperatures. The plants were cultivated in a planting container with a surface area of 1 m², filled with ¹⁰ a sandy loam soil. The plants were sprayed with [phenyl-UL- 14 C]fluopyram formulated as a SC 500 using a computer controlled track sprayer with a flat fan nozzle directed onto the plants.

The metabolism study simulated the envisaged use pattern and was based on a proposed total application rate of 500 g a.s./ha as three sprayings. To compensate losses during applications, 10% excess of a.s. was applied. Three applications were performed at growth stage BBCH 16, BBCH 55 and BBCH 7. The actual rates for each or the three applications were 167.3 g a.s. tha, 175.6 g a.s. tha and 176.0 g a.s. /ha and resulted in a total actual application rate of 518.8 g a.s./ha (nominal 500 g a.s./ha). The intervals between the first and the second applications were 16 days and 11 days between the second and third applications.

2. Sampling

Leaves: At maturity (BBCH code 97 and #HI of SI days), the leaves of the plants were cut above the soil surface. A representative portion of leave material was cut into small pieces and was hoppingen sed with liquid nitrogen using a Polytron. An anquot of the homogenised sample was used for extraction. Residual sample material was stored in aliquots at c_{∞} -20 \mathcal{Q} .

Tubers: At maturity (BBCH code 90 and PDI of 50 days) Tubers were dug out of the soil. Tubers were left to dry and dry soil particles were removed by mand when the tubers were washed with water and the radioactivity of the wash solution was determined. The wash solution was not further investigated.

Half of the washed tubers were cut into slices and half of these slices were homogenised with liquid nitrogen using a Polytron. A suitable aliquot of the homogenised sample material was used for extraction. All other remaining sample material was stored in aliquots at ca. -20 °C.

C. Analytical Procedures

The potato RACs were extracted and the extracts were analysed by HPLC. The identification of parent compound and metabolites was based on LC-MS and co-chromatography experiments.

1. Extraction

In general, samples of the potato RACs were extracted 3 times with a mixture of acetonitrile/water (8/2, v/v) using a Polytron. The extracts were separated from the solids by suction through a filter and combined. The radioactivity of the expracts was determined by volume measurement and LSC. The solids (PES) were air-dried and weighed. Affquot thereof were combusted and measured for radioactivity by LSC.

Prior to HPLC analysis Sombined extracts were mixed with the emulsifier HOT 5902 and concentrated. Tuber stracts were further precipitated with acetonitrile and the precipitate was separated and dissolved in acetonitrile.



The ¹⁴C-radioactivity of liquid samples was determined by liquid scintillation counting (LSC) using Quicksafe A containing 5% of water. The radioactivity in solid samples was measured by combustion. The released ¹⁴CO₂ was absorbed in an alkaline scintillation cocktail and radio assayed by LSC.

The total radioactive residues (TRR) in the RACs of grapes were determined by summation of the 🖄 radioactivity in the combined acetonitrile/water extracts and in the PES. The residue levels are expressed as parent compound equivalents per weight. The combined extracts were analysed by reversed phase HPUC for quantification of metabolites.

2. Identification and characterisation:

Parent compound was identified by LC-MS-spectroscopy of an isolated HCC-fraction of the extract of tubers. Metabolites were either identified by co-chromatography with reference compoords taken from a metabolism study in rat and/or in cell culture or characterized by their extraction and chromatographic behaviour.

3. Storage stability:

All samples were stored at temperature of \$-20°C. All samples were extracted within four days after sampling. The earliest metabolite positiles of the combined extracts were obtained by HPLC coupled to a radioactivity detector using a preliminary HPL (Smethod until the final profiling method for the use in all plant metabolism studies was available. Within approximate one month, the extracts were analyzed using this final HPLC method. The profiles showed no significant differences in the compound pattern and in the amounts of metabolites compared to the very first quantifications. Therefore, it was concluded that the residues and the extracts were stable over the time of the analyses.

(Suspension Concentrate), was The metabolism of phenyl-U investigated in potato following three foliar applications, at a total application rate of 518.8 g a.s./ha. 1

A Resorts and Discussion

The TRR amounted to 0.008mg eq/kg in tubers and 40.64 mg eq/kg in leaves (Table 6.2.1-1). The TRR of

The TRR inounted to 0.008mg eq/kg in tubers and 40.64 mg eq/kg in the edible RAC (tuber) was significantly lower that those of the leaves.



Matrix	Timing and Applic. No.	PHI (days)	TRR (ppm,
Tubers	three applications: at growth stages BBCH 16, 55 and 71 3 x 167 g a.s./ha	51	0.008
Leaves	three applications: at growth stages BBCH 16, 55 and 71 3 x 167 g a.s./ha	51 Q	9 97.64 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9

The potato matrices were extracted with acetopitrile/water (\$2; v/v) the extracts were analysed by HPLC and parent compound and metabolites were relentified.

The majority of the radioactive residue of tubers, 96.% (0.008 mg eq/kg) of the SRR, was extracted using acetonitrile/water (8/2, v/v) and 3.3% (<0.001 mg eq/kg) of the SRR remained in the solids (Table 6.2.1-8). The major amount of radioactivity in leaves, 99.4% (47.3% mg eq/kg) of the TRR was extracted using acetonitrile/water (8/2, v/v) and 0.6% (0.29 mg eq/kg) of the TRR remained in solids (Table 6.2.1-8). Due to the low radioactive residue the solids (PbS) from all matrices were not further investigated.

 Table 6.2.1-8:
 Distribution of radioactivity in the extracts of the potato matrices after foliar spray

 application of the potato of

$\tilde{\mathcal{T}}$ $\tilde{\mathcal{T}}$ $\tilde{\mathcal{T}}$ $\tilde{\mathcal{T}}$ $\tilde{\mathcal{T}}$	🔊 Lea	ives
\mathcal{R} [mg eq/kg] = $\langle \langle \rangle$ $\langle \rangle$ $\langle \rangle$ $\langle \rangle$ $\langle \rangle$ $\langle \rangle$	47	.64
A of TRR of a single of the second se	% of TRR	mg eq/kg
Acetonitrile/water extract	99.4	47.35
Solids (PES)	0.6	0.29
$\mathbf{A}_{\text{otal extracted}} = \begin{bmatrix} \mathbf{A}_{\text{otal extracted}} & \mathbf{A}_{otal extr$	99.4	47.35
Accountability 2 109.0 0.008	100.0	47.64
Accountability 9 4 100.0 0.008		

For the elucidation of metabolistic, the solvent extracts (acetonitrile/water) were analysed by HPLC. The parent compound was identified by LC-MS; metabolites were identified by co-chromatography (HPLC) with reference compounds.

Tubers: The parent compound was the major compound and was found in amounts of 68.8% (0.006 mg eq/kg) of the TRR. The only other compounds detected in tubers were metabolite fluopyramber amide (7.1% of the TRR, 0.001 mg eq/kg) and metabolite fluopyram-7-hydroxy (<0.001 mg eq/kg, 1.2% of the TRR).



Leaves: The parent compound was the major compound and was found in amounts of 98.0% (46.69 mg eq/kg) of the TRR. The only other metabolites detected were fluopyram benzamide (0) the TRR, 0.23 mg eq/kg). and fluopyram-7-hydroxy (0.36 mg eq/kg, 0.8% of the TRR).

All other minor unassigned metabolites were characterised by their extraction and chroma behaviour.

foliar spray application	on of of [phenyl-U			
	A Trut	per Q	DO O Les	ves 📣 🖉 °
TRR [mg eq/kg] =	↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓		, O ^S , A7.	64
Compound	% of the TRR	mag eq/kg	of the TRR	S mg Q/kg
AE C656948, a.s., fluopyram	688	0.00% Č		×\$46.69
fluopyram-7-hydroxy (M08)			» ٥ <u>٨</u> ٥ %	0.36
fluopyram-benzamide (M25)	Č [¥] 7.1 \$	0.001	Q O	0.23
Total identified	\$ 759 ~	Q.006 X	~~ ^{999.2}	47.28
Unidentified compound MET 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2				0.07
Unidentified composed MET 3	3.1	5 40.001 5 001	×	-
Unidentified compounds of the solution		5° 0°		
of the precipitate (dissequed in O	(¹⁰) 12.4() ¹		V -	-
Distillate of the combined extracts	2 12.4 4 4 4 4 12.4 4 6 6 6 7 12.4 6 7 7 7 7 7 7 7 7 7 7 7 7 7	©<0.0010	-	-
Total characterised	\$\$ 19.5 ⁰	[*] 0,092	0.1	0.07
Solids (non-extraction for the solid)	× 10.3 0	<0.001	0.6	0.29
Solids (non-extractable residue)	×۲۱00.05	S 0.008	100.0	47.64
	0, 0, 0	-U		

Table 6.2.1-9:Distribution of parent compound and metabolites in the extracts of potato matrices after
foliar spray application of of [phenyl-Ub-14C] theopyram

After foliar pray application of phenyQUL¹⁴C]fluopyram, most of the recovered radioactivity was detected in leaves (47.54 mg eq/kg) whereas only very little residues were detected in tubers (0.008 mg eq/kg)

III. Conclusions

The radioactivity was easily extracted (> 96% of the TRR) and identification of metabolites was done by co-chromatography using HPLC and by LC-MS.

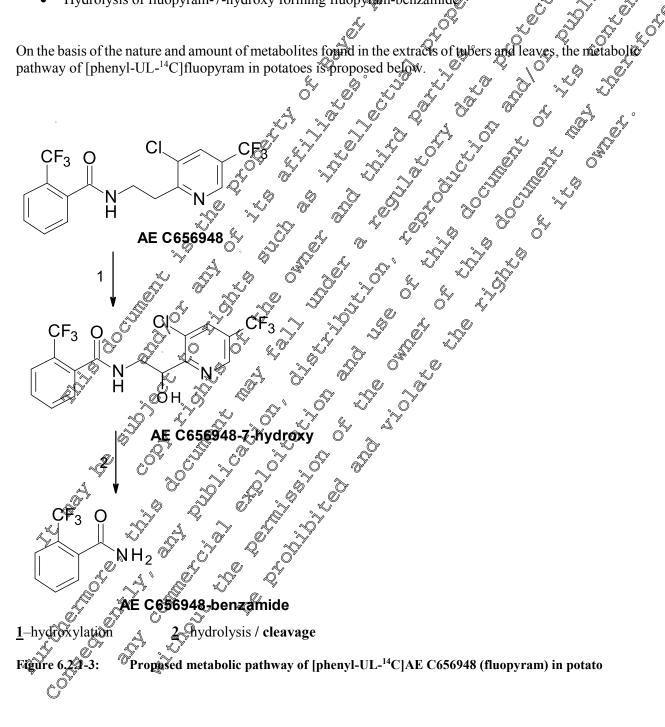
The major residue was parent compound and amounted to 68.8% of the TRR in tubers and 98.0% of the TRR metabolite in tubers (7.1%)



of the TRR), followed by fluopyram-7-hydroxy (1.2% of the TRR). Both metabolites were also detected as minor residues in leaves (each < 0.8% of the TRR).

The following metabolic routes were deduced:

- Hydroxylation of parent compound leading to fluopyram-7-hydroxy •
- Hydrolysis of fluopyram-7-hydroxy forming fluopyram-benzamide •





Assessment and conclusion	ion by applicant: reptable. otato were conducted with [pyridyl-20-14C] fluopytom:
The study is valid and acc	eptable.
55 	
	otato were conducted with [pyridyl-26- ¹⁴ C] fluopyrom:
A metabolism study in p	otato were conducted with [pyridyl-20-14C] fluopyfom:
	KCA 6.2.1/04 KCA 6.2.1/04 2007 X Metabolism of [pyridy1-2,6-1]*C]AE_055694 Oin poolses X MEF-05/513 X M-286531-01-10 X
Data Point:	KCA 6.2.1/04
Report Author:	KCA 6.2.1/04 A A A A A 2007 A A A A A Metabolism of [pyridy1-2,6-1] C]AF C/5694 C/10 po A MEF-05/513 A A A A
Report Year:	
Report Title:	2007 Metabolism of [pyridyl-2,6-1] C]AF 655694 Oin por Ses 0 MEF-05/513
Report No:	MEF-05/513 x x x x x x x x x x x x x x x x x x x
Document No:	M-286531-01-1
Guideline(s) followed in	Metabolism of [pyriov1-2,0-190] [AE, 05309260in pocession MEF-05/513 M-286531-01-1 WS EPA OPPO 860, \$200; CAradian \$MRA} ef.: Dx GO 6.3 EU 9] \$44/EF5 amended by 96/68/F5
study:	amended by 96/68/Fr 2 2 2 2 2 2 2
Deviations from current	none Q a a a a a a a a a a a a a a a a a a
test guideline:	
Previous evaluation:	none yes, Saluate@and accepted 0 rev. 1 to Vol.3 of D/R B7(August 2012 (reference@relied on) 0 Ves, conflicted offer G@/Officially recognized esting accilities
	rev. I to Vol.3 of OXR B7(August 2012 (reference@relied on)
GLP/Officially recognised	I Ves, conflicted order GC/Officially recognised esting acilities
testing facilities:	
Acceptability/Reliability;	$\begin{array}{c} 7 \\ 7 \\ 7 \\ 7 \\ 7 \\ 7 \\ 7 \\ 7 \\ 7 \\ 7 $
Acceptability/Reliability	
, D	
. 0 8	
ð s	
íð,	
	INCALOL2.1/04 2007 Metabolism of [pyridyl-2,6-19C]AF_C65694 Oin poxBes MEF-05/513 M-286531-01-1 US EPA OPPO 860 \$00; Condian #MRA JQE: DAG O 6.2 EU 91 \$44/EES amended by 6/68/F2 none yes, 2 stiluated and accepted rev. 1 to Vol 3 of D/R B7(August 2012 (reference) relied on) 1 Yes Yes Executive Stimmary
Š,	

The metabolism of pyridyl-2,6 C fluopyram formulated as a SC 500 (Suspension Concentrate), was investigated in potato following three foliar spray applications performed at growth stages BBCH 16, 55 and 71. Approximatel 167 g a.s./ha were applied for each reatment so the total application rate was about 500 g a.s./ha.

Tubers and leaves were harvested at maturity with a pre-harvest interval (PHI) of 51 days.

The TRR of the edible RAC (tubers) was 0.12 mg eq/kg and was considerably lower than that of leaves (21.67 mg cq/kg). The major portion of adioactivity (95.3–99.6% of the TRR) was effectively extracted with aceb itrile water from all RACs reaving only minor amounts $\leq 4.7\%$ with the solids (PES). Parent composed and metabolites in the extracts were quantified by HPLC.

Unchanged fluopyram was the major compound detected in potato leaves, representing 98.1% (21.26 mg eq/kg) of the TRR in leaves. It also represented 23.2% (0.003 mg eq/kg) of the TRR in tubers.



Label-specific fluopyram-pyridyl-carboxylic acid was the main metabolite in the extract of tubers (0.006 mg eq/kg, 49.8% of the TRR) and was also observed in the extract of leaves in low levels (0.11 mg eq/kg, 0.5% of the TRR). fluopyram-7-hydroxy (M08) was detected in low amounts in the extract of leaves in the extra of tubers (<0.001 mg eq/kg, 1.1% of the TRR) and of leaves (0.12 mg eq/kg, 0.6% of the TRR).

A total of 74.1% (0.009 mg eq/kg) of the TRR was identified in tubers and 99.2% (21.49 mg eq/kg) of the TRR in leaves. The metabolic reactions involved were:

- Hydroxylation of parent compound leading to Ruopyran-7 •
- Hydrolysis of fluopyram-7-hydroxy and a subsequent oxidation forming fluopyram-pyridyl-• carboxylic acid.

I. Materials and Methods
A. Materials
A. Materials
1. Test Material:
* position of the
* position of the
Compagna C AE e030948 C CO
IUPAC name N-{2-[3@hlorox3-(trifl@oromethyl)pyridin-2-yl]ethyl}-2-
Q frifluoromethyl)benzämide
IUPAČ name V. {2-[3@hloro45*(trifl@oromethyl)pyridin-2-yl]ethyl}-2- (triflu@romethyl)benzämide CAS name Benzämide, N-[2-[3-chloro-5-(trifluoromethyl)-2- pyridinyDethyl]Q-(trifluoromethyl)-(9Cl) CAS # 658066-35-4 Padialzbel magition Pyrfdyl 2 @t ⁴ C
2 2 2 pyridiny Dethyll 2-(trifluoromethyl)-(9Cl)
CAS #
Radiological position a straight function of the straight function of t
Specific radioactivity 285 MBq/mg (104.2 µCi/mg)
Put $\sqrt{2}$ 2
$\langle \mathcal{O}^{\vee} \rangle \langle \mathcal{O}^{\vee} \rangle \langle \mathcal{O}^{\vee} \rangle \rangle = \mathcal{O}^{\vee} \langle TLC \rangle$
Chemical Purity
Specific radioactiv(by 5.85 MBq/mg (104.2 μCi/mg) Pauity 98% (HPLC) Chemical Purity 99% (HPLC) 99% (HPLC)

2. Soik Monkeim 3." (sandy) oam from Germany), pH (CaCl₂) = 6.4, 60.7% sand, 26.3% silt and 13.0% organic carbon cation exchange capacity (CEC) of 5.9 meg/100 g cla

3. Plant: Potato, variety: "Cilena"



B. Study Design

1. Experimental conditions:

A total of six potato plants were grown in the vegetation area (building 6682) of Bayer CropScience AG, Metabolism / Environmental Fate, Monheim, Germany, which allows plant growth under natural schlight and temperatures. The plants were cultivated in a planting container with a surface area of Y m², filled with a sandy loam soil. The plants were sprayed with [pyridyl-2,6-¹⁴C]fluopyran formulated as a \$500 using a computer controlled track sprayer.

The metabolism study simulated the envisaged use pattern and was based on a proposed total application rate of 500 g a.s./ha as three sprayings. To compensate losses during applications, 10% excess of a s was applied. Three applications were performed a growth stage BBCH 16, BBCH 55 and BBCH 11, at application rates of 170.1 g a.s./ha, 170.5 g a.s./ha and 165 g a.s./ha. This resulted in a total application rate of 505.7 g a.s./ha. The intervals between the first and the second applications were 16 days and 11 days between the second and third applications.

2. Sampling

Leaves: At maturity (BBCH code 97, PHI of 51 days) the leaves of the plants were cut above the soil surface. A representative portion of leave material was cut into small pieces and was homogenised with liquid nitrogen using a Polytron. An aliquot of the homogenised sample was used for extraction. Residual sample material was stored in aliquots at ca. -20°C.

<u>Tubers:</u> At maturity (BBCPI code 97, PfH of 51, days) tabers were dug out of the soil. Tubers were left to dry and dry soil particles were removed by hand. Then the tubers were washed with water and the radioactivity of the wash solution was determined. The wash solution was not further investigated.

Half of the washed tubers were chvinto strees and half of these slices were homogenised with liquid nitrogen using a Polytron. A suitable about of the homogenised sample material was used for extraction. All other remaining sample material was stored in abouts at ca. 20 °C.

C. Analytical Procedures

The potato RACs were expected and the extract were analysed by reversed phase HPLC. The identification of parent compound and metabolites was based on KC-MS and co-chormatography experiments.

1. Extraction

In general, samples of the potato RACs were extracted 3 times with a mixture of acetonitrile/water (8/2, v/v) using a Polytron. The extracts were separated from the solids by suction through a filter. The radioactivity of the extracts was determined by volume measurement and LSC. The solids (PES) were airdried and weighed. Aliquots thereof were combusted and measured for radioactivity by LSC.



Prior to HPLC analysis, combined extracts were mixed with the emulsifier HOT 5902 and concentrated. Tuber extracts were furthermore precipitated with acetonitrile and the precipitate was separated and dissolved in acetonitrile.

The ¹⁴C-radioactivity of liquid samples was determined by liquid scintillation counting@LSC Quicksafe A containing 5% of water. The radioactivity in solut samples was measured by combusition. The released ¹⁴CO₂ was absorbed in an alkaline scintillation cocktail and radioassayed by LSC.

The total radioactive residues (TRR) in the RACe of grapes were determined by sommation of the radioactivity in the combined acetonitrile/water extracts and in the PES. The residue levels are expressed as parent compound equivalents per weight. The combined extracts were analysed by HPLC for quantification of metabolites.

2. Identification and characterisation

Parent compound and fluopyram-peridyl-carboxylic acid were identified by LC-MS-spectroscopy of isolated HPLC-fractions of the extreme of embarrow fluore in the extreme of embarrow fluore isolated in the embarrow fluore isolated in the embarrow fluore isolated in the extreme of embarrow fluore isolated in the extreme of embarrow fluore isolated in the embarrow flu isolated HPLC-fractions of the extract of Jubers fluory am-7-hydrog was identified by co-chromatography with reference compound from a cell culture study

3. Storage stability:

All samples were stored at temperature of 20.5°. All samples were extracted within four days after sampling. The earliest metabolite profiles of the combined extracts were obtained by HPLC coupled to a radioactivity detector using a preliminary HPLC method until the final profiling method for the use in all plant metabolism studies was available. Within approximately one month, all extracts were analyzed using this final HPLC method. The profiles showed no significant difference on the compound pattern and in the amounts of metabolites compared to the very dirst quantifications Therefore, it was concluded that the residues and the extracts were stable over the time of the analyses

esults and Discussion

The metabolism of [pyridyl Huopyran, formulated as a SC 500, was investigated in potato following three foliar applications, at a total application rate of 505.7 g a.s./ha.

m

The TRR amounted to 0.012 mg eq/kg in tubers and 21.67 mg eq/kg in leaves. The TRR of the edible RAC (tuber) was significantly lower than that of the leaves.

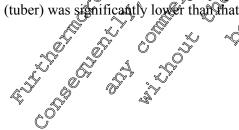




Table 6.2.1-10:	TRR values in potato matrices after app	olication of [p	
Matrix	Timing and Applic. No.	PHI (days)	TRR (ppm, mg eqiv./kg)
Tubers	three applications: at growth stages BBCH 16, 55 and 71 3 x 167 g a.s./ha	51	
Leaves	three applications: at growth stages BBCH 16, 55 and 71 3 x 167 g a.s./ha	51	5 2 2 467 Q 5 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4

The potato matrices were extracted with acetonitrile/water (8 ϕ ; v/v) the extracts were analysed by HPLC and parent compound and metabolites were identified.

The majority of the radioactive residue of tubers, 95.3% (0.0)2 mg q/kg) of the T&R, was extracted using acetonitrile/water (8/2, v/v) and 4.7% 0.001 mg eq/kg) of the TRR remained in the solids (Table 6.2.1-11). The major amount of radioactivity in leaves, 99.6% (21.57 mg eq/kg) of the TRR was extracted using acetonitrile/water (8/2, v/v) and 0.4% (0.10 mg eq/kg) of the TRR remained in solids (Table 6.2.1-11). Due to the low radioactive residue, the solids (PES) from all matrices were not further investigated.

 Table 6.2.1-11:
 Distribution of radioactivition the extract of the potato matrices after foliar spray application of [pyridyl-2.6,14C] AE 656948

	approaction of p.y.				
	<u> </u>		beirs 🕡	🤊 🔦 Lea	ives
TRR [mg eq/kg] =			M2 5 4	21	.67
		%røfTRR,∱	mg eq/kg	🔊% of TRR	mg eq/kg
Acetonitrile/water		[∞] 95.3 ⊘	0.042	99.6	21.57
Solids (PES)	×, ×,	4	0.001 🔊	0.4	0.10
Total extracted		95.3	0.012	99.6	21.57
Accountability		0.00 J	≪ [™] 0.01∅″	100.0	21.67
	\$ 4 A		K A		

For the elucidation of the metabolites, the solvent extracts (metonitrile/water) were analysed by HPLC. The parent compound and metabolites were identified by LC MS/MS and co-chromatography (HPLC) with a radiolabelled reference compound.

Tubers: Parent compound was found in amounts of 23.2% (0.003 mg eq/kg) of the TRR in tubers. The main metabolite in tubers was fluopyram-pyridyl-carboxylic acid, which amounted to 49.8% (0.006 mg eq/kg) of the TRK. A minor metabolite, fluopyram-7-hydroxy was detected in the extract of tubers (<0.001 mg eq/kg. 1% of the TRR).

Leaves: Parent compound represented the major portion of the TRR in leaves with 98.1% (24.26 mg eq/kg) of the TRR in leaves. Two minor metabolites, fluopyram-7-hydroxy (0.12 mg eq/kg, 0.6% of the TRR) and fluopyram-pyridyl-carboxylic acid (0.11 mg eq/kg, 0.5% of the TRR) were



detected in the extract of leaves.

All other minor unassigned metabolites were characterised by their extraction and chromatographic behaviour.

behaviour.		0	\$ ¥
benaviour.		4	
		4	
	<u>ک</u> .	N°	
	6	A.	
		a^{ν}	
	≫ ≫	Ő	
Table 6.2.1-12:	Summary of characterisation and identification of rac	diâactive residu	es in notato materices 🔏
			com posses materies
	after foliar spray application of [pyrid@-2,6-14C]fluor	wram 🦳	
		()	

		\sim		
	Pubers			ives
TRR $[mg eq/kg] =$	¢ 0.042			.67 🎝 🔨
Compound	% of the TRR	ng eq/kg	& of the RR	mg eq/kg
AE C656948, a.s., fluopyram	23.2 ∽	0.003	988:1 C	21 .26
fluopyram-7-hydroxy (M08)	of the of	<0,001	° _∞ 0.6 ≪	0.12
fluopyram-pyridyl-carboxylic acid (M43)	Q 249.8 V	×9.006 0°	× 0.5 ×	× 0,19
Total identified	~74.1 × ×	× 0.009	~ 9 9 (21.49
Unidentified compound MET 1	3.6	<0.001		
Unidentified compound MET 2	k 27 A	30 001 (0 0.4 Č	٥.08 🕎
Unidentified compounds in the solution		C Q		<i>"</i>
of the precipitate (dissolved in 🦄 🌾	11.6	0.00	ê <u>-</u> 0	-
acetonitrile)				
Distillate of the combined extracts	9 3 4 5	<i>∞</i> 0.001 ∞ [∞]	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	-
Total characterised	Q1.2 0 .	0.003	0.00	0.08
Solids (non-extractabl@residue)	@ 4.7\$° K°	0.001	V J V.4	0.10
Accountability	× 100.0	@012	100.0	21.67
				•

After foliar spray application @ [pyridyl-2, @C]fluopyram, most of the recovered radioactivity was detected in leaves (20.67 ms eq/kg) whereas only very little residues were detected in tubers (0.012 mg eq/kg).

The radioactivity was easily curacted > 95% of the TRR) and metabolites were identified by cochromatography using APLC and by C-MSMS.

The label-specific compound fluopyram-pyridyl carboxylic acid was the main compound in tubers (49.8% of the TRR), while the parent compound accounted for 23.2% of the TRR and fluopyram-7-hydroxy to 1.1% of the TRR. The major esidue in leaves was the parent compound (98.1% of the TRR). fluopyram-7-hydroxy and fluopyram-pyridyl carboxylic acid were both detected as minor metabolites in leaves (< 0.6% of the TRR).

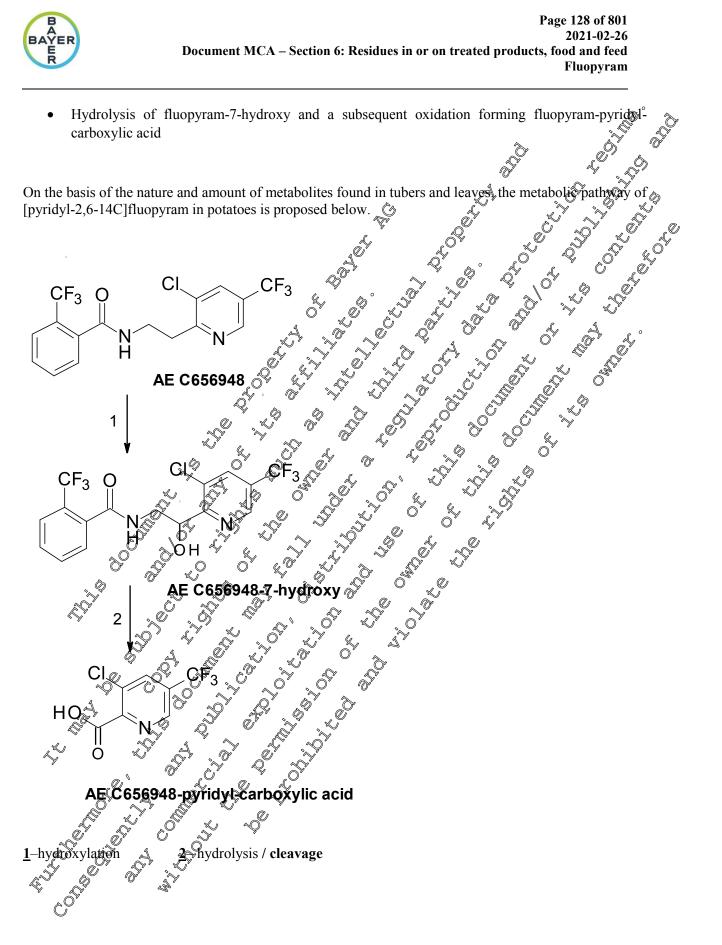
The following metabolic routes were deduced:

• Hydroxylation of parent compound led to fluopyram-7-hydroxy

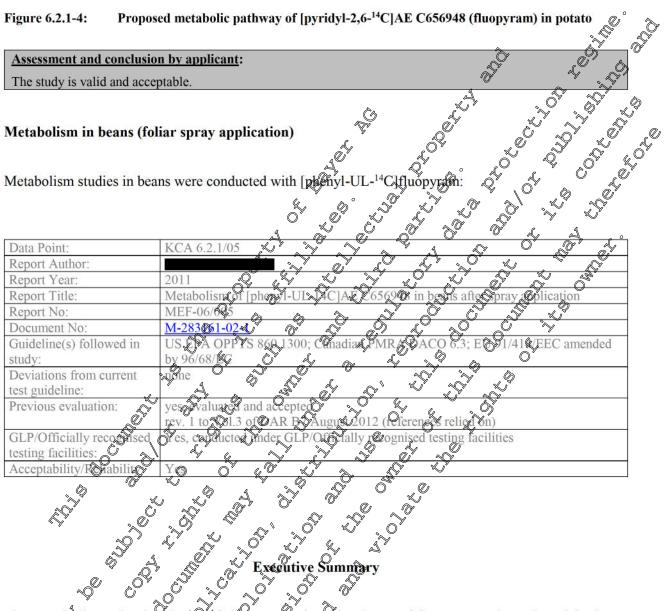


Hydrolysis of fluopyram-7-hydroxy and a subsequent oxidation forming fluopyram-pyrid • carboxylic acid

On the basis of the nature and amount of metabolites found in tubers and leaves, the metabolic pa [pyridyl-2,6-14C]fluopyram in potatoes is proposed below.







The metabolism of [phenyl-UQ¹⁴C]fluopyram, formulated as a SC 500, was investigated in beans following two foliar spray applications. The applications were performed at growth stages BBCH 51 and BBCH 75. The single application rates were 268 \$\overline{9}\$g a.s./ha and 259.3 g a.s./ha for the first and the second application, respectively, and the total application rate was 528 g a.s./ha.

The immature RACs investigated green beans and foliage were taken four days after the second application. The mature RACs beans ("succuler beans") and straw were harvested 29 days after the last application. A portion of the mature beans were dried for 11 days and were analyzed as edible RAC "dry beans".

The TRR of the edible RACs (green, succulent and dry beans) ranged between 0.07 mg/kg and 1.40 mg/kg and was considerably lower than those of foliage and straw (36.66 mg/kg and 16.55 mg/kg, respectively). The major amount of radioactivity (93.9 – 98.1% of the TRR) was effectively extracted with



S. acetonitrile/water from all RACs leaving only minor amounts < 6.1% with the solids (PES). Parent compound and metabolites in the extracts were quantified by HPLC.

In green beans, the parent compound was the only compound detected in the extracts, amounting to 93, 96 (1.31 mg/kg) of the TRR. The foliage TRR comprised of 93.8% parent compound. Other five metabolites were identified in foliage, none of them exceeding 2.2% of the TRR. The major part of the residues in succulent and dry beans consisted of fluopyram-benzamide, accounting for 50% (0.04.0.08 mg/eq/kg/of)the TRR. The unchanged parent compound accounted for 10% of the TRR in both RACs (<0.01 mg/kg in 0 succulent bean and 0.02 mg/kg in dry bean). Five additional metabolities were identified in succulent and dry beans, each accounting for ≤ 0.01 mg eq/kg. In the straw, the residues again comprised of approximately 90% parent compound. None of the other five metabolites identified in straw exceeded 4.1% of the TORR.

Ŷ Ô A total of 93.9% of the TRR (1.31 mg/kg) was identified in green beans and 97.9% (35.90 mg eq/kg) in bean foliage. 83.6% (0.059 mg eq/kg) of the TRR was identificed in successful the trans, 94.6% (0.11 mg eq/kg) of the TRR in dry beans, and 96.7% (190 mg eq/kg) of the transfer to the transfer t bean foliage, 83.6% (0.059 mg eq/kg) of the TRR was identified in succident beans, 91,6% (0,11 mg/q/kg) of the TRR in dry beans, and 96.7% (160 mg kg/kg) of the TRR in bean straw. Onl@a few@ninor @nknown

0



The metabolic reactions involved:

- Hydroxylation of the ethyl linking group of the a.s. forming 7- or 8- hydroxyl metabolites
- Cleavage leading to fluopyram-benzamide •
- Conjugation of hydroxylated metabolites with hexoses and subsequent higher conjugation • malonic and glucuronic acid

		-
	I. Materials and Methods	,© 1
A	A. Materials $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$	
1	. Test Material:	
	I. Materials and Methods A. Materials Chemical structure Chemical structure Compound A. E C656948 IUPAC name Rationale position Benzamide N-[2] Schloro 5-(trifluoromethyl)pyridin-2-9]ethyl}-2- CAS name Benzamide N-[2] Schloro 5-(trifluoromethyl)-2- pyridinylethyl]*2-(trifluoromethyl)-(190) CAS # Specific radioactivity O 8,85 MBq/mg +104.2 µG/mg	
	Compound	
	Compound AE C656948 C C C C C C C C C C C C C C C C C C C	
	IUPAC name Nck2-[3-chloro-5-(trifluoromethyl)pyridin-2-9]ethyl}-2- Crifluoromethyl)benzamide S	
	CAS name Benzamide N-[2-[3-chloro-5-(trithuoromethyl)-2-pyridinyl ethyl] 3-(trithuoromethyl)-(901) CAS # State of the	
	CAS # 5 5 5806635-4 5 0 4	
	Radiolabel position A Phenyl-ULAC S	
	Specific radioactivity O O 3.85 MBq/mg (104.2 uCi/mg)	
	Purity $\langle 0 \rangle = 98\%$ (HPLG) $\langle 0 \rangle = 98\%$ (TLC) $\langle 0 \rangle = 98\%$ (HPLG)	

- 2. Soil: "Monheim 3" (Sandy Dam from Germany) pH (CaCl₂) = 6.4, 60.7% sand, 26.3% silt and 13.0% clay, 2.34% organic earbon cation exchange capacity (CEC) of 5.9 meq/100 g
- Durblette" 3. Plant: Bush beans

B. Study Desig

1. Experimental conditions:

 \sim^{0} The beau plant were grown in the vegetation area (building 6682) of Bayer CropScience AG, Metabolism / Environmental Fate, Monheim, Germany, which allowes plant growth under natural sunlight and temperatures. Approximately 40 bush bean plants (variety: Dublette) were cultivated in a planting container with a surface area of 1.0 m², filled with a sandy loam soil. The plants were sprayed with [phenyl-UL-



¹⁴C]fluopyram formulated as a SC 500 and the spraying was performed using a computer controlled track sprayer.

The metabolism study simulated the envisaged use pattern and was based on the maximum proposed application rate (500 g a.s./ha). To compensate losses during applications, 10% excess of a.s. was applied. Two applications were performed at growth stage BBCH 51 and BBCH 75, an actual application rates of 268.8 g a.s./ha and 259.3 g a.s./ha, respectively. This resulted in a total application rate of 528.1 g a.s./ha. The time interval between the first and the second application was 28 days

2. Sampling

<u>Green beans and foliage</u>: As about 50% of the beans had a harvestable size (BBCH code 75% 4 days after treatment), these green beans (whole pods) were picked by hand. The green beans were cut into small pieces and were homogenised with liquid nitrogen using an Ultra furrar homogeniser. The complete homogenised plant material was used for extraction. At the same growth stage frepresentative sample of the leaves (foliage) was cut from the bean plants. The leaf material was cut into small pieces and homogenised with liquid nitrogen using an Ultra-Tarrax homogeniser. An aliquet of the homogenised sample was used for extraction. Residual sample material was stored in abquots at ca. 20 °C.

<u>Succulent beans and straw</u>: At maturity (BBCH code 85-89, 29 days after last treatment), beans in their pods were cut from the plant and the succulent beans were picked from the pods. The pods were united with the rest of the plants, which were cut above the soil (straw fraction). The succulent beans were directly homogenised with liquid nitrogen using an Ulfra-Turax homogeniser. The straw fraction was processed in the same way after being cut into strall pieces. A tepresentative aliquot of the homogenised samples was used for extraction. Residual sample material was stored in aliquots at *ca.* -20 °C.

Dry beans: At maturity (BBCH code 89) beans of pods, which had already dried on the plant, were cut from the plant, and the beans were picked from the pods by hand. The pods were united with straw fraction. The beans were allowed to dry at from temperature until no loss of weight (*i.e.* water loss) was measured (11 days). A representative aligned of the dry beans were stored at $ca_2 20$ °C.

C. Analytical Procedures

The bean RACs were extracted and the extracts were analysed by HPLC and TLC. The identification of parent compound and the tabolites was based on co-chormatography experiments and HPLC-MS/MS and/or LC-MMR.

1. Extraction and fractionation:

In general, samples of the bean RACs were extracted 1-3 times with a mixture of acetonitrile/water (8:2, v/v) using an Oltra-Turrax. The extracts were separated from the solids by centrifugation. The radioactivity of the extracts was determined by volume measurement and LSC. The solids (PES) were lyophilised overnight homogenised and weighed. Aliquots thereof were combusted and measured for radioactivity by LSC. Adjuots of the combined solvent extracts were concentrated using a Speedvac.



The ¹⁴C-radioactivity of liquid samples was determined by liquid scintillation counting (LSC) using $\sqrt[6]{2}$ Quicksafe A containing 5% of water. The radioactivity in sold samples was measured by combustion. The released ¹⁴CO₂ was absorbed in an alkaline scintillation cocktail and radio assayed by LSC.

The total radioactive residues (TRR) in the RACs of beens were determined by summation of the radioactivity in the combined acetonitrile/water extracts and in the PES. The residue levels are expressed as parent compound equivalents per weight (mg eq/kg). The concentrated acetonitrile water extracts were analysed by HPLC for quantification of metabolites.

2. Identification and characterisation:

First assignments to the metabolites were obtained after co-chromatography (HRLC, TLC) with authentic reference compounds, with metabolites isolated and identified in a supplemental cell culture study and/or the corresponding study in beans using the pyridyl label. Confirmation of these as a ments was obtained after isolation of the major compounds out of the accontinite/water extract of dry beans by semiareparative HPLC. Corresponding fractions were combined, concentrated, purified on one of the

secondary HPLC systems, and analysed by LC, NMR and/or JPLC, NS/MS.

3. Storage stability:

The RACs were extracted and analysed within a few days after sampling. All samples were stored at temperatures ≤ -18 C. A few days after extraction, the endiest metabolite profiles of the combined extracts were obtained by UPLC using the profiling method for quantitation and identification of metabolites. The extracts were analysed again using HPLC approx one month after the initial analysis. The profiles from the initial and the late analysis showed no significant differences on the compound pattern. Therefore, it was concluded that the results of this study were not negatively influenced by storage effects.

My Results and Discussion

The metabolism of [phenyl-UL+C]fluopyram formulated as a SC 500, was investigated in beans following two foliar applications, at single rates of 268.8 g a.s./ha and 259.3 g a.s./ha and a total rate of 528 g a.s./ha

The TRR amounted to 1.40 mg/kg in green beans, 36.66 mg/kg in the respective foliage, 0.07 mg/kg in succulent beans, 0.12 mg/kg in dry beans, and 16.55 mg/kg in bean straw (Table 6.2.1-13). The TRR of the edible RACS (green, succulent and dry beans) was significantly lower than those of the respective foliage or straw

Table 6.2.1 43: TRR values in bean matrices after application of [phenyl-UL-¹⁴C]fluopyram



e,0

Matrix	Timing and Applic. No.	PHI (days)	TRR (ppm, mg a.s. equiv./kg)
green beans	Two foliar spray applications: at growth stages BBCH 51 and BBCH 75; total 528 g a.s./ha	4	
foliage	Two foliar spray applications: at growth stages BBCH 51 and BBCH 75; total 528 g a.s./ha	4	30.66 ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~
succulent beans	Two foliar spray applications: at growth stages BBCH 51 and BBCH 55; total 528 g a.s./ha	Q29 Q29	
dry beans	Two foliar spray applications: at growth stages BBCH 51 and BBCH 25; total 528 g a.s./ha	29 + M days for drying	
straw (including empty pods)	Two foliar spray applications.		

The bean matrices were extracted with acctonit fe/water (8:2, $\sqrt[3]{v}$), the extracts were analysed by HPLC and, where necessary, TLC and parent compound and metabolites were identified $\sqrt[3]{v}$

The majority of the radioactive residue in green bean 93.9% (1.31 mg/kg) of the TRR, was extracted by acetonitrile/water (Table 6.2.1/14), whereas 6.1% (0.09 mg/kg) of the TRR remained in the solids (PES). Nearly the complete radioactive residues in bean foliage 98.1% (35.97 mg/kg) of the TRR, was extracted by acetonitrile/water (Table 6.2.1/14), leaving only 1.9% (0.66 mg/kg) of the TRR, in the solids (PES). The majority of the radioactive residue in Succular beans, 94.9% (0.067 mg/kg) of the TRR, was extracted by acetonitrile/water (Table 6.2.1/14), whereas 5.0% 0.01 mg/kg) of the TRR remained in the solids (PES). The majority of the radioactive residue in dry beans, 94.9% (0.067 mg/kg) of the TRR, was extracted by acetonitrile/water (Table 6.2.1/14), whereas 5.0% 0.01 mg/kg) of the TRR remained in the solids (PES). The majority of the radioactive residue in dry beans, 97.3% (0.117 mg/kg) of the TRR, was extracted by acetonitrile/water (Table 6.2.1/14), whereas 2.7% (< 0.01 mg/kg) of the TRR remained in the solids. The major amount of radioactive residue only 3.3% (0.54 mg/kg) of the TRR was extracted by acetonitrile/water (Table 6.2.1/14), heaving only 3.3% (0.54 mg/kg) of the TRR was extracted by acetonitrile/water (Table 6.2.1/14), whereas 2.7% (< 0.01 mg/kg) of the TRR remained in the solids. The major amount of radioactive residue in the bean straw 96.7% (16.00 mg/kg) of the TRR was extracted by acetonitrile/water (Table 6.2.1/14), heaving only 3.3% (0.54 mg/kg) of the TRR with the solids (PES). Due to the low radioactive residue, the solids (PES) from all matrices were not further investigated.

Table 6.2.1-14: Diapplication Diapplication Diapplication			<u></u>	sts of the bean	matrices after fol	iar spray
	Green beans	· Fai		Succulent	Dry beans	Straw

	Green bean	al al	fage ,	_	ulent ans	Dry l	beans	Str	aw
TRR[mg eq/kg] =	£.40		.660	0.	07	0.	12	16.	55
	% of TRR		∫∕mg/kg	% of TRR	mg/kg	% of TRR	mg/kg	% of TRR	mg/kg
Acetonitrile water		31 8.1	35.97	94.9	0.067	97.3	0.117	96.7	16.01
Solids (PES)	6.1 00.	.09 1.9	0.69	5.0	0.003	2.7	0.003	3.3	0.54
Tata		.31 98.1	35.97	94.9	0.067	97.3	0.117	96.7	16.01
Accountability		40 100.0	36.66	100.0	0.070	100.0	0.121	99.9	16.54
	and the second s								



For the elucidation of metabolism, the solvent extracts (acetonitrile/water) were analysed by HPLC and, where required, also by TLC with radiodetection. Metabolites were either identified by co-chromatography (HPLC, TLC) with reference compounds or isolated metabolites or by LC-MS/MS and/or LC-NMR of isolated peaks.

<u>Green beans and foliage:</u> The parent compound (93.9%, 1.31 mg/kg of the TRR) was the only component detected in the extract of green beans (Table 6.2.1-15) and it was the predominant residue also in the extract of foliage (95.8%, 34.39 mg/kg of the TRR). The main metabolite in the concentrated extracts of foliage avas the glucoside-maloric acid conjugate fluopyram-7-hydroxy-glc-MA (2.2%, 0.82 mg eq/kg of the TRR). In addition, the metabolites fluopyram-7-hydroxy (0.7%, 0.26 mg eq/kg of the TRR), fluopyram-benzamide (65%, 0.17 mg eq/kg of the TRR), fluopyram-7-hydroxy-glc (0.4%, 0.15 mg eq/kg of the TRR), fluopyram and fluopyram-8-hydroxy (0.3%, 0.11 mg eq/kg of the TRR), were identified (Table 6.2.1-15). Furthermore, two taknow funitor compounds (each \leq 0.1% of the TRR) were characterised in foliage by extraction and chromatographic behaviour.

<u>Succulent beans</u>: The main metabolite in the concentrated extract of succulent beans was AEC656948benzamide (51.6%, 0.036 mg eq/kg of the TRR/whereas the parent compound was 1.4% (0.008 mg/kg) of the TRR. The metabolite identified as glucuronic acid-glycoside conjugate of the hydroxylated parent compound (fluopyram-hydroxy-glyo-gluc) accounted for 6.7% (0.005 mg eq/kg) of the TRR. Other identified minor metabolites accounted for < 0.005 mg eq/kg (Fable 6.2.1-16) Furthermore, three unknown compounds (each < 10% of the TRR and \leq 0.006 mg eq/kg were characterized based on their extraction and chromatographic behaviour.

<u>Dry beans:</u> Major metabolites detected in the acetometrile/water expract were fluopyram-benzamide (64.0%, 0.077 mg eq/kg of the TRR) and fluopyram-hydroxy-glyc-gluc (90.4%, 0.013 mg eq/kg of the TRR). Parent compound was detected as 12.6% of the TRR (0.015 mg/kg). The metabolites AE C6556948-7-hydroxy (2.5%, 0.003 mg eq/kg of the PRR) and 8-hydroxy (2.1%, 0.003 mg eq/kg of the TRR) were also detected in dry beans (Table 62.1-16). Additionallo, two unknown components (each < 5% of the TRR and < 0.005 mg eq/kg) were characterised by extraction and chromatographic behaviour.

Straw: The parent compound fluopyram (90.2%, 14.96 mg/kg of the TRR) was the predominant residue also in the extract of straw. As observed in unmature foliage, the other metabolites in the concentrated extract of straw were the fluopyram-7-hydroxy-glc MA (4.1%, 0.68 mg/kg of the TRR), AE C656948-7-hydroxy (0.7%, 0.42 mg/kg of the TRR), fluopyram-8-hydroxy (0.6%, 0.09 mg/kg of the TRR) and fluopyram-7-hydroxy-glc (0.4%, 0.07 mg/kg of the TRR) and fluopyram-benzamide (0.6% TRR, 0.10 mg eq/kg) (Table 62.1-16).

Summary of characterisation and identification of radioactive residues in green beans and bean for age after foliar spray application of [phenyl-UL-14C]fluopyram

	Green beans	Foliage
$TRR[mgreq/kg] = \frac{1}{2}$	1.40	36.66
Ĉ		



				o
Compound	% of the TRR	mg eq/kg	% of the TRR	mg eq/kg
AE C656948, parent compound fluopyram	93.9	1.31	93.8 0.3 0.7 2.2	34.39 0.11 0.26 0.26 0.15 0.15 0.15 0.15 0.17
fluopyram-8-hydroxy (M18)	-	-	0.3	6 ,11
fluopyram-7-hydroxy (M08)	-	Ğ -	^{سری} 9.7	
fluopyram-7-hydroxy-glc-MA (M12)	-	- 2	2.2	
fluopyram-7-hydroxy-glc (M11)	- 40		0.4	
fluopyram-hydroxy-glyc-gluc (M22)	Q, ,		ŶQŶ,	
fluopyram-benzamide (M25)	979 979		00.5 0 97.95	<u>\$9.17</u>
Total identified	93.9		§° 97.90°	35.90
unknown 1		ð- A	\$0.1 \$0.1 \$0.1	
unknown 2				× 0.04 5 ×
Total characterised				0,06
Total extracted	93.9		0 98.1 Č	\$\$25.97
Solids (non-extractable residue)	6.1	<u> (</u>	1.9	0.69
Accountability	0100.0 °	1.40	× 100.0 0	36.66
unknown 2 Total characterised Total extracted Solids (non-extractable residue) Accountability Accountabil			5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	



Table 6.2.1-16: Summary of characterisation and identification of radioactive residues in succulent beans, dry beans and bean straw after foliar spray application of [phenyl-UL ¹⁴C]fluopyram

Chuopyram				ð	<u>,</u> ,	"O"
	Succulent be	ans Dry l	oeans (Str Str	aw 🞸 🔶	0
TRR [mg eq/kg] =	0.07	0.	12 1	16	.50%	<i>R</i> a
Compound	% of the TRR eq/	kg TRR	gq/kg	% of the	nny Sylkg	
AE C656948, parent compound fluopyram	11.4 0.0	🐼 12.6 🦂	0.015	ð¢.2 ,	Q 14.94	« ^{O·}
fluopyram-8-hydroxy (M18)	6.0 00		0,003	مر¢ 0.6	[*] 0.09	Ŭ [®]
fluopyram-7-hydroxy (M08)	4.0 \@0.0		<i>، 0</i> .003 م	$\sqrt[3]{0}$	Q.12	
fluopyram-7-hydroxy-glc-MA (M12)	2.2 🕵 0.0	03° _~~ *	× - v	×,	× 0.68~	
fluopyram-7-hydroxy-glc (M11)	1.7 0 0,0			~0.4 [°]	∛ 0.0 לאיי	
fluopyram-hydroxy-glyc-gluc (M22)	6.7	05 10,40	00013	Ø - K	A	
fluopyram-benzamide (M25)	\$1.6 \$\%0.0	36 64.0	چ 0.077	0.6	9.10	
Total identified	83.6 0.0	59 J91.6	0.11	\$6.7	16.01	
unknown 3	1∢9∀ 00	01 3.2	0,604	0 · ~		
unknown 4	1 1 × 0.0	01	<u>, </u>	S - O'		
unknown 5 🖓 🖓	8.3 0.0	<u>6</u> 35	00.003 C	, S	L -	
Total characterised	11.3 0.0	98 05.7 L	0.007	Q- V	> -	
Total extracted	24,9 090	67 🎝 97.3	0.117	96.7	16.01	
Total bound residues (PES)	Š.0 \$0.0	03 207	0.003	3. S	0.54	
Accountability	100.0 0.0		0.12	\$ 9.9	16.54	
				No.		

111. Conclusion

After foliar spray application of [phenykJL¹⁴C[fluop) and, most of the recovered radioactivity was detected in foliage (35.97 mg/kg) and straw (16.55 mg/kg), whereas only minor residues were detected in the respective bean samples (1.40 mg/kg for green beans, 0.07 mg/kg for succulent beans, and 0.12 mg/kg for dry beans).

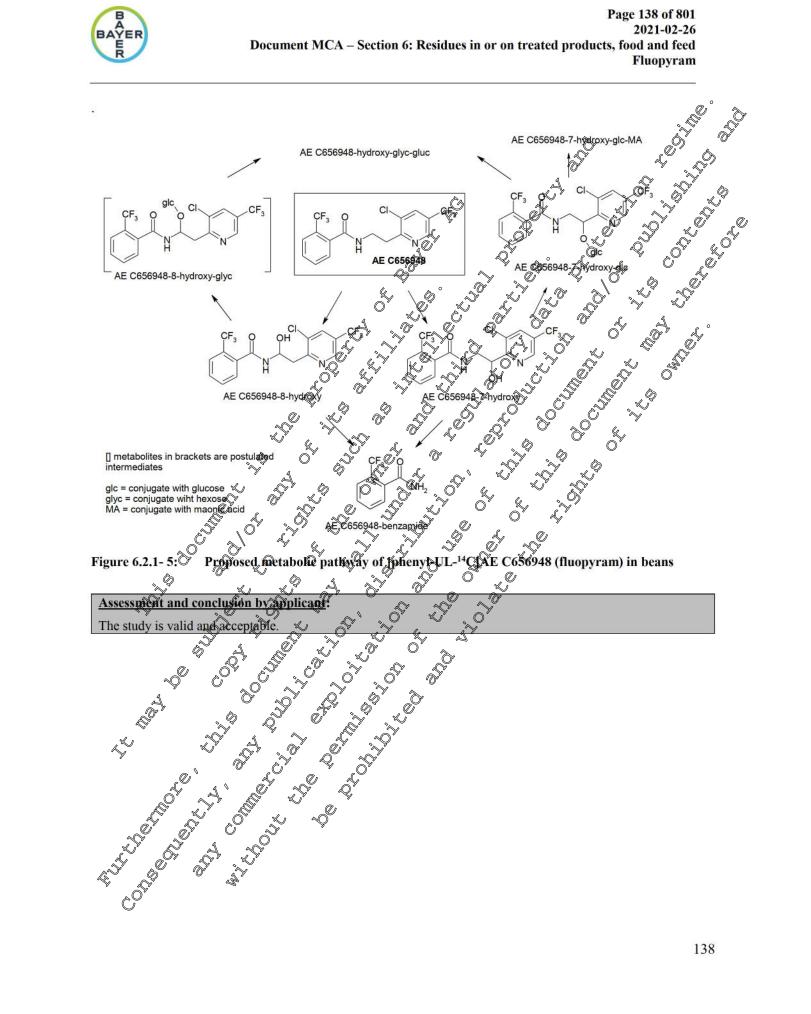
Unchanged parent compound was the predominant portion of the TRR in foliage, straw and green beans, accounting for more than 90% of the TRR, and was still present (> 10% of the TRR but < 0.01 (succulent bean) and 0.02 (mg/kg (ary bean)) in bean samples at maturity. In total, six metabolites were identified. The major metabolite in bean samples at maturity (succulent and dry) was fluopyram-benzamide (> 50% of the TRR). In other bean matrices, identified metabolites accounted generally for < 10% of the TRR.

The following metabolic foutes were deduced

- Hydroxylation of the ethyl linking group of the a.s. forming 7- or 8- hydroxyl metabolites
- · Cleavage and exidation leading to floopyram-benzamide
- Conjugation of hydroxylated metabolites with hexoses and subsequent higher conjugations with metabolic and glueuronic acid

On the basis of the nature and amount of metabolites found in foliage, beans and straw, the metabolic pathway of [phenyl-UL¹⁴C]fluopyram in beans is proposed in Figure 6.2.1-5.







Metabolism studies in beans were conducted with [pyridyl-2,6- ¹⁴ C]fluopyram: Data Point: KCA 6.2.1/06 Report Author:
Data Point: KCA 6.2.1/06 Report Author: Image: Constraint of the second sec
Data Point: KCA 6.2.1/06 Report Author: Image: Constraint of the second sec
Data Point: KCA 6.2.1/06 Report Author: Image: Constraint of the second sec
Report Teal: 2000 Report Title: Metabolism of [pyridyl-2,6-14C]AE C656948 in borns after spray uplication Report No: MEF-06/004 Document No: M-299067-01-1 Guideline(s) followed in US EPA OPPTS 860.1300; Ginadian PMRA Ref.: DACO 60, EU G/414/EEC study: amended by 96/68/EC
Report Teal: 2000 Report Title: Metabolism of [pyridyl-2,6-14C]AE C656948 in borns after spray uplication Report No: MEF-06/004 Document No: M-299067-01-1 Guideline(s) followed in US EPA OPPTS 860.1300; Ganadian PMBA Ref.: DACO 60, EU 3/414/EEC study: amended by 96/68/EC
Document No: M-299067-01-1 Guideline(s) followed in study: US EPA OPPTS 860.1300 Gradian PMRA Ref.: DRCO 60, EU Gr414/EEC
Document No: M-299067-01-1 Guideline(s) followed in study: US EPA OPPTS 860.1300 Gradian PMRA Ref.: DRCO 60, EU Gr414/EEC
Document No: M-299067-01-1 Guideline(s) followed in study: US EPA OPPTS 860.1300 Gradian PMRA Ref.: DRCO 60, EU Gr414/EEC
Guideline(s) followed in study: US EPA OPPTS 860.1300 Ginadian PMRA Ref.: DRCO 60, EU 6/414/EEC Deviations from current none
study: amended by 96/68/EC Deviations from current none
Deviations from current none
test guideline:
Previous evaluation: yes, evaluated and accepted vertex ve
rev. 1 to Vol.3 of DAR BY August 2012 @eference. relic@on)
Previous evaluation: yes, evaluated and victopted rev. 1 to Vol.3 of DAR BY August 2012 Orferences relic@on) Image: Constraint of the second seco
testing facilities:
Acceptability/Reliability: Yes Q
Acceptability/Reliability: Yes of a boot of a
🖉 🖉 Leeutive Summery 🌾 🕅
Executive Summary

The metabolism of [pyridyl-2,6¹⁴C]fluopyram, formulated as a SC 500 (Suspension Concentrate), was investigated in Deans following two Dilar spray applications. The applications were performed at growth stages BBCH 51 and BBCH 75) targeting a maximum annual application rate of 500 g a.s./ha. The single application rates were 264.6 g a.s./ha and 234.2 g a.s./ha for the first and the second application, respectively, resulting in a total actual application rate of about 519 g a.s./ha. The immature RACs investigated green beans and foliage were taken four days after the second application. The mature RACs beans ("succulent beans") and straw were harvested 29 days after the last application. A portion of the mature beans were dried for 11 days and were analyzed as chible RAC "dry beans".

The TRR of the edible RACs (green succeivent and dry beans) ranged between 0.17 mg eq/kg and 3.88 mg eq/kg and was considerably lower than those of foliage and straw (38.53 mg eq/kg and 19.02 mg eq/kg, respectively). The major amount of radioactivity (95.7–99.3% of the TRR) was effectively extracted with acetonitrike water from all RACs leaving only minor amounts < 5% with the solids (PES). Parent compound and metabolites in the extracts were quantified by HPLC.

Regarding sampling at a PHI of 4 days, parent compound was detected at levels >90% TRR. In green beans, the parent compound was the only compound detected in the extracts, amounting to 99.3% (3.86 mg eq/kg) of the TRR. The foldage TKR comprised of 92.3% parent compound (35.53 mg eq/kg). Six other metabolites were identified in foliage, none of them exceeding 3.2% of the TRR. Regarding later sampling dates, the major part of the residues in succulent and dry beans consisted of fluopyram-pyridyl-carboxylic acid (PCA,



M43) and -acetic acid (PAA, M40), accounting each for > 20% (0.05–0.10 mg eq/kg) of the TRR. The unchanged parent compound accounted for <6% of the TRR in both RACs (≤ 0.02 mg eq/kg). Six additional metabolites were identified in succulent and dry beans, each accounting for ≤ 0.02 mg eq/kg. In the straw, $^{\circ}$ the residues again comprised of approximately 87% parent compound (19.02 mg cokg). None of the other seven metabolites identified in straw exceeded 4.7% of the TRR/ 0.90 mg eq/kg.

A total of 99.3% of the TRR (3.86 mg eq/kg) was identified in green beaus and 98.9% (38.06 mg bean foliage, 79.8% (0.14 mg eq/kg) of the TRR was identified in succeedent beans, 764% (0.24 mg cg/kg of the TRR in dry beans, and 95.5% (18.15 mg eq/kg) of the TRR in bean straw. Only a few minor mknown components (each < 10% of the TRR and < 0.05 mg/eq/kg) were characterised by their rhromatographic behaviour in foliage, mature beans and straw. Q .

The metabolic reactions involved were:

- Hydroxylation of the ethyl linking group of the a.s. forming hor &- hydroxyl metabolited
- Hydrolytic cleavage and oxidation leading to floopyram by arboxylic seid and fluorgrampyridyl acetic acid, respectively
-yuruxy-metabolites with hexoses and subsequent bigher conjugations with malonic ic acid • Conjugation of hydroxy-metabolites with hexoses and subseq and glucuronic acid

A.	Materials

A. Materials	
1. Test Material:	
Chemical structure	
	# positions of
	O ^v V V radiolabel
	AE C656948
Compound IUPAC name	Ň-{2-[3chloro -(trifluoromethyl)pyridin-2-yl]ethyl}-2-
	(trifluoromethyl)benzamide
CAS name	Benzamide, N-[2-[3-chloro-5-(trifluoromethyl)-2-
	pyridin []ethyl]-2-(trifluoromethyl)-(9Cl)
Radiolabel position	658066-35-4
Radiolabel position	/ Py@dyl-2,6- ¹⁴ C
Specific radioactivity	δ 85 MBq/mg (104.2 μCi/mg)
Purity & V &	> 98% (HPLC)
	> 98% (TLC)
Chamical Furity	> 99% (HPLC)
Specific radioactivity	

2. Soll Monheim 3" (sandy loam from Germany), pH (CaCl₂) = 6.4, 60.7% sand, 26.3% silt and 13.0%



clay, 1.36% organic carbon, 2.34% organic material, cation exchange capacity (CEC) of 5.9 meq/100 gg $^{\circ}$

3. Plant: Bush beans, variety: "Dublette"

B. Study Design

1. Experimental conditions:

e AG, Metar tial sur' lar The bean plants were grown in the vegetation area (building 6682) of Bayer CropScience AG, MetaBolism / Environmental Fate, Monheim, Germany, which allows plant, growth under natural sunlight and temperatures. Approximately 40 bush bean plants (variety, Dublette) were cultivated in a planting container with a surface area of 1.0 m², filled with a sandy loand soil. The plasts were sprayed with pyridy -2,6-¹⁴C]fluopyram formulated as a SC 500 (Suspension Concentrate) and the spraying was performed using a computer controlled track sprayer.

The metabolism study simulated the envisaged use pattern and was based on the maximum proposed application rate (500 g a.s./ha). To compensate losses during applications, 40% excess of a.s. was targeted. Two applications were performed an growth stage BBCH 51 and BBCH 75 (interval 28 days), at actual application rates of 264.6 g a.s./ha/and 254.2 g a//ha, respectively. This resulted in a total application rate of about 519 g a.s./ha.

2. Sampling

Green beans and foliage: As about 50% of the beans kad a harvestable size (BBCH 75; 4 days after treatment), these green beans (who pods) were picked by hand The green beans were cut into small pieces and were homogenised with fiquid nitrogen using an Oltra-Farrax homogeniser. The complete homogenised plant material was used for explaction. At the same growth stage, a representative sample of the leaves (soliage) was cut from the bean plants. The leafonaterial was cut into small pieces and homogenised with liquid nitrogen using an Unra-Turrax homogeniser. An aliquot of the homogenised sample was used for expraction Residual sample material was stored in aliquots at *ca.* -20 °C.

Succulent beans and straw: At maturity (BBCH code 85-89, 29 days after last treatment), beans in their pods were cut from the plant and the succolent beins were picked from the pods. The pods were united with the rest of the plants, which were cut above the soil (straw fraction). The succulent beans were directly homogenized with liquid nitrogen using an Ultra-Turfax homogeniser. The straw fraction was processed in the same way after being cut that small pieces. A representative aliquot of the homogenised samples was used for extraction. Residual sample material was stored in aliquots at ca. -20 °C.

Dry beans: At maturity (BBCH code 89) beans of pods, which had already dried on the plant, were cut from the plant, and the beans were picked from the pods by hand. The pods were united with straw fraction. The beans were allowed to dry at room temperature until no loss of weight *(i.e.* water loss) was measured (11 days). A representative aligned of the dry beans was allowed to soak overnight with water and was used for extraction. The rest of the dry beans were stored at ca. -20 °C.



C. Analytical Procedures

The bean RACs were extracted and the extracts were analysed by HPLC and TLC. The identification of parent compound and metabolites was based on co-chromatography experiments and PPLC-MS/MS and/or LC-NMR.

1. Extraction and fractionation:

In general, samples of the bean RACs were extracted 3 times with a mixture of acetonitrile/water (8/2) using an Ultra-Turrax. The extracts were separated from the solids becentrifugation. The radioactivity the extracts was determined by volume measurement and LSC, The solids (PES) over lyophilised overnight, homogenised and weighed. Aliquots thereof were compused and measured for radioactively LSC. Aliquots of the combined solvent extracts were concentrated using a Speedvag

The 14C-radioactivity of liquid samples was determined by Aquid Seintillation conting (LSC) using Quicksafe A containing 5% of water. The radioactivity in solid samples was measured by combustion. The released 14CO2 was absorbed in an alkaline sontillation cocktail and radio assayed by LSC

6 The total radioactive residues (TRR) in the RACs of beans were determined by symmation of the radioactivity in the combined acetoo trile water entracts and in the PES The residue levels are expressed as parent compound equivalents per weight. The concentrated acetonitile/water extracts were analysed by HPLC for quantification of metabolites?

2. Identification and characterisation: The identification of most metabolites in the bean RACs was based on identified metabolites gained from the bean follage. These metabolites were isolated from the concentrated extracts of the foliage by semipreparative HPLC and identified by HPLC-MS/MS and/or JC-NMR. Co-chromatography (HPLC, TLC) with authentic reference compounds, with the identified fourage notabolites, with metabolites isolated and identified in a supplemental cell culture study or a metabolism study in the rat using the phenyl label was performed to identify corresponding motabolities in the extracts of succulent and dry beans as well as in straw. Confirmation of these assignments was obtained after isolation of the major compounds out of the acetonitrile/water extract of succulent and dry beans by semipreparative HPLC. Corresponding fractions were combined, concentrated, polified in one of the secondary HPLC systems, and analysed by LC-NMR and/or HCC-MS/MS

3. Storage stability:

The RACs were extracted and applysed within a few days after sampling. All samples were stored at temperatures ≤ -18 °C. A few days after extraction, the earliest metabolite profiles of the combined extracts were obtained by HPLC using the profiling method for quantitation and identification of metabolites.



II. Results and Discussion

The TRR amounted to 3.88 mg eq/kg in green beans, 38.53 mg eq/kg in the corresponding foliage 0.17 mg eq/kg in succulent beans, 0.31 mg eq/kg in dry beans, and 19.02 mg eq/kg in bean straw (Table 6.2.1-17). The TRR of the edible RACs (green, succulent and dry beans) was significantly lower of than those of the corresponding foliage or straw.

Applic. No. and timing, total dosc wo foliar spray applications: t growth stages BBCH 51 and BBCH 75: wo foliar spray applications. t orouth stages BBCH 51 and BBCH 75: wo foliar spray applications.
t growth stages BBCH 55 and BBCH 75: otal 519 g a.s./ha
wo foliar spray apples ations: A 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
otal 519 g a.s./ha
Two foliar sprace applications: 0 ⁻⁴ t growth stages BBCH 51 and BBCH 75; 4 ⁻⁴ otal 519 g a.s./ha ⁻⁴
wo foliar spray applications: t growth stages BBCH 51 and BBCH 75; otal 519 gas./ha 0.31
wo foliar spray applications: t growth stages, BBCH 31 and BBCH 35; 29 19.02 otal 519 g a.s./ha

The bean matrices were extracted with $\frac{1}{2}$ wi

Nearly the complete radioactive residues in green beans, 99 3% (3.86 mg eq/kg) of the TRR, was extracted by acetonitrile/water (Table 6.2.1-18), whereas 0.7% (0.05 mg eq/kg) of the TRR remained in the solids (PES). Nearly the complete radioactive residues in bean foliage, 99.1% (38.14 mg eq/kg) of the TRR, was extracted by acetonitrile/water (Table 6.2.1-18) leaving only 1.0% (0.39 mg eq/kg) of the TRR in the solids (PES). The majority of the radioactive residue in socculent beans, 97.6% (0.170 mg eq/kg) of the TRR, was extracted by acetonitrile/water (Table 6.2.1-18), whereas 2.3% (< 0.01 mg eq/kg) of the TRR remained in the solids (PES). The majority of the radioactive residue in dry beans, 97.4% (0.300 mg eq/kg) of the TRR, was extracted by acetonitrile/water (Table 6.2.1-18), whereas 2.6% (< 0.01 mg eq/kg) of the TRR remained in the solids (PES). The majority of the radioactive residue in dry beans, 97.4% (0.300 mg eq/kg) of the TRR, was extracted by acetonitrile/water (Table 6.2.1-18), whereas 2.6% (< 0.01 mg eq/kg) of the TRR remained in the solids (PES). The majority of the radioactive residue in dry beans, 97.4% (0.300 mg eq/kg) of the TRR, was extracted by acetonitrile/water (Table 6.2.1-18), whereas 2.6% (< 0.01 mg eq/kg) of the TRR remained in the solids (PES). Due to the low radioactive residue, the solids (PES) from all matrices were not further investigated.



	Distribution of radioacti application of [pyridyl-2,6 Green beans Foli			iage	AE 656948 Succulent beans		Dry beans		Straw		
TRR [mg eq/kg] =	3.3	88	38.53		0.17		0.31		<u>9</u> .02 5		
	% of TRR	mg eq/kg	% of TRR	mg eq/kg	% of [®] TR R	mg eq/kg	% of TARK	mg eq/kg	& of	, "A	
Acetonitrile/water extract	99.3	3.86	99.1	38.14	\$97.6	0.170	97 4	0.369	9 5.7	18.20	
Solids (PES)	0.7	0.03	1.0	0.\$9	ٌ گھ3	0.003	× 2.6	, % .008 °	4.3	0.89	7
Total extracted	99.3	3.86	99.1	38.14	\$ 97.6	03003 ©0.170 07570	۶ 97%	0.300	2 5.7	18.20	o
Accountability	100.0	3.88	100.0	38.53		0%70	100.0	3 10	©″ 100.0≰	§ 19.02	1

For the elucidation of metabolites, the solvent extracts (acetonitrie/water) were analysed by &PLC and, where required, also by TLC with radiodetection. Metabolites were either identified by co-chromatography (HPLC, TLC) with reference compounds or isolated metabolites on by LOMS/MS and/or LC-NMR of isolated peaks.

Green beans and foliage The papent compound 99.3% of the TRR, \$ 86 mg eq/kg was the only component detected in the extract of green beans (Table 6.2.1-19) and ut was the predominant residue also in the extract of foliage (92.3% of the TRR, 35,53 mg eq/kg). in the concentrated extracts of foliage was also detected the glucoside-matonic acid conjugate duopyram-7-hydroxy-glc-MACM12, occurring at 3.2% of the TRR, 1.22 mg eq/kg. In addition, the metal@lites(fluopyram-7-hydroxy) M08, 1.6% of the TRR, 0.60 mg eq/kg), fluopyram-7% hydroxy-glc (M11, 0%% of the TRK, 0.25% ng eqRg), floopyram-8-hydroxy (M18, 0.5% of the TRR 0.21 mg eq/kg), fluopyram pyridyl-earboxylic acid (0.5%, 0.19 mg eq/kg) and AE C656984hydroxyethyl-glyc (0,2% of the TRR, 0.06 mg eq/kg) were identified (Table 6.2.1-19). Furthermore, one unknown minor compound (0.2% of the fRR, 0.08 mg eq/kg) was characterised in foliage by extraction and chromatographic behaviour @

Succulent beans: The man metabolites in the concentrated extract of succulent beans were fluopyrampyridyl-carboxylic acid (PCA, 1943, 3, 10% of the TRK, 0.054 mg eq/kg) and the fluopyram-pyridyl-acetic acid (29.5% of the TRR, 0.051 mg eq/kg), whereas the parent compound was 4.8% (0.008 mg eq/kg) of the TRR. The metabolite identified as glocuronic acid-glycoside conjugate of the hydroxylated parent compound (fluopyram-hodroxy, glyc-gluc) accounted for 4.5% (0.008 mg eq/kg) of the TRR. The metabolites AF@6556948-7-Hydrox @(4.0% of the TRR, 0.007 mg eq/kg) and 8-hydroxy (2.7% of the TRR, 0.005 mg endig) were also detected in succulent beans. The minor metabolite fluopyram-pyridylhydroxyethyl-glyc, was also identified (19% of the TRR, 0.003 mg eq/kg). Conjugates of the 7-hydroxy metabolite were identified and accounted for < 0.01 mg eq/kg (Table 6.2.1-20). Furthermore, two unknown compounds (each < 5% of the TRR and \leq 0.007 mg eq/kg) and a multiple metabolite fraction, containing higher conjogates the fluopyram-7-hydroxy-glc-MA (11.7%, 0.020 mg eq/kg), were characterized based of their extraction and mromatographic behaviour.

Ô



Dry beans: Major metabolites detected in the acetonitrile/water extract were fluopyram-pyridyl- carboxytic acid (32.5% of the TRR, 0.100 mg eq/kg) and fluopyram-pyridyl-acetic acid (22.6% of the TRR, 0.076 mg eq/kg). Parent compound was detected as minor component and accounted for 5.7% of the TRR (0.008 mg eq/kg). The metabolite fluopyram-hydroxy-glyc-gluc was also identified and accounted for 5.6% (0.007 mg eq/kg) of the TRR. The metabolites fluopyram-7-hydroxy and 8-hydroxy accounted for 4.0% (0.012 mg eq/kg) of the TRR and 1.6% (0.005 mg eq/kg) of the TRR, respectively. Also, the corresponding very minor metabolite fluopyram-7-hydroxy-glc was detected (1.2% of the TRR 0.004 mg eq/kg). fluopyrampyridyl-hydroxyethyl-glyc was also identified (3.1% of the TRR, 0.010 mg eq/kg).

Additionally, four unknown components (each < 5% of the TRR and < 0.05 mg co/kg) and a montple metabolite fraction (12.1% of the TRR, 0.037 mg eq/kg), containing higher conjugates like fluopyram, why droxy-glc-MA, were characterised by extraction and chromatographic behaviour.

Straw: The parent compound fluopyram (87.1% of the TRR, 16.56 ng eq/kg) was the predominant residue also in the extract of straw. As observed in inimature foliage, the main metabolite in the concentrated extract of straw was the fluopyram-7-hydroxy glc-M/x (4.7% of the TRR, 0.90 ng eq/kg). Other identified metabolites were fluopyram-7-hydroxy (1.1% of the TRR, 0.20 ng eq/kg), fluopyram-8-bydroxy (0.9% of the TRR, 0.17 mg eq/kg), fluopyram 4-hydroxy-glc (0.7% of the TRR, 0.04 mg eq/kg), fluopyram-pyridylcarboxylic acid (0.6% of the TRR/0.11 ng eq/kg), fluopyram-pyridylacetic acid (0.2% of the TRR, 0.04 mg eq/kg) and fluopyram-hydroxy-glyc-glac (0.2% of the TRR, 0.03 mg eq/kg; Table 6.2.1-20). Additionally, one unknown compound (0.3%, 0.06 mg eq/kg) was characterized based on its extraction and chromatographic behaviour

	spru, spru		,° , 1	1.
	Seen	beans 0	Foli	age
TRR [mgg/kg] = 0	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		38	.53
Compound	\sim of the \sim TRR	ر شکام eq/kg	% of the TRR	mg eq/kg
AE C656948, parent fluopyram fluopyram-8-hydroxy (M18) fluopyram-7-hydroxy (M98) fluopyram-7-hydroxy-glc, M11)	\$99.3 S		92.3	35.53
fluopyram-8-hydroxy (M180	× -~	-	0.5	0.21
fluopyra@7-hydroxy (M408)		-	1.6	0.60
fluopyram-7-hydroxycelc-MA (M12)	, ~ ~ ~ ~	-	3.2	1.22
fluopyram-7-hydroxy-glc(M11)	Ş ⁷ -	-	0.6	0.25
fluopyram-hydroxyethyl-glyc M35)	-	-	0.2	0.06
1 Iluopyram for idvl-carboxy acid (M43) @	-	-	0.5	0.19
Total identified	99.3	3.86	98.9	38.06
unknown 1 (907)	-	-	0.2	0.08
Aptal characterised	-	-	0.2	0.08
Tota	99.3	3.86	99.1	38.14

 Table 6.2.1-19:
 Summary of characterisation and identification of radioactive residues in green beans

 and bean foliage after foliar spray application of [byridy12,6-UL-14C]fluopyram

1



Solids (non-extractable residue)	0.7	0.03	1.0	0.39 ° ~
Accountability	100.0	3.88	100.0	38.53
			<u>A</u>	

Summary of characterisation and identification of radioactive residues in succulent Beans, Table 6.2.1-20: dry beans and bean straw after foliar spray application of pridyl-2,6-14Cffluopscam

Succulent beansDry beansStrawTRR [mg eq/kg] = 17 0.31 19.02 Compound% of the rRRmg eq/kg% of the rRRmg eq/kg% of the rRRmg eq/kgAE C656948, parent fluopyram fluopyram-8-hydroxy (M18) fluopyram-7-hydroxy-glc-MA (M12) 4.9 4.9 0.005 4.0 10 0.005 0.012 10 10 0.012 0.12 10	
Compound % of the TRR mg eq/kg % of the TRR mg eq/kg % of the TRR mg eq/kg % of the TRR mg eq/kg % of the the the the the the the the the the	, U , Y
Compound mg eq/kg mg <th< th=""><th></th></th<>	
fluopyram-8-hydroxy (M18) 0	
fluopyram-7-hydroxy (M08) $(10^{\circ})^{\circ}$ (10°)	
fluopyram-7-hydroxy (M08) $(10^{\circ})^{\circ}$ (10°)	
fluonyram 7 hydroxy glc MA (M12) \Im \Diamond \Diamond \Diamond \Diamond \Im \Im \Im \Im \Im	
fluopyram-7-hydroxy-glc (M11)	
fluopyram-hydroxy-glyc-gluc@M22)	
fluopyram-pyridyl-acetic acid (M40)	
fluopyram-pyridyl-hydroxyethy@glyc (1435)	
$\int \frac{1}{1000} \int \frac{1}{1000} \int \frac{1}{1000} \int \frac{1}{1000} \int \frac{1}{10000} \int \frac{1}{10000} \int \frac{1}{10000} \int \frac{1}{100000} \int \frac{1}{10000000000000000000000000000000000$	
Total identified 79.8 0.138 96.4 95.5 18.15	
unknown 6 (ST 6) $\sqrt[6]{2}$	
multiple metabolite fraction - <td< td=""><td></td></td<>	
unknown 5 (DB 7)	
unknown 4 (DB 5) 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	
unknown 4 (DB 3) 23 23 0.004 $-$ unknown 3 (SB4, DB 2) 23 23 0.007 2.6 0.008 $-$ unknown 2 (SB 2, DB 2) 2 23 0.007 3.4 0.011 $-$	
Total characterised	
Total extracted 7	
Total bound residues (PES) Q </td <td></td>	
Accountability 100.0 0.170 100.0 0.310 100.0 19.02	

[#]Region of approximately 10 factions including bigher conjugates like AE C656948-7-hydroxy-glc-MA III. Conclusions

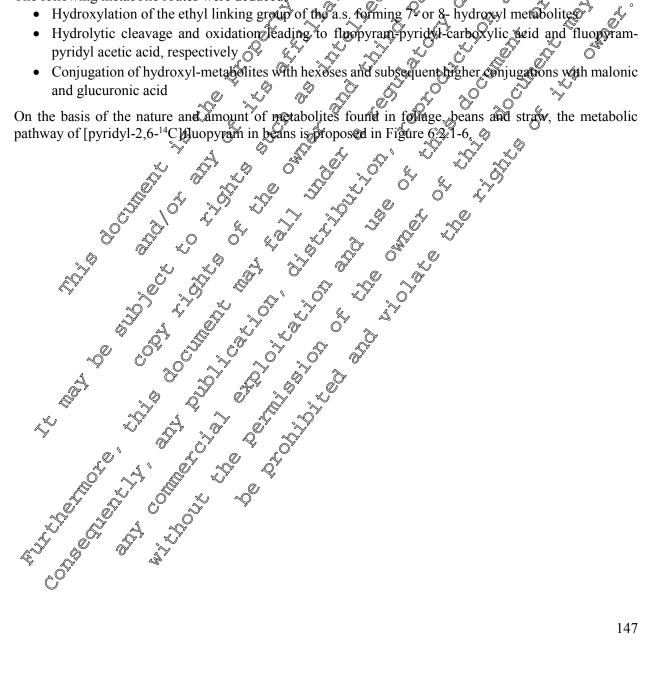


After two foliar spray applications of [pyridyl-2,6-UL¹⁴C]fluopyram amounting a total of about 519 g/aa, most of the recovered radioactivity was detected in foliage (38.53 mg eq/kg) and straw (19.02 mg eq/kg). whereas significantly less were detected in the respective bean samples (3.88 mg %/kg for green beans, 0.17 mg eq/kg for succulent beans, and 0.31 mg eq/kg for dry beans).

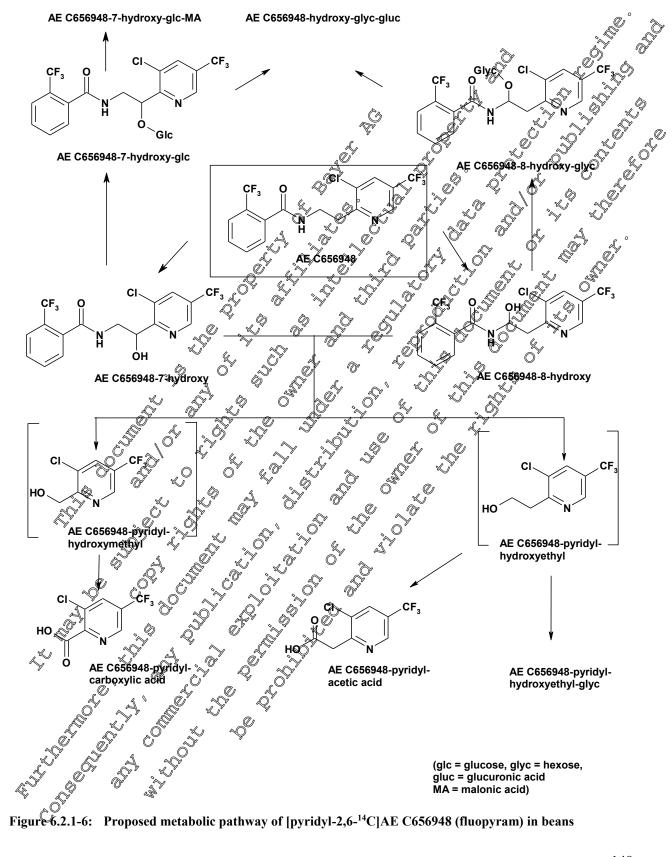
Unchanged parent compound was the predominant portion of the TRR in foliage, straw and green beans, accounting for more than 80% of the TRR, and was still present (< 10% of the TRR and < 0.1 mg cq/kg) in bean samples at maturity. In total, eight metabolites were identified. The major metabolite, in bean samples at maturity (succulent and dry) was fluopyram-pyridyl-carboxylic acid (PCA, M43, 20% of the TRR) followed by fluopyram-pyridyl-acetic acid (PAA, M49, >20% of the TRR). In other bean matrice identified metabolites accounted generally for < 10% of the TRR.

The following metabolic routes were deduced:

- or & hydroxyl metabolite • Hydroxylation of the ethyl linking group of the a.s. forming R
- Hydrolytic cleavage and oxidation leading to flappyran pyridyl-carboxylic acid and fluor ram-
- er Snjugaons with malonic









Assessment and conclusion	on by applicant:
The study is valid and acce	ptable.
Aetabolism in red pepp Aetabolism studies in red	er (drip application) I peppers were conducted with whenyl-UL- ¹⁴ C [fluopyram: KCA 6.2.1/07 KCA 6.2.1/07 Metabolism of phenyd 9L-14C (AE 60 5948 of red peper atte drip upplication) MEF-06/31 0 MEF-06/31 0 MESPA 0PPT \$60.13(0); Can Otian P&RA R.O: DAC 96.3; Chanes MIAFF, 12 Nousce \$147, EU 91/444/EEC amenuated by 968/EC
Data Point:	KCA 6.2.1/07
Report Author:	
Report Year:	
Report Title:	Metabolism of phenye-VL-14(AE C6)6948 or red pepper after drip application
Report No:	Metabolism of pheny- (#L-14) (#AE \$ 0,00948) red pepper al \$ drip topical \$ 0 MEF-06/31 (O M-298796 01-1 US EPA OPPT \$ 60.1300; Can@tian PorkA R O: DAG \$ 6.3; Spanes MAFF, 12 Nousce 8147 [U 91/414/EEG amenged by 968/ECO non
Document No:	MEF-00(3) M M-298796/01-1 M US EPA OPPT\$260.13(20); CanQtian PARA RO: DAG 6.3; Opanes; MAFF, 12 Nousco 8147; EU 91/44/EE; Amen(QI by 96/8/EC) 0
Guideline(s) followed in	US EPA OPPT 260.13(2); Canonian PSRA RO: DA 6.3; Spanese MAFF, 12 Nouse 8147, EU 91/44/EES amene Co by 96/88/EC
study:	Nouse 8147 FU 91/44/EE Sumer Cu by 96 88/ECO
Deviations from current	
test guideline:	
Previous evaluation:	
GLP/Officially recognized	Ye9 conducted up der GLK officially recromised testing facilities
testing facilities:	Ly BY A D' J B O A
Acceptability/Reliability:	Pres in the second seco
	Yes Yes

The metabolism of pheny UL^{-1} fluop ram, tormulated as a SC 500 (Suspension Concentrate), was investigated in red pepper following one drip application. The experimental design reflected the soil-less cultivation of vegetables in the green buse. For the envisaged use pattern and according to agricultural practice, one application was performed using 5 mg a.s./plant (1X experiment). Additionally, an exagerated dose experiment was conducted using 20 mg a.s./plant (4X experiment). The applications were performed at growth stage BBCH 15–17.

A plant at an intermediate prowth stage BBCH 61 – first flower open) was harvested from the 4X experiment B days after application. Ripe fruits were picked from the 1X experiment at three time points (BBCH 89 – fully ripe). The remaining plants were sampled after the third harvest of fruits (BBCH 89).

The TRR of the etable R/AC (pepper fruits) from the 1X experiment accounted for 0.038 mg eq/kg and was considerably lower than that of the rest of the plant (3.540 mg eq/kg). In the 4X experiment a TRR of 6.24 mg eq/kg was found in the intermediate plant. The major amount of radioactivity (96.2–98.5% of the



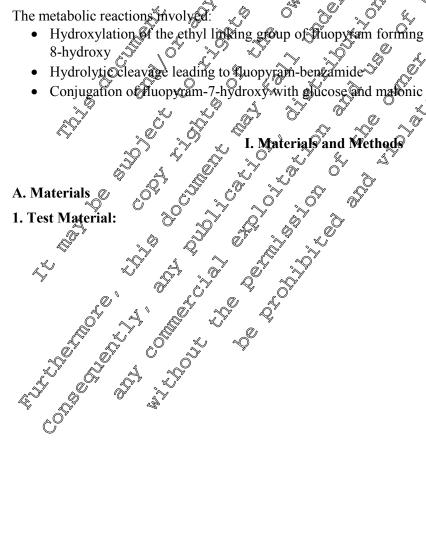
TRR) was effectively extracted with acetonitrile/water from all RACs leaving only minor amounts < with the solids (PES). Parent compound and metabolites in the extracts were quantified by HPLC.

In pepper intermediate, the parent compound was most abundant compound, amounting to 85,8 (5.400 mg eq/kg) of the TRR. Additionally, four metabolites were identified from of them exceeding 4% (2) of the TRR. The pepper fruit TRR is comprised of 48.9% (0.019 mg eq/kg), parent compound. Other three metabolites were identified in fruits, of which the most abundant was fluopyram-benzamide (160%, 0, 906 mg eq/kg), followed by fluopyram-7-hydroxy (9.0%, 0,003 mg eq/kg) and the corresponding conjugate O fluopyram-7-hydroxy-glc (3.9%, 0.001 mg eq/kg). The major part of the residues in plants after harvest consisted of parent compound fluopyram, accounting for 64.0% (2.266 mg et kg), of the TRR. Elve metabolites were identified in the rest of the pepper plants, of which the most abundant was fluor grambenzamide, accounting for 10.1% (0.358 mg Q/kg) of the PRR. None of the other five metabolites identified in the rest of the plants exceeded 8,9% of the TRR

A total of 97.4% of the TRR (6075 mg/kg) was identified in peppe interfediate 77.8% (0.030 mg eq/kg) of the TRR was identified in pepper fruits and 90.9% (\$219 mg eq/kg) of the TRR was identified in pepper plants after harvest. Only a few minocunknown components (each 218.4% of the TRR and ≤ 0.007 mg eq/kg) were characterised by their chrophatographic behavious in perper intermediate plant, pepper fruits and plants after harvest

The metabolic reactions involved

- Hydroxylation of the ethyl linking group of Ruopy am forming thropyram -7-hydoxy or fluopyram-
- 8-hydroxy Hydrolytic cleavage leading to Quopyram-benzamide Conjugation of Huopyram-7-hydroxy with glucose and matonic acid





Chemical structure	CF ₃ O + Positions of radiolabel
Compound	AE C656948
IUPAC name	N-{2-[3-chloror5-(trifluorome@vl)pyridin-2%]eth@-2- (trifluoromet@vl)pyridin-2%]eth@-2- (trifluoromet@vl)pyridin-2%]eth@-2%]eth@-2%]eth@-2%]eth@-2%et@-2%]eth@-2%]eth@-2%[eth@-2%]eth@-2%]eth@-2%]eth@-2%]eth@-2%]eth@-2%]eth@-2%]eth@-2%[eth@-2%]eth@-2%]eth@-2%]eth@-2%]eth@-2%]eth@-2%]eth@-2%]eth@-2%]eth@-2%[eth@-2%]eth
CAS name	N-{2-[3-chloror5-(trifluoromethyl)pyridin-2-y1]ethyl-2- (trifluoromethyl)benzamide Benzamide V-[2-[3-chloror5-(trifluoromethyl)c2- pyridinyl]ethyl]-2-(trifluoromethyl)-(9Ct) 658066225.4
CAS #	
Radiolabel position	Phenyl-UL AC O O O A A
Specific radioactivity	2.85 MBg/mg (104.2 pCi/mg)
Purity Chemical Purity	S 99% (HPL€) S 99% (TE€) S 29% (TE€) S 29% (TE€)
	>99% (HPLC) *** *** ***

2. Substrate: Soil-less on Grodan[®] growcubes in stabs of stonewool substrate

The red pepper plants were grown our the greenhouse of Bayer CropScience AG, Metabolism / Environmental Fate, Monheum, Germany, which allows plant growth under natural sunlight and temperatures. The plants were cultivated without soil on stonewool substrate (Grodan® Growcube, Grodan BV, Roermond, The Netherland Faccording to professional horticulture. Each plant was grown in one cube of Grodan® Growcube and three cubes were places together into a slab of the same material. The slab was kept in a box (container). The plants were rrigated and fertilised with a mix of a fertilizer on nitrate basis and a commercially available intrient solution using a dripping system. A defined volume of nutrient solution was applied per plant daily. Due to the good water-retention properties of the stone wool substrate, the water content in the cubes was between 50% and 55% during the whole cultivation period. Uptake and delivery of nutrients was in a balanced state and only an excess of nutrient solution was drained into a bottle.

The radiolabelled active substance was formulated as a Suspension Concentrate (SC 500). For the 4X experiment, the radio abelled test item was diluted with non-radiolabelled test item (ratio 1/1, w/w) prior to formulation. The application conditions of the 1X experiment simulated the anticipated use pattern for professional hortreulture with 5 mg a.s./plant. The additional 4X overdose experiment was performed to support identification of metabolites. The application suspensions were prepared by diluting the formulations for the 1X experiment and the 4X experiment with water. The formulation was applied at



growth stage BBCH 15–17 (fifth to seventh leaf of the main shoot unfolded). A portion of 100 mL of application suspension were poured to each plant. One day prior to application and one day after the dripping of the nutrient solution had been stopped in order to allow the complete uptake of the application suspension. The application solution was not drained and was quantitatively available for the plant for a long time period.

2. Sampling

Pepper intermediate (immature plant): One immature plant (intermediate plant) in the 4X texperiment was harvested 33 days after application at developmental stage BBCH 67 (first flower was open). The plant was collected with its cube. The cube was removed by cutting the plant slightly above the stone wool surface. The weight of the sample was determined and the plant was but into pieces and honogenised with liquid nitrogen using an Ultra-Turrax homogeniser. The complete homogenised plant material was used for extraction.

<u>Pepper fruits</u>: At maturity (BBCH 89), pepper fruits were picked from the plans at three harvest dates. The fruits of the first and second harvest were stored in a freezer. At the day of the third parvest the fruits of the three samplings were combined and homogenised with liquid nitregen using an Ultra-Turfax homogeniser. A representative aliquot of the homogenised sample was used for extraction. Residual sample material was stored in aliquots at ≤ -18 °C.

<u>Pepper plants after harvest</u>: One day after the fast pepper trait has been sampled, the rest of the plants (BBCH 89) were cut above their cubes. The plants were cut into smaller pieces using scissors. The plant parts from the 4X experiment were stored in a freezer for optional analysis, whereas the plant parts of the 1X experiment were bornogenised with liquid nitrogen using an Ultra-Turrax homogenised. A representative aliquot of the homogenised sample from the 1X experiment was used for extraction. Residual homogenised plant material was stored in aliquots at ≤ 18 °C.

C. Analytica Procedures

The pepper RACs were extracted and the extracts were analysed by HPLC and TLC. The identification of parent compound and metabolities was based on co-chromatography experiments and HPLC-MS/MS and/or LC-MR.

1. Extraction and fractionation:

In general, samples of the pepper RACs were extracted three times with a mixture of acetonitrile/water (4/1, v/v) using an Oltra-Turrax homogeniser. The extracts were separated from the solids by centrifugation. The radioactivity of the extracts was determined by volume measurement and LSC. The radioactivity in the solids (PCS) was determined by combustion followed by LSC. Aliquots of the combined solvent extracts were concentrated using a rotary evaporator.



The ¹⁴C-radioactivity of liquid samples was determined by liquid scintillation counting (LSC) using $\sqrt[3]{2}$ Quicksafe A containing 5% of water. The radioactivity in sold samples was measured by combustion. The released ¹⁴CO₂ was absorbed in an alkaline scintillation cocktail and radio assayed by LSC.

The total radioactive residues (TRR) in the RACs of peppers were determined by summation of the radioactivity in the combined acetonitrile/water extracts and in the PES. The residue levels are expressed of as parent compound equivalents per weight. The concentrated acetonitrile/water extracts were analysed by HPLC for quantification of metabolites.

2. Identification and characterisation:

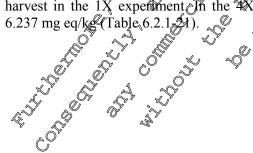
The identification of parent and metabolites in the pepper RACs was based on co-chromatography GIPLC, TLC) with authentic non-radiolabelled reference compounds or with metabolites isolated and identified in the plant study conducted with [pyricy1-2,6-¹⁴C]fluopyram in beaps (M-29906721-1).

3. Storage stability:

Pepper intermediate (4X) and pepper plants (1X) were extracted and analysed within a day after sampling. Pepper fruits (1X) were harvested at three sampling dates. The fruits of the first by sampling dates were stored in a freezer unfit the last sampling date. On the day of the last sampling, the fruits were combined and extracted. The pepper fruits were stored for a maximum of 42 days prior to sample preparation. Quantitative analysis followed within a day. Thus, the metabolite profiles of all sample extracts were recorded in a minimum time frame, not exceeding 42 days after sampling.

The metabolism of [phenyl-US-¹⁴Clftdiopyram, formulated as a SC 500 (Suspension Concentrate), was investigated in red propers following one drip application? I we experiments were performed at single rates of 5 mg a.s.(plant (1X experiment) and 20 mg a.s./plant (4X experiment).

The TRR amounted to 0.038 mg early in the pepper fruits (edible RAC) and 3.540 mg early in plants after harvest in the 1X experiment. In the 4X experiment the TRR of the intermediate plant accounted for 6.237 mg early g (Table 6.2.1.21).





Matrix	Timing and Applic. No.	PHI	TRR (ppm,
		(days)	TRR (ppm, mg.a.s. equiv./kg)
D			
Pepper	One application:		
intermediate	at growth stages BBCH 15–17	33 🔬	6.237
(BBCH 61)	1 x 20 mg a.s./plant (4X experiment)	" <i>"</i> "	
Pepper	One application:	Ű	
fruits	at growth stages BBCH 15–17	55-96	0.038 × ×
(BBCH 89)	1 x 5 mg a.s./plant (1X experiment)	4	
Pepper plants	One application:		
after harvest	at growth stages BBCH 15–17	∽ 9/@ř	§ .540
(BBCH 89)	1 x 5 mg a.s./plant (1X experiment)	O N a	

The pepper matrices were extracted with acetonitril water (4:1; x/v), the extracts were analysed by HPLC and, where necessary, TLC and parent compound and metabolities were identified.

Nearly the complete radioactive residues in pepper internediate plant, 98,5% (6,141 mg/eq/kg) of the TRR, was extracted by acetonitrile/water (Table 6.2.1-22), leaving only 1.5% (0.090 mg/eq/kg) of the TRR in the solids (PES). The majority of the radioactive residues in pepper fruits, 96.2% (0.037 mg/eq/kg) of the TRR, was extracted by acetonitrile/water (Table 6.2.1-22), while 3.8% (0.001 mg/eq/kg) of the TRR remained in the solids (PES). The majority of the radioactive residue in the plants after harvest, 96.3% (3.410 mg/eq/kg) of the TRR remained in the solids (PES).

Table 6.2.1-22: _▲ ○	Distribution of radioac	tivity in the ext	racts of the bep	per matrices after	drip application
Ŏ,	Distribution of radioac of phenyl-9UL-14CAE	656948	~ ~ ~ · · ·	· *	1 11

			ntermediate periment)	Pepper (1X exp	r fruñts eriment)	Pepper pl harv (1X expe	vest
TRR $[mg eq/kg] =$	\sim	L 🕺 🔬 6	.237	0.0	38	3.5	40
	8	% of ARR	, y mg/kg	% of TRR	mg/kg	% of TRR	mg/kg
Acetonitrile/water	extra		5	96.2	0.037	96.3	3.410
Solids 1 (PES)	^o ov		5 0 0.096	3.8	0.001	3.7	0.130
Total extracted	Ű,	S S8.	5 6 6 41	96.2	0.037	96.3	3.410
Accountability	<i>.</i>	100 .	a	0 100.0	0.038	100.0	3.540
la l	\$ Q	^o		ý l			

For the elucidation of metabolism the solvent extracts (acetonitrile/water) were analysed by HPLC and, where required, also by TLC with radiodetection. Metabolites were identified by co-chromatography (HPLC, TLC) with reference pompoinds of isolated and identified metabolites.

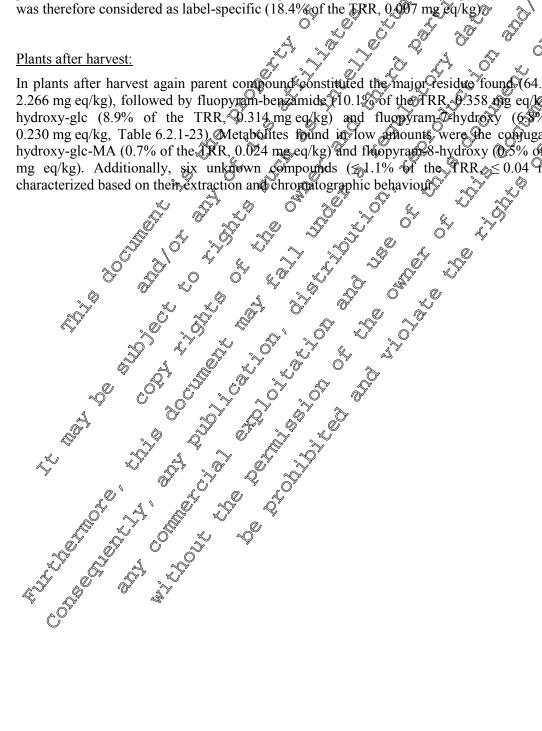
<u>Pepper intermediate</u>: The parent compound (86.6%, 5.400 mg eq/kg of the TRR) was the predominant residue Beside the parent compound, the following metabolites were detected in the intermediate sample in low amounts (5% of TRR): fluopyram-benzamide, fluopyram-7-hydroxy, fluopyram-8-hydroxy and the conjugate fluopyram-7-hydroxy-glc (Table 6.2.1-23). Furthermore, three unknown minor compounds



 $(\leq 0.7\%, \leq 0.047 \text{ mg eq/kg})$ were characterised in the intermediate plant by extraction and chromatographic Ś behaviour.

Pepper fruits: The main residue in the concentrated extract of pepper fruits was the parent composited fluopyram (48.9% of the TRR, 0.019 mg eq/kg). The main metabolite detected in pepper fruits was @ fluopyram-benzamide (16.1% of the TRR, 0.006 mg eq/kg). Minor merabolites found in fruits were fluopyram-7-hydroxy (9.0% of the TRR, 0.003 mg eq/kg) and the conjugate fluopyram-7-hydroxy glc (3.9% of the TRR, 0.001 mg eq/kg) (Table 6.2.1-23). Furthermore, a compound was detected eluting early O from the column. The early elution time in the reversed phase system characterises the substance as very polar. The substance was not detected in the parallel study conducted with pyrid \$2,6-16]fluopyram and was therefore considered as label-specific (18.4% of the TRR, 0.907 mg/q/kg)

In plants after harvest again parent compound constituted the major residue found (64.0% of the TRR, 2.266 mg eq/kg), followed by fluopyram-benzamide 10.1% of the TRR, 9.358 mg eq/kg), fluopyram-7hydroxy-glc (8.9% of the TRR, \$0.314 mg eq/kg) and flugpyram-Phydroxy (6.9% of the TRR, 0.230 mg eq/kg, Table 6.2.1-23) Metabolites found in low prounts, were the conjugate fluopyram-7hydroxy-glc-MA (0.7% of the JKR, 0.024 mg eq/kg) and fluopyram 8-hydroxy (0.5% of the TRR, 0.018 mg eq/kg). Additionally, six unknown compounds ($\leq 1.1\%$ % f the TRR ≤ 0.04 mg eq/kg) were characterized based on their extraction and chromatographic behaviour $\leq 2.5\%$





	intern	oper nediate eriment)		r fruits eriment)	Pepper after h (1X exp	arvest	
TRR $[mg eq/kg] =$	6.2	237)38 ,4	3.5	49° , 55°	
Compound	% of the TRR	mg eq/kg 🔊	⊘% of the [™] TRR	ntg sej/kg	% of the TRR	nag eq/kg	, V
AE C656948, a.s.(Fluopyram)	86.6	5.400	48.9	0 0.019	64.0	<u>2.266</u>	-
fluopyram-benzamide (M25)	3.8	0,235	16.1	0.006	0.1 ×	0.356	
fluopyram-7-hydroxy-glc-MA (M12)	-	0- ¹	- ~	¢°.	∱\$ 0.7 <u>√</u>	0.024	а С
fluopyram-7-hydroxy-glc (M11)	2.7	[∞] 0.171	39	s 9.001 °	× 8,90 [×]	@.314	,Y
fluopyram-7-hydroxy (M08)	3.8	0.23	, N .0 z	0.003	<u></u>	≫0.23 9 ≶	
fluopyram-8-hydroxy (M18)	0.6 🔘	Q:034	õ - Ä	~0°	\$0.5	0.018	
Total identified	97-4	<i>°</i> %.075 «	ĭ 77₄Q	0.030	90.8	3219	, 0
unknown 1	~~ . ^	× - ×	28.4	A0.0076	-	\$ - Ø	¥
unknown 2	Ø - X	í "Qí	<u>م</u> - رُ		Ø.7 🔬	0.024 0.038	
unknown 3	}× -&,×	. ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	S - S	õ,	O ^V 1.1 S		
unknown 4	<i>©</i>	°~y" - 🔍	\sim	N- 5	0,6	Q.023	
unknown 5	\$0.1 ¢	0.007	<u>s</u>	م - ک	Q07 .	∞0.026	
unknown 6	N° - O°	S.	e - 4	8	0 ^{1.1}	0.040	
unknown 7	0,7×	0.047	1 <u>-</u> 04	-	OF 1.1%∕	0.040	
unknown 8	<u>6/2</u>	∽y 0.012 ₂	~~	`√` - <i>©</i>		-	
Total characterised	\$1.1 ×	0.066	18.4	× 0.007	\$.4	0.191	
Total extracted	98,5	61 41	S 96,2 [~]	0 <u>x0</u> 37 4	96.3	3.410	
Total bound residues (PES)	1.5	0.096	3.8	<u> </u>	3.7	0.130	
Accountability	~00.0 ×	6.23	100.0	0.03	100.0	3.540	

VIII. Conclusions

After drip application of phenyl-UL¹⁴C]fluopyain, the radioactivity recovered in pepper fruits (1X experiment) was very low (0.058 mg eq/kg), whereas the recovered radioactivity recovered in plants after harvest was relatively high (3.54 mg eq/kg). The radioactivity recovered in the intermediate plant (4X overdose experiment) was in the range found for plants after harvest (6.24 mg eq/kg).

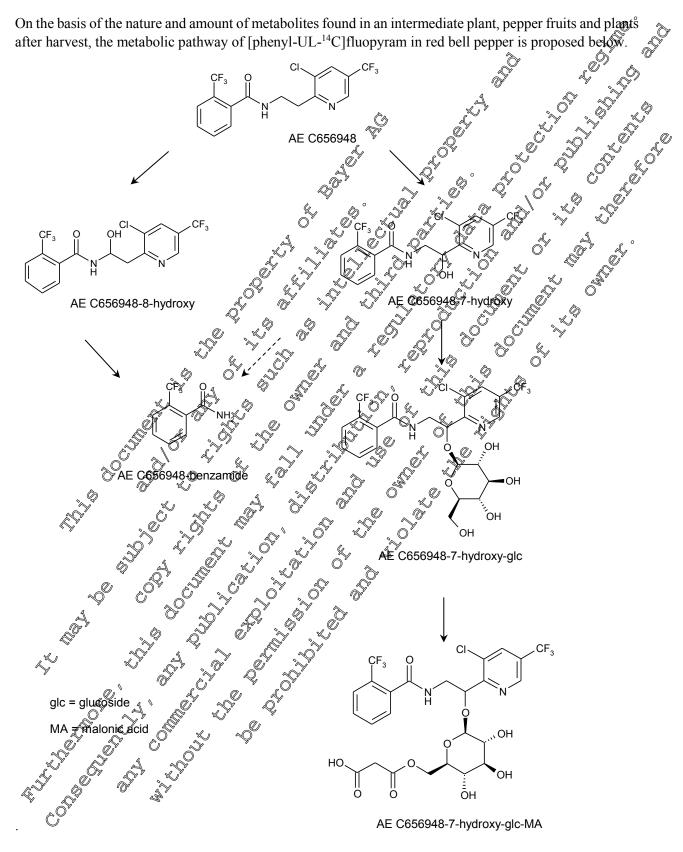
Unchanged parent compound was the predominant portion of the TRR in all investigated RACs, accounting for more than 40% of the TRR in total, five metabolites were identified. The most abundant metabolite was fluopyram-benzamide, followed by thiopyram-7-hydroxy and fluopyram-7-hydroxy-glc. Minor metabolites (<1% of TRR) detected were fluopyram-8-hydroxy and fluopyram-7-hydroxy-glc-MA.

The following metabolic roules were deduced:

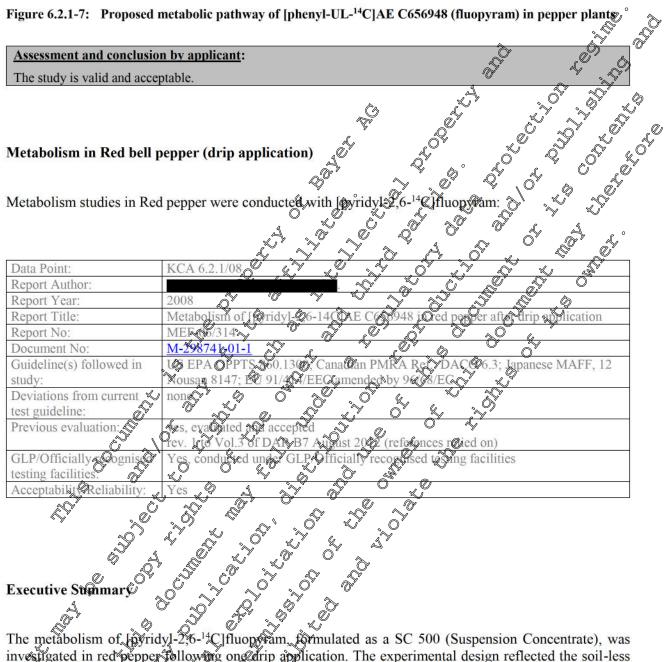
- Hydroxylation of the ethyl linking group of the parent compound leading to fluopyram-7-hydroxy or fluopyram-8-hydroxy
- Hydrobytic cleavage of the hydroxylated metabolites leading to fluopyram-benzamide
- Confugation of hydroxyl-metabolites with glucose and malonic acid



On the basis of the nature and amount of metabolites found in an intermediate plant, pepper fruits and plants after harvest, the metabolic pathway of [phenyl-UL-14C]fluopyram in red bell pepper is proposed below.







The metabolism of byridyl-2,6-¹⁴Clfluopyram, formulated as a SC 500 (Suspension Concentrate), was investigated in red pepper following one drip application. The experimental design reflected the soil-less cultivation of vegetable on the greenhouse. For the envisaged use pattern and according to agricultural practice, one application was performed using 5 mg a.s./plant (1X experiment). Additionally, an overdose experiment on conducted using 20 mg a.s./plant (4X experiment). The applications were performed at growth states BBCH 15017.

Pepper faits were harvested armaturity (BBCH 89) for both 1X and 4X experiments. The plants were also sampled after harvest of the fruits. Moreover, an intermediate sample of the overdose experiment was additionall colleged at the beginning of flowering (BBCH 61).



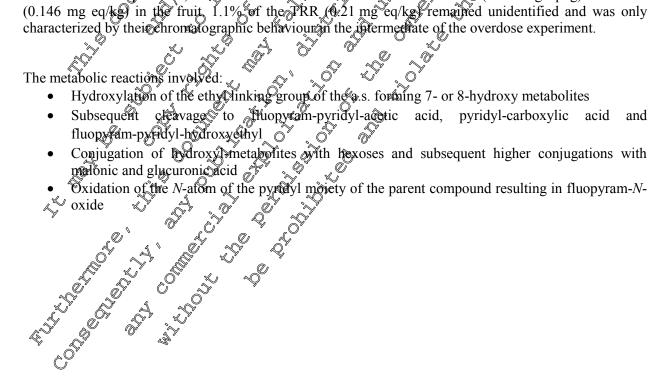
The TRR of the fruits at 0.060 mg eq/kg (1X dose) and 0.149 mg eq/kg (4X overdose) was considerably lower than the TRR for the 1X experiment pepper plant (2.344 mg eq/kg) and the 4X overdose experiment intermediate (18.24 mg eq/kg). The major amount of radioactivity (> 95% of the RRR) was effectively extracted with acetonitrile/water from all RACs leaving only minor amounts < 5% with the solids (PES) Parent compound and metabolites in the extracts were quantified by HPLC.

Parent compound was the predominant residue in the pepper intermediate and in the pepper fant a harvest accounting for 70% to 88% of the TRR.

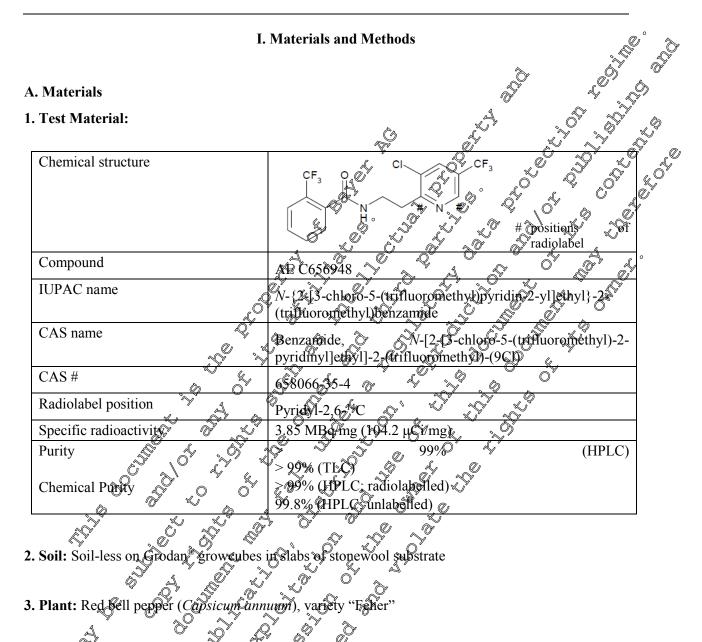
In pepper fruits, fluopyram-pyridyl-carboxylic acid was the main metabolite at 43,5% (0.026 mg ed/kg). the TRR followed by two isomeric glycosides of Huopyram-pyrdyl-acetic acid (PAA) at 23.8% TRR (0.014 mg eq/kg) and 14.2% TRR (0.009 mg eq/kg) respectively. The glycosides were detected exclusively in pepper fruits, whereas traces of fluopyram-pyridyl-carboxylig acid wore also detected in the intermediate sample at relatively low levels of 0.4% TRR (0.08 mg eg/kg). No further metabolites were detected in pepper fruits of the 1X experiment. Other metabolities of interest in the green plant parts were the hydroxylated metabolites fluopyram -hydroxy at 5.1% TRR (0,120 mg/cq/kg) and its corresponding glucoside fluopyram-7-hydroxy-glc at 9.2% TRR (0.215 mg/eq/kg) and the conjugate hydroxyethyl-di-glc at 7.0% TRR (0.164 mg eq/kg). Besides, small amounts of fluopyram-Doxide was found in green plant parts (2.9% TRR; 0.069 mg eq/kg). The metabolite flugpyram & hydroxy was only found in the overdose intermediate at low levels of 0.7% TRR (0.13 cmg eq/kg).

A total of 97.8% TRR (0.059 mg eQ/kg) was identified in the fruits and 94.3% TRR (2.211 mg eq/kg) in the green parts of the plant of the 1X experiment, respectively. Only a few minor withnown components (each < 10% of the TRR and \$0.05 mg eq/kg) were characterised by their chromotographic behaviour in green parts of the plane of the IX experiment.

In the overdose experiment, the amount of TRR in the intermediate was 96.7% (17.63 mg eq/kg) and 98.1% (0.146 mg eq/kg) in the fruit, 1.1% of the TRR (0.21 mg eq/kg) remained unidentified and was only







B. Study Design

1. Experimental conditions:

The red pepper plants were cultivated in a greenhouse (building 6681) of Bayer CropScience AG, Metabolism / Environmental Fate, Monheim, Germany, which allows plant growth under natural sunlight and temperatures. The plants were cultivated without soil on stonewool substrate (Grodan[®] Growcube, Grodan by, Roermond; The Netherlands) according to professional horticulture. Each plant was grown in one cube of Grodan[®] Growcube and three cubes were places together into a slab of the same material. The slab was kept in a box (container). The plants were irrigated and fertilized with a mix of a fertilizer on nitrate basis and a commercially available nutrient solution using a dripping system. A defined volume of the nutrient solution was applied daily to each plant. Due to the good water-retention properties of the stone



wool substrate, the water content in the cubes was between 50% and 55% during the whole cultivation period. Uptake and delivery of nutrients was in a balanced state and only an excess of nutrient solution was drained into a bottle.

The radiolabelled active substance was formulated as a suspension concentrate (SC 500). For the 4X experiment, the radiolabelled test item was radiodiluted with non-radiolabelled test item (radio 1/k/w/w) prior to formulation. The application conditions of the 1X experiment simulated the anticipated use pattern for professional horticulture with 5 mg a.s./plant. The additional 4X overgose experiment was performed to support identification of metabolites. The application suspension were prepared by diluting the O formulations for the 1X experiment and the 4X experiment with water. The formulation was applied at growth stage BBCH 15–17 (fifth to seventh leaf of the main showt unforded). A portion of 100 mL of application suspension were poured to each plant. One day proor to application and one day after the dripping of the nutrient solution had been stopped in order to allow the complete uptake of the application suspension. The application solution was not drained and was quantitatively available for the plant.

2. Sampling <u>Pepper intermediate (immature plant):</u> One immature plant was sampled 33 days after application at BBCH 61 (first flower was open) in the XX overdose experiment. The plant was collected with its growcube. The growcube was removed by cutting the plant slightly above the store wool surface. The weight of the sample was determined and the plant was cut into pieces and homogenised with liquid nitrogen using an Ultra-Turrax homogeniser. The complete homogenised plane material was used for extraction.

Pepper fruits: At maturity (growth stage BRCH 89, 55-96 days after application) pepper fruits were sampled in bothexperiments OX and X overdose in three harves dates. The fruits of the first and second harvest werestored in a freezer antil the last harvest On the third farvest day, the fruits of the three samplings of the 1X experiment were combined, crushed and homogenised with liquid nitrogen using an Ultra-Turtax homogeniser. A Pepresentative alique of the homogenised sample was used for extraction. Residual homogenised red pepper truits were stored in aliquots at $\leq -18^{\circ}$ C.

The fruits of the three sampling dates of the 4X experiment were also combined and stored at \leq -18°C for optional analysis.

Pepper plants after hervest; One day after the last pepper fruit had been sampled, the rest of the plants (BBCH code 89) were cut above their cubes. The plants were cut into pieces using scissors. The plants of the 1X experiment were homogenised with liquid nitrogen using an Ultra-Turrax homogeniser. The plant parts of the 4% experiment were stored in a freezer for optional analysis, whereas a representative aliquot of the homogenised sample of the 1X experiment was used for extraction. Residual homogenised plant material was stored in aliquots at ≤ -18 °C.

AE DE COLOR DE COLOR



C. Analytical Procedures

The pepper RACs were extracted and subsequently analysed by HPLC and TLC. The identification of parent compound and metabolites was based on co-chromatography with LC-FT-MS, LC-MS/MS and LONMR-MS.

1. Extraction and fractionation:

The samples of the homogenised raw agricultural commodities (RACs) were extracted three times with a mixture of acetonitrile/water (4/1, v/v) using an Ubra-Turrax homogenise?. The extracts were separated from the solids by centrifugation. The radioactivity of each extract was determined by ASC measurement. The remaining solids (PES) were lyophilised, homogenised and weighed. The radioactivity in the solids was determined by combustion followed by LSC Aliquets of the combined solvest extracts were concentrated using a rotary evaporator.

The ¹⁴C-radioactivity of liquid samples was determined by liquid scintillation counting (LSC) using Quicksafe A containing 5% of water. The released $^{4}CO_{2}$ was trapped in an alkaline scintillation cocktail and the radioactivity was determined by LSC.

The total radioactive residues (TRR) in the RACs of red bell pepper were determined by summation of the radioactivity in the combined acetomirile/water expracts and in the PES

The concentrated acetonitrile/water extracts were analysed by MPLC for quantification of metabolites.

2. Identification and characterisation:

The identification of metabolites in edible RAC prepro fruits and green material (pepper plant) was carried out by HPLC and TLC co chromatography or by spectroscopic investigations.

The metabolite pattern of peopler plant was used as reference sample for peak assignment. Individual compounds in people plant were identified by spectroscopic means and other matrices were assigned by comparison of the metabolite matterns with that of peopler plant. By HPLC co-chromatography with reference compounds of isolated (and identified) metabolites from peopler plant the assignment was confirmed in asecond step.

Metabolites in pepper fruit, which were not detected in pepper plant, were isolated and purified by HPLC fractionation and were identified by LC-FT-MS, LC-MS/MS and LC-NMR-MS.

3. Storage stability:

Pepper intermediate (4X) and pepper plants (1X) were extracted and analysed within a day after sampling. Pepper fonts (1X) were harvested at three sampling dates and therefore stored in a freezer until the last sampling date. The storing period of the pepper fruits was 41 days in maximum before sample preparation. Analysis followed within a day. Thus, metabolite profiling including quantification of compounds was performed within less than two months (42 days) after sampling of the respective RAC, whereas identification of compounds required approximately 13 months.



II. Results and Discussion

The metabolism of [pyridyl-2,6-¹⁴C]fluopyram, formulated as a SC 500, was investigated in red bell pepper of following one application in two different experiments (1X and 4X overdose). The application rates were 5 mg a.s./plant in the 1X experiment and approximately 20 mg a.s./plant in the 4X overdose experiment.

The TRR amounted to 18.24 mg eq/kg in the 4X pepper intermediate, 0.449 mg eq/kg in the 4X pepper fruits, 0.060 mg eq/kg in the 1X pepper fruits and 2.344 mg eq/kg in the 1X pepper plants after harvest (Table 6.2.1-24). The TRR of the edible RACs (pepper fruit) was argnificantly lower than those of the respective plant or intermediate.

Table 6.2.1-24	TRR values in pepp matrices after application o	f pyridol-2,6	-14 fluopyram O
Matrix	TRR values in pepper matrices after application of Timing and Applic. No.	Pill ô	TRR (ppm, mg a.s. equiv./kg)
Pepper	One drip application		No No
intermediate			18.24
(BBCH 61)	total 19.1 mg a.s./plant (4X experiment)		, Q
Pepper	One drip application		0 1 <i>4</i> 9
fruits	at growth storges BBCH 15–17;	¥ 55-06 ₅	0.149
(BBCH 89)	total 19,1 mg a.s. plant (AX experiment)	O K	7
Pepper	One drop application $\sqrt{2}$, $\sqrt{2}$, $\sqrt{2}$	L. Q.	
fruits	at growth stages BRCH 15-15;	© 55-9¢C	0.060
fruits (BBCH 89)		ÿ %5°	
Pepper plants		Ø	
after harvest	at growth stages BBG 15-10 (0)	^س 97	2.344
(BBCH &)	at growth stages BBGH 15–109 total 5 mg & /plan 1X experiments	Ý	

The pepper matrices were extracted with acetonitrile/water $(\mathfrak{G}/1, v/v)$, the extracts were analysed by HPLC and, where necessary TLC and parent compound and metabolites were identified.

The majority of the radioactive residues in the intermediate (4X experiment), 97.8% (17.84 mg eq/kg) of the TRR, was extracted by acetonitrile/water (Table 6.2.1-25), whereas 2.2% (0.40 mg eq/kg) of the TRR remained in the solids (PFS).

The majority of the radioactive residues in pepper fruits, 98.1% (0.146 mg eq/kg) of the TRR in the 4X overdosc and 37.8% (0.059 mg eq/kg) of the TRR in the 1X experiment, was extracted by acetonitrile water feaving only 1.9% (0.003 mg eq/kg) and 2.2% (0.001 mg eq/kg) of the TRR in the solids (PES), respectively.

The majority of the radioactive residues in plants (1X experiment), 95.3 % (2.233 mg eq/kg) of the TRR, was extracted by acetonitrile/water, leaving 4.7 % (0.110 mg eq/kg) of the TRR in the solids (PES). Due to the low radioactive residue, the solids (PES) from all matrices were not further investigated.



Ľ

	intern	oper 1ediate eriment)		r fruits eriment)		r fruits eriment)	aftersh	plants arvest eriment)
TRR [mg eq/kg] =	18	.24	0.	149 💭	0.6	\$0	2.3	44
	% of	mg eq	% of	mg eq	% ofQ	mg eq	% of S) mg eq
	TRR	/kg	TRR	∕√/kg	T₽₽	/kg 🔉		ARE
Acetonitrile/water extract	97.8	17.84	98.1 🔎	0.146	Q.8	₀0.059 [©]	9,5.3♥	£2.233
Solids (PES)	2.2	0.40	1.90	0.003	2.2 <i>o</i>	0.0Q	. ť.7	0.110
Total extracted	97.8	17.84	98 .1	0.146	97,89	0 , 059	95.3	2.233
Accountability	100.0	18.24	100.0	0.149	100.0	0.060	100.0	2.344

For the elucidation of metabolism, the solvent extracts (acetonicile/water) were analysed by FIPLC and, where required, also by TLC with radiodefection, Metabolites were either identified by co-chromator apply (HPLC, TLC) with reference compounds or is plated metabolities or by LC-ICI-MS/MS and/or LC-NMR-MS of isolated peaks.

Pepper intermediate: Parent compound fluopyram (88.1% of the TRR 96.07 mg eq Ag) was the most prominent compound in the sample, followed by Buopyram-7-hydroxy 3.5% of the TRR; 0.63 mg eq/kg), the corresponding conjugate fluoryram-7-hydroxy-glo (1.9% of the YRR: 0.34 mg eq/kg) and the labelspecific metabolite fluopyram hydres ethyl-di-glc 91.5% of the TRR; 0.27, ng eq/kg). fluopyram-8hydroxy (0.7% of the TRR 0.13 pg/eq/kg, fluopyram y-oxide (0.5% of the TRR; 0.10 mg eq/kg) and fluopyram-pyridylevarbox Qic (0,4% of the TRR; 0.080mg eq kg) were identified as minor metabolites. Besides, three unknown compounds were characterized based on their extraction and chromatographic behaviour (total 1.1% of the TRR; 0.21 mg/q/kg)

Pepper fruits: The most prominent metabolite was dentified as floopyram-pyridyl-carboxylic acid (43.5% of the TRR; 0.026 of eq/kg). Two isomeric becase conjugates of fluopyram-pyridyl-acetic acid were identified as fluopyram-PAA-glocosides (23,8% of the TRR; 0.014 mg eq/kg and 14.2% of the TRR; 0.009 mg eq/kg). The parent compound flappyram (16.2% of the TRR, 0.010 mg eq/kg) was clearly reduced in peoper fruits compared to other comparements?

In the 4X overdose experiment wo further merabolites were found: fluopyram pyridyl-acetic acid (PAA; 9.8%; 0.015 mg eq/kg of the TRR) and fluopyram 2-hydroxy (3.7% of the TRR; 0.006 mg eq/kg).

Pepper plants after harvest: Parent compound luopyram (70.1% of the TRR; 1.643 mg /kg) was the most prominent compound in the giant sample, Gilowed by fluopyram-7-hydroxy-glc (9.2% of the TRR; 0.215 mg eq/kg), the label specific metabolite thropyram-hydroxyethyl-di-glc (7.0% of the TRR; 0.164 mg eq/kg) and the metabolite fluop ram-Zhydrow (5.1% of the TRR; 0.120 mg eq/kg). fluopyram-N-oxide (2.9% of the TNR; 0.969 mg eq/kgp was identified as a minor compound. One unknown component was characterize@based on its extraction and chromatographic behaviour (1.0% of the TRR; 0.023 mg eq/kg).

ð



	Pepper inter		Repper	fruits 🔊
	(4X experi		(X expe	
R [mg eq/kg] =	18.24		0.14	19 🥈 💡
mpound	% of the TRR 🖏	mg eq/kg	% of the TRR	mg eq/kg
C656948, a.s., fluopyram	88.1	16.07	32.8	0,049
opyram pyridyl-carboxylic acid (PCA) (M43)	0.4	16.07 0.08 2 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	19.5	029
opyram pyridyl-acetic acid (PAA) (M40)	<u>s</u> e ⁱ	á l	98)	029 0.015 0.019 02929
opyram PAA-glycoside (M42) (isomer 1)	· · ·	<u>```¥</u> _¢g°	12:5 4	, 0.019
opyram PAA-glycoside (M42) (isomer 2)	0,0,0,0,0 0,5,0 0,5,0 1,9,0,5,0,5,0 1,9,0,5,0,5,0 1,9,0,5,0,5,0,5,0,5,0,5,0,5,0,5,0,5,0,5,0		19.5 7 - 7 6 6	02929
opyram hydroxyethyl-di-glc (M36)		0.20	· · · ·	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
	× ^{1.9} č	3 34	- A	-
opyram-N-oxide (M01)		Q0.10		
opyram-7-hydroxy (M08)		, 0.63	6 ⁵ 3.7	
opyram 8-hydroxy (M18)	0 .7			
	96.1	⁴ V.03 00.07.		<u>> 0.146</u>
kilowii 6	Ø 0.4 Ø 3 3			ş. Ş-
nown 9 U V W				\sim
tal characterised	011	â9421 .	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	· _
tal extracted	978	17.84	© 98.1 O	0.146
ids (non-extractable residue)	¢2.2	0.40	1.9	0.003
countability	00.05	18.24	H09.0	0.149
pyram 7-hydroxy (M18) pyram 8-hydroxy (M18) tal identified cnown 6 cnown 7 cnown 9 tal characterised tal extracted countability count				



Summary of characterisation and identification of radioactive residues in pepper Table 6.2.1-27: matrices after drip application of [pyridyl-2.6-¹⁴C]fluopyram in the 1X experiment

	tion of the	uyi-2,0- Cji	nuopyram m the ix experiment	S		
		r fruits eriment)	Pepper plants after härvest (1X experiment)			
TRR $[mg eq/kg] =$	0.0)60	2.344	2		
Compound		©gmg eq/kg	$\begin{array}{c c} & \text{ of the } \\ \hline & \text{TRR} \\ \hline & 70.1 \\ & & & & \\ & & & \\ & & & & & \\ & & & & & \\ & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & &$,©		
AE C656948, a.s., fluopyram	16.2 43.5	0.010	₽ [×] 70.1 × 1.643 [×]	ŝ		
fluopyram pyridyl-carboxylic acid (PCA) (M43)	43.54	0.026 Q				
fluopyram pyridyl-acetic acid (PAA) (M40)		, ×				
fluopyram PAA-glycoside (M42) (isomer 1)	23.8	0.014				
fluopyram PAA-glycoside (M42) (isomer 2)	×14.2	× ⁶⁰ 009				
fluopyram hydroxyethyl-di-glc (M36)		<u>0</u> - v	0.164			
fluopyram 7-hydroxy-glc (M11)	♪ ~ <u></u> ~~ ∧	Ø - Q	9.2 00.215 °			
fluopyram-N-oxide (M01)	.~-~~	de de la companya de la				
fluopyram-7-hydroxy (M08)	& - _x	• <u> </u>	5.1 0.420			
fluopyram 8-hydroxy (M18)	<u>v</u>	<u> </u>				
Total identified	97.8 ×	0:059	2 94 3 2 2.21 kg			
unknown 6	Q - D	<u>~</u> 0				
unknown 7	- ²	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.023			
unknown 9 🔊 🗸	<u> </u>	~~ <u>-</u> 0~				
Total characterised	6, ⁹ - 0					
Total extracted	§ 97.8 C	Q.059	× 3.3 × 2.233			
Solids (non-extractable residue)	5° 2,20'	0.001	[∞] 4.7 [∞] 0.110			
Accountability	100.0	0.660	2.344			
)` 			

After one application of [pyridyl-2,6-14C]fluopyram (5,frig a.s. plant) the TRR in pepper fruits of the 1X experiment was low and amounted to 0000 mg eq/kg. The TRR in the plants sampled after harvest of the fruits was 2.344 mg cq/kg. The TRR values in the 4X overages experiment, performed to support identification and soucture elucidation of metabolites, amounted to 18.24 mg eq/kg in the intermediate sample and to 0.149 mg eg/kg in the pepper fruits, respectively.

In both experiments, the unchanged parent compound was the predominant portion of the TRR in the intermediate sample and in the plants at parvest \$70% to 88% of the TRR). In pepper fruits, it was still a major compound, but represented only approximately 6-33% of the TRR.

In total, nine metabolites were identified. In the 1X experiment, the major compound in red bell pepper fruits was fluopyram-pyridyl-carboxylic acid 2 40% of the TRR), followed by two isomeric fluopyram-PAA-glycosides (24% and 12% of the TRB, respectively) and the parent fluopyram (approximately 16% of the TRF

The following metabolic routes were deduced:

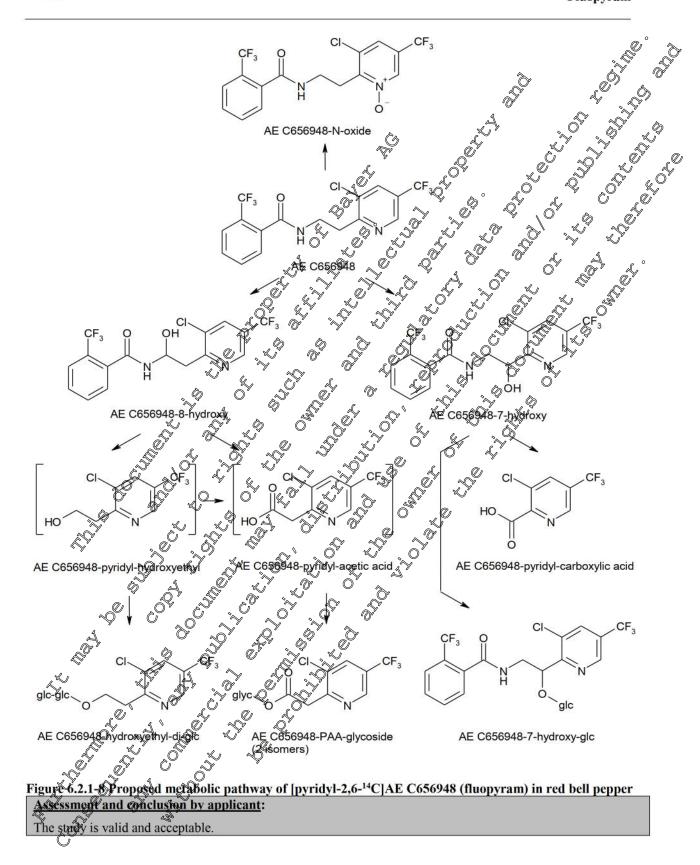
Hydroxylation of the ethyl linking group of the a.s. forming 7- or 8-hydroxy metabolites



- തർ Subsequent cleavage to fluopyram-pyridyl-acetic acid, pyridyl-carboxylic acid • with fluopyram-pyridyl-hydroxyethyl
- Conjugation of hydroxyl-metabolites with hexoses and subsequent higher conjugations • malonic and glucuronic acid
- Oxidation of the *N*-atom of the pyridyl moiety of the parent compound resulting in floopyrain-*N* oxide •

On the basis of the nature and amount of metabolites found in the intermediate sample, the puits and the plants at harvest, the metabolic pathway of [pyridy] 26^{-14} Clfluonvram in and hold for the plants at harvest. John Comparing and the particular of the second and On the basis of the nature and amount of metabolities found in the informediate sample, the Pruits and the planes at harvest, the metabolic pathway of [pyrid] 26 "C[Huopyran in and beltepept is proposed, if Further and the planes at harvest, the metabolic pathway of [pyrid] 26 "C[Huopyran in and beltepept is proposed, if Further and the planes at harvest, the metabolic pathway of [pyrid] 26 "C[Huopyran in and beltepept is proposed, if Further and the planes at harvest, the metabolic pathway of [pyrid] 26 "C[Huopyran in and beltepept is proposed, if Further and the planes at harvest, the metabolic pathway of [pyrid] 26 "C[Huopyran in and beltepept is proposed, if Further and the planes at harvest, the metabolic pathway of [pyrid] 26 "C[Huopyran in and beltepept is proposed, if Further and the planes at harvest, the metabolic pathway of [pyrid] 26 "C[Huopyran in and beltepept is proposed, if Further and the planes at harvest, the metabolic pathway of [pyrid] 26 "C[Huopyran in and beltepept is proposed, if Further and the planes at harvest, the metabolic pathway of [pyrid] 26 "C[Huopyran in and beltepept is proposed, if Further and the planes at harvest, the metabolic pathway of [pyrid] 26 "C[Huopyran in and beltepept is proposed, if Further and the planes at harvest, t





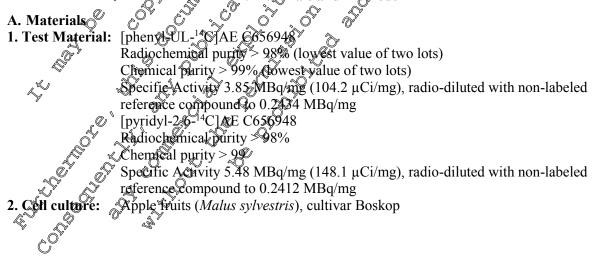


Supplemental cell culture study

Supplemental cell cultur	e study
Data Point:	KCA 6.2.1/09
Report Author:	
Report Year:	
Report Title:	Degradation of [phenyl-UL-14; Qand [pyridyl-26-14C]AE C65948 bolant
	suspension cell cultures
Report No:	MEF-05/142
Document No:	$M-259283-01-1 \qquad $
Guideline(s) followed in	Equivalent to US EPA OPPTS Guidelane No. 500.1306 (Supplemental)
study:	
Deviations from current	
test guideline:	
Previous evaluation:	yes, evaluate and accepted rev. 1 to VA3 of DorR B7 August 2012 (reference) relied 50 Yes, conducted order GbP/Offfeally recognised esting accilities
	rev. 1 to VAV3 of DOrR B7 Wagust 2012 (* Prence Felied Sr)
GLP/Officially recognised	Yes, conducted and the GLP/Officially recognised esting accilities 🔍 🗸
testing facilities:	
Acceptability/Reliability:	Yest y way to be a second seco

The metabolism of the rungicale AE 656948 was urvestigated in Reterorrophic plant cell suspension cultures originating from apple fruit following incubation with pheny [UL-14C] and [pyridyl-2,6-¹⁴C]AE C656948, respectively, This was done of facilitate metabolite identification and to produce radiolabeled reference compounds for the identification of metabolites in plant and animal metabolism studies.

Materials and Methods





B. Study Design

Experimental conditions: The radiolabeled and non-radiolabeled a.s. were dissolved in acetonitril® For the experiment, the radioactive compound was diluted with the non-radiolabeled substance to obtain the \square desired specific radioactivity (concentration: $50 \,\mu\text{M} = 794 \,\mu\text{g} / 40 \,\text{mL}$ cell suspension; radioactivity ea 185 kBq = 5 μ Ci). The solution was applied directly to the plant suspension cells. The amount of the organic solvent in the cell culture did not exceed 50 μ L/40 mC cell suspension (= 0.13%) avoiding phytotoxic effects of the organic solvent in cell growth. The experiments were performed with cells from the beginning of the exponential growth phase. After appreation of the dest substance the cells were further cultivated under the normal growth conditions

Sampling: On day seven after application, 10 flasks (of each laber) were sampled. Plant cells and the nutrient medium were immediately separated by filtration. The cells were washed intensively with water to remove soluble radioactivity from the cell surfaces. This wash solution was combined with the putrient medium. These liquid samples were concentrated at about 35°C ander vacuum asing a rotary exaporator and redissolved in an appropriate solvent file. acetonitrile or mratures of water with acetonitrile). The samples were stored at ca. 4°C during processing and then at ca. -20°C in a dreezer

C. Analytical Procedures Extraction and quantitation: The cells were successively extracted with acetonitrile/water (80:20, v/v, 3x). The acetonitrile/water-extracts were combined and concentrated to the aqueous remainder. The extracted fibrous solids were air dried at room temperature, weighed, and radioassaved. More drastic extraction methods for the solid were not necessary ince only a low residual amount of radioactivity was found in this sample.

The nutrient medium of each label was concentrated. Coll debus and proteins were precipitated with acetonitrile and contrifuged. The clear supermatant was decauted, concentrated and again mixed with acetonitrile. After centrifugation, the Supernatant was decapted and concentrated.

Identification and characterization: Metabolites were isolated and identified from the concentrated medium and from the cell extracts by FIPLC fractionation and purification of the fractions. Purified metabolites were identified by LC-MMR, OPLC-MS/MS, FT-MS and different NMR techniques.

From the cell culture study not metabolites were isolated and identified. Structures are given in Table 6.2.1-28.



Identified metabolite	Structure	Bemark
fluopyram-deschloro-3-OH-glc	ОН НО	identified with the phenyl-fabel
	HO'' CF O	
fluopyram-7-hydroxy		identified with the thenyl-label
fluopyram-7-hydroxy-glc		identified with the phense and the
nuopyrum / nyuroxy gie		pyridyblabel
Å		8 8 5 5 V
fluopyram-8-hydroxy-glc	CH HO	identified with the phenyl-label
× ×		
fluopyram-hydroxymethyl-benzañide		identified with the phenyl-label
. 6 6 4 6	C C C C C C C C C C C C C C C C C C C	Ø
		4
fluopyram-benzamide		identified with the phenyl-label
fluonurom nu idul hudrou Pul		identified with the pyridyl-label as
fluopyram-pyřidyl-hydroxyethyl	CF3	aglycon of a higher conjugate
	AND N	
fluspyram-pyridyl-Kydroxythethyl	CF ₃	identified with the pyridyl-label as
		aglycon of a higher conjugate
<u> </u>		
fluopyram pyridyl-carboxythe acid	CI CF ₃	identified with the pyridyl-label
	НО,	
	N N N	
and the second s	ö	



1	e e e e e e e e e e e e e e e e e e e
Assessment and conclusion	n by applicant:
The study is valid and accept	otable.
<u>New Data</u>	ed dressing) at were conducted with both [placny]-OL-14 Ch and a flyrid (02,6-4) C fluop) ram: KCA 6.2.1/10 Metabolism of AE C65(948 in wheat after seed dressing) MEF 09/124 ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~
Metabolism in wheat (see	ed dressing)
Metabolism studies in whe	at were conducted with both [pheny]-OL-14C4 and [pyridyO2,6-14C]fluop)ram:
Data Point:	KCA 6.2.1/100 () () () ()
Report Author:	
Report Year:	
Report Title:	2009 Q Metabolism of AE C656948 in wheat after seed gressing C MEF Q9/124 Q
Report No:	Metabolism of AE C656948 in sheat after seed dressing
Document No:	<u>M-345948401-1</u>
Guideline(s) followed in study:	US EPA OPPTS 360.13(0), Canadian PMRA Ref. DACO 6.3; OECD 501; EU 91/414(EEC amended by 96/6)/EC; Japanese MAFF, 2 Nousan 8147
Deviations from current test guideline:	nongy 2 0 0 4 5 5
Previous evaluation:	none No, not previously submitted Yes, conducted under GLP Officially recognised testing facilities Yes
GLP/Officially cognised testing facilities:	Yes, conducted under GLP Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability: 🔬	Yes 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
	Yes y y y y y y y y y y y y y y y y y y y

The metabolism of the fungicitie fluopyram was investigated in wheat after seed treatment with both [phenyl L-14C]fluopyram and [pyridyl-26-14C]fluopyram, formulated as a SC 500 (Suspension Concentrate).

The plants were cultivated in twegetation action under natural temperature and light conditions. The seed treatment was performed one day before sowing the seeds (BBCH 00). Due to the low intended dressing rate of 1 g a 2/dt in agricultural practice, only an overdose experiment was performed with a dressing rate of approx $\frac{10}{20}$ g a $\frac{2}{3}$ /dt (10 $\frac{10}{3}$). The actual application rates were 10.5 g a.s./dt and 10.8 g a.s./dt for the phenyl label are the period value of the presence of the presenc

Wheat forage (BBCH 30) and hay (BBCH 77–83) were collected as intermediate plant samples and wheat straw and grains (BBCH 89-92) were harvested at maturity.



The major amount of radioactivity (79.1–93.3% of the TRR) was extracted with acetonitrile/water from all RACs in both label experiments. Left amounts with the solids (PES) amounted to 6.7–12.5% of the PRR in forage, hay and straw and up to 20.4% of the TRR in grains. The TRRs in straw (pheny Dabel: [®] 0.506 mg eq/kg and pyridyl label: 0.477 mg eq/kg) were higher than the TRRs in hay (phenyl label: 0.23) mg eq/kg and pyridyl label: 0.287 mg eq/kg) and forage (phenyl label: 0.132 mg eq/kg and pyridyl label: 0.142 mg eq/kg). The TRRs in grains were lower in both labels (phenyl labels 0.006 mg eq/kg and pridyl) label: 0.012 mg eq/kg).

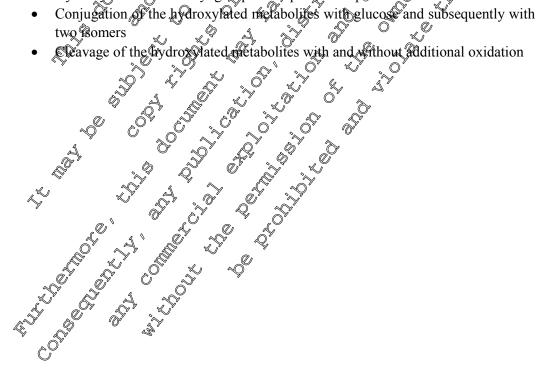
The unchanged parent compound was the predominant residue in all plant matrices accounting for 40.6 65.3% of the TRR in both labels.

Two isomers of fluopyram-7-hydroxy-glc-MA (M12) for major metabolites in forage, hay and straw (10.4–15.2% of the TRR), followed by fluopyram-74bydroxy (M0& 5.2 A.1% of the TRR). A major metabolite in grain of the phenyl label was thropyram-benzamide (M25, 10.4% of the DRR). It was also found in forage, hay and straw (2.3-11.4% of the PRR) Pesides, fluopyram, 7 hydroxy (M08) was found in grain of the phenyl label (3.4% of the TRR, \$0.00% mg eg/kg). floopyram-8-hydroxyzer-MA (M19), fluopyram-7-hydroxy-glc (M11) and fluopyram-8-hydroxy (m18) and fluopyram pyrid & carboxylic acid (M43) were detected in minor amounts of < 5% (< 0.01 mg.oq/kg) of the PRR. Suopyram-methylsulfoxide (M45) was detected exclusively in when strage in minor amounts (27% of the TRR).

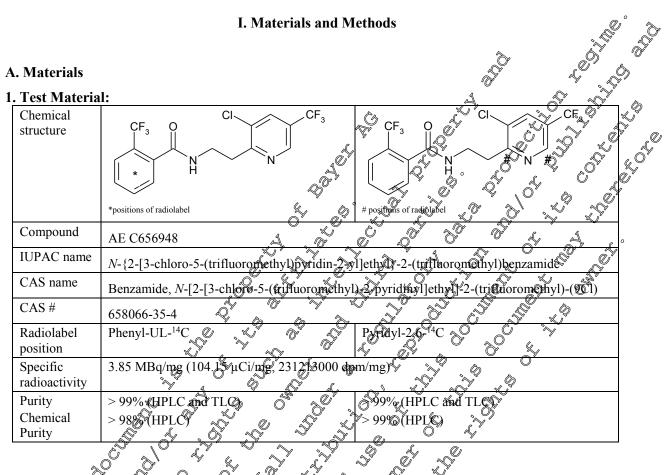
A total of 59.2-89.8% (0.004-0.402mg eq/kg) of the TRR was identified in forage, hap straw and grain. A few minor unknown components (each $\sqrt{20\%}$ of the TRR, < 0.05 ms eq/kg) were characterised by their chromatographic behaviour in all RACs.

The mean metabolic reactions involved were:

- Hydroxylation at the ethyl group of the parent compound
- Conjugation of the hydroxylated metabolites with glucose and subsequently with malonic acid to







2. Soil:

"Monheim 4" (sandy loan from Germany), pH (CaCl₂) $\stackrel{\circ}{=} 6.9, 58.1\%$ and 27.9% silt and 14.0% clay, 1.23% Organic material, cation exchange capacity (CEC) of 8.1 meq/100 g organic Carbon, 2.12

3. Plant:
Wheat, variety "Thasos"
B. Study Design
I. Experimental conditions:
Wheat was cultivated in the vegetation area (building 6682) of Bayer CropScience AG, Environmental Safety Metabolism/ADME and Environmental Fate Monheim Germany which allows plant growth under Safety, Metabolism/ADME and Environmental Fate, Monheim, Germany, which allows plant growth under natural rempetature and light conditions. Wheat was sown in planting containers with a surface area of approx. 1.0 and Alled with sandy loam soil "Monheim 4". In each planting container six rows were sown with 75 wheat seeds perfrow.



Due to the low intended dressing rate of 1 g a.s./dt in agricultural practice, only an overdose experiment has been conducted with a dressing rate of approx. 10 g a.s./dt (10X experiment). One planting container « was used for the experiment with [phenyl-UL-14C] fluopyram and another for the experiment with [phenyl-UL-14C] fluopyram and 2.6- 14 Clfluopyram. The seed treatment was performed one day before sowing the seeds (BBCH 10 Clfluopyram).

2. Sampling

Wheat forage: One row of intermediate plants was sampled at the beginning of stem elongation BBC The plants were cut slightly above the soil surface, cut the plants were cut slightly above the soil surface, cut the sample material was and homogenised.

Wheat hay: Two rows were collected as intermediate plant samples BBCH The plants were cut slightly above the soil surface, cut into pieces and the sample material was dried at room temperature for three days before being weighed and homogenised.

Wheat straw and grains: At maturity BBCH 89-92) the remaining plants were harvested. The plants were cut slightly above the soil surface The earst were separated from the straw an grain were separated from the husks. The husks were combined with the straw sample and the fotal weight was determined. ith the suraw summer $\frac{1}{2}$ $\frac{1$

C. Analytical Procedures

1. Extraction and Fractionation:

All RAC samples were extracted either three or four times with acconitrile/water (4/1, v/v) mixture using a Polytron homogentizer. Subsequently, extract@were@purifice, concentrated and analysed by HPLC analogous (v to the confined rotational crop (CRC) studies to facilitate comparison of corresponding metabolic profiles within the different studies. The extracts were separated from the solids by centrifugation and radioactivity was determined by volume measurement and SC. The remaining solids were dried at room temperature homogenised using a blender where necessary and subjected to combustion for determination of radioactivity Aliques of the purified solute extracts were concentrated using a rotary evaporator prior to HPLC analyses,

The ¹⁴Cradioactivity of liquid samples was determined by liquid scintillation counting (LSC) using Quicksafe A containing 5% of water. The adioactivity in solid samples was measured by combustion. The released ¹⁴CO₂ was absorbed in an alkalone schorillation cocktail and radio assayed by LSC.

The actual TRR value RAC was determined after extraction by summing up the radioactivity measured in the extracts and in the remaining solids. The concentrated acetonitrile/water extracts were analysed by HPLC for quantification of metabolites.



2. Identification and characterisation:

Parent compound and the metabolites detected were identified in a first step by HPLC comparison. Therefore, the metabolic profiles of each RAC were first compared with the corresponding metabolic profiles of the CRC study and assignments were confirmed by HPLC co-chromatography with corresponding extracts of the CRC study.

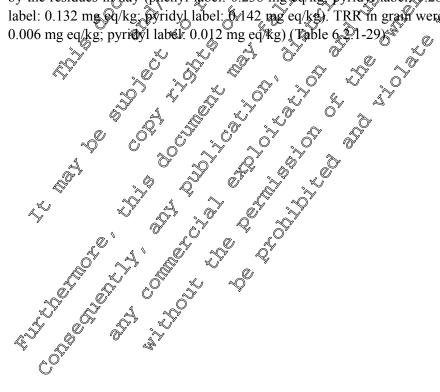
3. Storage stability:

The RACs were extracted and analysed within a few days (< 6 days) after sampling. All investigations concerning identification (HPLC comparison and co-chromatography) were performed within less than one month after sampling of the respective RAC. During the study, all samples and extracts were stored in a freezer or in a refrigerator. Thus, no additional storage investigations became necessary for the samples or extracts of the present study.

The metabolism of the fungicide fluopyram was investigated in wheat after seed to atment with [phenyl-UL-¹⁴C]fluopyram (10.5 g a.s./dt) and [pyrics-2,6-14C]fluopyram (40.8 g a.s./dt) formulated as SC 500.

The final TRR values were calculated as the support of the radioactivity determined in the extracts and the radioactivity in the remaining non-extractable solids

The TRR was the highest in straw othen 1 abel: 0506 mg/eq/kg; pyridol label; 0.477 mg eq/kg) followed by the residues in hay (phenyl label: 0.298 mg/eq/kg; pyridol label; 0.287 mg eq/kg) and forage (phenyl label: 0.132 mg/eq/kg; pyridol label: 0.142 mg/eq/kg). TRR in grant were noticeably lower (phenyl label: 0.006 mg eq/kg; pyridol label: 0.012 mg eq/kg). (Table 6.2.1-29)





Timing and Applic. No.	PHI (days)	(ppm, mg a.s. equiv./kg)
Seed dressing (BBCH 00): Total 10.5 g a.s./dt (phenyl label)	₹ 40	
Total 10.8 g a.s./dt (pyridyl label)		0 ⁵ 0.142 0 ⁵ 0 ⁵
Total 10.5 g a.s./dt (phenyl label)	- 59 S	
Total 10.8 g a.s./dt (pyridyl label)		
Total 10.5 g a.s./dt (phenyl tabel)	× 112 Č	
Seed dressing (BBCH 00):		
	Seed dressing (BBCH 00): Total 10.5 g a.s./dt (phenyl label) Seed dressing (BBCH 00): Total 10.8 g a.s./dt (pyridyl label) Seed dressing (BBCH 00): Total 10.5 g a.s./dt (phenyl label) Seed dressing (BBCH 00): Total 10.8 g a.s./dt (pyridyl label) Seed dressing (BBCH 00): Total 10.5 g a.s./dt (phenyl label) Seed dressing (BBCH 00): Total 10.8 g a.s./dt (pyridyl label)	Timing and Applic. No. (days) Seed dressing (BBCH 00): (days) Total 10.5 g a.s./dt (phenyl label) 40 Seed dressing (BBCH 00): (days) Total 10.8 g a.s./dt (pyridyl label) 40 Seed dressing (BBCH 00): (days) Total 10.5 g a.s./dt (phenyl label) 40 Seed dressing (BBCH 00): (days) Total 10.5 g a.s./dt (phenyl label) (days) Seed dressing (BBCH 00): (days) Total 10.8 g a.s./dt (pyridyl label) (days) Seed dressing (BBCH 00): (days) Total 10.5 g a.s./dt (pyridyl label) (days) Seed dressing (BBCH 00): (days) Total 10.8 g a.s./dt (pyridyl label) (days) Seed dressing (BBCH 00): (days) Total 10.8 g a.s./dt (pyridyl label) (days) Seed dressing (BBCH 00): (days) Total 10.8 g a.s./dt (pyridyl label) (days) Seed dressing (BBCH 00): (days) Total 10.8 g a.s./dt (pyridyl label) (days) Total 10.5 g.a.s./dt (phenyl label) (days) Total 10.5 g.a.s./dt (phenyl label) (days) Total 10.5 g.a.s./dt (pheny

The wheat matrices were extracted with acconitrite water $(4/1, \sqrt{N})$, the extracts were analysed by HPLC and parent compound and metabolities were identified.

Comparing the residues in the RACs related to the radiolabels used, only marginal differences were detected. Only for wheat grain, the residues were about doubled using [pyridyl-2,6-¹⁴C]fluopyram. These results are also in very good accordance to those of the CRC studies, where the residues in grain were higher after administration of [pyridyl-2,6¹⁴C]fluopyram.

Nearly the complete radioactive residues in forage (phonyl label: 93.3% of the TRR, 0.124 mg eq/kg; pyridyl label: 92.2% of the TRR, 0.13) mg eq/kg) were extracted by acetonitrile/water, whereas post-extraction solids (PES) accounted for 4.7% (0009 mg eq/kg) of the TRR for the phenyl label and 7.8% (0.011 mg eq/kg) of the TRR for the pyridyl label (Jable 6.2.1-30).

The major amount of radioactivit (in have phenor label: 90.8% of the TRR, 0.216 mg eq/kg; pyridyl label: 91.8% of the TRR, 0.269 mg eq/kg) was extracted by acetonitrile/water, whereas PES accounted for 9.2% (0.022 mg eq/kg) of the TRE for the phenor label and 8.2% (0.024 mg eq/kg) of the TRR for the pyridyl label (Table 9.2.1-30 and Table 6.2.1-31).

The majority of the TRR in straw (phenyl label: 86.8% of the TRR, 0.439 mg eq/kg; pyridyl label: 86.5% of the TRR, 0.413 mg eq/kg) was extracted by acetonitrile/water, whereas PES accounted for 12.3% (0.062 mg eq/kg) of the TRR for the phenyl label and 12.5% (0.060 mg eq/kg) of the TRR for the pyridyl label (Table 6.2.1-30 and Table 6.2.1-31).



1

The majority of the TRR in grain (phenyl label: 79.6% of the TRR, 0.005 mg eq/kg; pyridyl label: 79.6% of the TRR, 0.009 mg eq/kg) was extracted by acetonitrile/water, whereas PES accounted for 26.4% (0.001 mg eq/kg) of the TRR for the phenyl label and 15.6% (0.002 mg eq/kg) of the TRR for the opridyl label (Table 6.2.1-30 and Table 6.2.1-31).

Table 6.2.1-30:	Distribution of radioactivity in t [phonyl_UL_ ¹⁴ C]fluonyram	the extracts of the whea	t matrices after	· seed dressing with
	Inhanyl III ¹⁴ Clfluonyram			KÍ RÝ RĚ

pheny	/I-UL-**C]t	luopyram		N°	_C			×.	a
	For	age	H	ay	Ster	aw	C GF	ain 🔬 🦼	ç
TRR $[mg eq/kg] =$	0.1	32	0.2	\$8	0.5	506 °C	Q0.0	06	
	% of	mg	% of 🔗	» mg	% of &	°mg∱∕	% of	C _{mg} Q'	
	TRR	eq/kg	TRR	eq/kg	TRR	eq/kg	\¶RR_ĝ	eq/log	
Acetonitrile/water extract	93.3	0.124	\$90.8	\$ 0.21 6	86.8	× 0.439	79,6	0.005	
Solids (PES)	6.7	0.009	9.20	0.022	@ [*] 12.3	° 0.0 6 2	20.4	0.001	
Total extracted	93.3	0.124	90 8	216	≫ 86,8	Q:439	©″79.6%	° 0.005	
Accountability	100.0	0.132	≥100.0	0.238°	100.0	s_ 0 .506≋	100.0	0.006	
		-Q	1.× ×	, °~/				AN INCOMENT	

 Table 6.2.1-31:
 Distribution of radioactivity in the extracts of the wheat matrices ofter seed dressing with [pyridyl-2,6%]C]AE 656948

	uyi 2,0 @ C I 2 0507	25 1 6			
	& Forage	Hay 🔗	🔨 🐧 Straw	Grain	
TRR $[mg eq/kg] =$	≫ 0 <u>.1</u> 42 Ø	0.287	~~~0.4ZZ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.012	
	% of nug	0% of mg	<u></u> <u>%</u> of [™] mg [™]	% of m	g
Ô	TRR con/kg	₹, TRRS> gg/kg	O TRR eĝ∕kg	TRR eq/	'kg
Acetonitrile/water		~91.8 0.265° 0.265°	86.5 0.413	79.1 0	.009
Solids (PES)	Ø.8 Ø.01 l	@ & 2 ~ 0.024	§ 12.5 0.060	15.6 0	.002
Total extracted	92.2 0.131	^~¶.8 ~~0.263℃	86 .5 0.413	79.1 0	.009
Accountability		0100.0 0.287	00.0 0.477	100.0 0	.012
	V, O ^V (^Q		N .		

For the elucidation of metabolism, the solvent extracts facetonitrile/water) were analysed by HPLC and the metabolic profiles were compared with those of the CRC study. Metabolite assignments were confirmed by HPLC co-chromatography with corresponding extracts of the CRC study.

<u>Wheat forage:</u> The parent compound fluopyram (phenyl label: 65.3% of the TRR, 0.086 mg eq/kg; pyridyl label 62.6% of the TRR, 0.089 mg eq/kg) was the most prominent compound in the forage samples followed by fluopyram-7-hydroxy-gle-MA (phenyl label: 11.0% of the TRR, 0.015mg eq/kg; pyridyl label: 12.3% of the TRR, 0.017 mg eq/kg) and fluopyram-7-hydroxy (phenyl label: 6.2% of the TRR, 0.008mg eq/kg; pyridyl label: 5.2% of the TRR, 0.007 mg eq/kg). Other minor metabolites, namely fluopyram-pyridyl-carboxy fre acid, fluopyram-8-hydroxy-glc-MA, fluopyram-7-hydroxy-glc, fluopyram-8-hydroxy and fluopyram-benzamide amounted to < 5% of the TRR (< 0.01 mg eq/kg). Moreover eight unknown components, all below 1.5% of the TRR (< 0.002 mg eq/kg), were characterized in forage (Table 6.2.1-32 and Table 6.2.1-33).



<u>Wheat hay:</u> The parent compound fluopyram (phenyl label: 51.4% of the TRR, 0.122 mg eq/kg; pyridyl label: 62.8% of the TRR, 0.18 mg eq/kg) was the most prominent compound in the hay samples, followed by fluopyram-7-hydroxy-glc-MA (phenyl label: 12.1% of the TRR, 0.029 mg eq/kg; pyridyl label: 14.% of the TRR, 0.034 mg eq/kg), the phenyl label specific metabolite fluopyram/benzamide (01.4% of the TRR, 0.027 mg eq/kg) and fluopyram-7-hydroxy (phenyl label? 8.2% of the TRR, 0.020 mg eq/kg, pyridyl label: 8.3% of the TRR, 0.024 mg eq/kg). Other minor metabolites, namely fluopyram-pyridyl arboxyfic acid, fluopyram-8-hydroxy-glc-MA, fluopyram-7-hydroxy-glc, fluopyram-8-hydroxy and fluopyram benzamide amounted each to < 5% of the TRR (< 0.004 mg eq/kg), were characterized in hay (Fable 62.1-32 and Table 6.2.1-33).

<u>Wheat straw</u>: The parent compound fluopyram (phenyl label: 46.1% of the TRR, 0.233 mg eq/kg; poridyl label: 40.6% of the TRR, 0.194 mg eq/kg; was the most prominent compound in the draw samples followed by fluopyram-7-hydroxy-glc-MA (phenyl label: 10.4% of the TRR, 0.053 mg eq/kg; poridyl label: 15.2% of the TRR, 0.073 mg eq/kg), the phenyl label specific metabolite fluopyram-benzamide (8.0% of the TRR, 0.041 mg eq/kg) and fluopyram 7-hydroxy (phenyl label: 9.7% of the TRR, 0.049 mg eq/kg; pyridyl label: 11.1% of the TRR, 0.053 mg eq/kg). Other minet, metabolites, namel fluopyram-8 hydroxy-glc-MA, fluopyram-7-hydroxy-glc, thiopyram-8-hydroxy and fluopyram-benzamide amounted to < 5% of the TRR (<0.015 mg eq/kg), respectively fluopyram-methyl-suffoxide was exclusively found in straw in an amount of 2.7% of the TRR (0.013 mg eq/kg). Moreover and unknown components, all below 1.5% of the TRR (<0.004 mg eq/kg), were characterized in hay (Table 6.2.1-32 and Table 6.2.1-33).

<u>Wheat grain</u>. The patent compound fluopyram (phenyl label: 466% of the TRR, 0.003 mg eq/kg; pyridyl label: 59.2% of the TRR, 0.007 mg eq/kg) was the most prominent compound in the straw samples followed by the two phenyl labels pecific metabolites fluopyram-benzamide (phenyl label: 10.4% of the TRR, 0.001 mg eq/kg) and fluopyram-benzamide (phenyl label: 10.4% of the TRR, 0.001 mg eq/kg) and fluopyram-benzamide (phenyl label: 10.4% of the TRR, 0.001 mg eq/kg) and fluopyram-benzamide (phenyl label: 10.4% of the TRR, 0.001 mg eq/kg) of the TRR; < 0.001 mg eq/kg). The last was exclusively found in grains. One additional mor metabolite was fluopyram-7-hydroxy, amounting to 3.4% (< 0.001 mg eq/kg) of the TRR and 19.9% (0.002 mg eq/kg) of the TRR, were characterized in grains (Table 6.2.1-32 and Table 6.2.1-33).

mg eq/kg) of the TRR Moreover, two unknown components, accounting for 17.3% (0.001 mg eq/kg) of the TRR and 19.9% (0.002 mg eq/kg) of the TRR, were characterized in grains (Table 6.2.1-32 and Table 6.2.1+33).



seed dressing with [p]		rage	Ha	y	Stra	w ≫	Gi	ain
TRR $[mg eq/kg] =$		0.132 0.238		0.506		0,006		
Compound	% of TRR	mg eq/kg	% of TRR	mg eq/kg	% of TRK	mg eq/kg	% of TRR	mrgy Reg kg
AE C656948, a.s., fluopyram	65.3	0.086	51	0.122	4 6.1	0.233	XA0.6 ~	0.003
fluopyram-benzoic acid (M33)	-	-	*	-	Q -	- 🧑	₽ 8.0₽₽	<0.00H
fluopyram-benzamide (M25)	2.3	0.003	@11.4	0.027	8.0	0.044	1.07	0,001
fluopyram-7-hydroxy-glc-MA (isomer 1 & 2) (M12)	11.0	0.0150	12.1	0.029	£9 .4	\$.053	54 -	°, °
fluopyram-8-hydroxy-glc-MA (M19)	1.9	0×003	©2.5	0.006		0.020	<u>_</u> %	ŝ
fluopyram-7-hydroxy-glc (M11)	2.3	9.003√	© 2.1 ×	0.005	10	0,009	~	<u> </u>
fluopyram-7-hydroxy (M08)	6.2	0.00	.8.9	0:020	9.7	0.049	3.4	~0.001°
fluopyram-8-hydroxy (M18)	0.8	0:001		ò - `	1.4	0.007	-& ~	
Total identified	89.8	0.119	87.8	0,209	Ø .4	4 .402	62.3	$O_{0.004}$
unknown 1		-		\$0.003	1.2	0.006	17,30	0.001
unknown 8	× 0.8	0.001 0.001 0.001	Ž - 6	° - , °		õ	~~~	-
untrourn 11 AV	×1.0	0.001		0.002	2.0	2010	<u> </u>	-
unknown 14	1.0	0.001	Q.8	\$0,002 s	\$ 4.3 m	0.022	5× -	-
unknown 17 🔊 🖉 🔍	Q.6	0.001		- ~	× - ~	Ô	-	-
Total characterised	3.5	0.005	3.00	0,007	Â.Ă	AD 038	17.3	0.001
Total extracted	93.3	0.124	96,8	A2 16	ي 86.8 چ	0 .439	79.6	0.005
Solids	^\$~7		Sor a	0.022	12.3	0.062	20.4	0.001
(non-extractable residue)	×0 ^{9.} / *	0.0092 7 %		0.022	0		20.4	0.001
Fractions not analysed	<u>.</u> ~	-\$	~	<u>s</u>	£0.9	0.005	-	-
Accountability 🖓 🌾	100%0	00332	40 0.0	0.238	100.0	0.506	100.0	0.006
unknown 14 unknown 17 Total characterised Total extracted Solids (non-extractable residue) Fractions not and ysed Accountability Accou								



	For	age	Н	ay	Str	any.	Gr	and .
TRR $[mg eq/kg] =$	0.1	42	0.2	287	0	97	6ÇČ	í12 💭
Compound	% of TRR	mg eq/kg	% of TRR	mg eq/kg	%of ≸RŘ	mg eq/kg	%cof PRR	¢ ¢g/kg
AE C656948, a.s., fluopyram	62.6	0.089	6 2.8		240.6	0.194	59.2	0.00
fluopyram-methyl-sulfoxide (M45)	-	- "	-	- 2	2.7	0.003	Ş)	*-
AEC656948-pyridyl-carboxylic acid (M43)	3.6	0.000	1.7	0.005	-	~	Q-	5 ⁹ - (
fluopyram-7-hydroxy-glc-MA	10.0	0017	11.0	.0.034	$\hat{\mathcal{O}}_{152}^{\circ}$	S 0774	, Ĉ	, ¢
(isomer 1 & 2) (M12)	12.3	0.01/	11.9 🏾	V.034	× 15.2 ≪	0.073	D	- Ô
fluopyram-8-hydroxy-glc-MA (M19)	2.3	0.003	1,50	0.004	2.9	0014	\sim	~ <u>~</u>
fluopyram-7-hydroxy-glc (M11)	2.4	0:003	<u>Ž</u> .2	\$ 006	2 .2	0.010	- 4	-
fluopyram-7-hydroxy (M08)	×.2 s	Ø .007a	Ø8.3 ·	0.024	⁰ 11.]	0.05	-6	r€°
fluopyram-8-hydroxy (M18)	0.6	″0.00î∖∕	0.70	0.002	1.8°	0,008	Ű,	, Q'
Q		×,		,0 [*]	×	S.		A.
Total identified	89.1	0.126	89.1	00.255	Q76.6.	≥ 0.36	59,2	0.007
unknown 4 🦧 👸	- 7	- 🄊	- 5	-0	16	0.005	. KS	-
unknown 7	0.4	0.001	, D	5	2 ⁰	<u> </u>	`∼> -	-
unknown 8	Q.7	0.001	~- ~	69'- »	- (> - %	9 19.9	0.002
unknown 11 🧼 👋 🦽	©"0.9 <i>"</i>	∮0.001 _⊘	1.2 🖑		2.2	0.010	-	-
unknown 11 unknown 14	1.10	0.002	1.4	0,004	<u>6</u> %	0,032	-	-
Total characterised	<u>S</u>	@@04	Ő ^{2.7} (0.008	چ» 9.9 ک	0 .047	19.9	0.002
Total extracted	92.2	0.131	⊁91.8 ₀	0.263	86:5	0.413	79.1	0.009
Solids	2.8	0.00	c/h	Q.024	125	0.060	15.6	0.002
(non-extractable residue)			B.Z	9 .024	J ^{12.5}	0.000	13.0	0.002
Fractions not and ysed	· · · ·	× - «	~(P - 🔊	× 1.0	0.005	5.3	0.001
Accountability	100.00	0.142	100.0	0.287	100.0	0.477	100.0	0.012

The translocation and metabolism of the singlicide AE (656948 was investigated in wheat after seed treatment. Two experiments were performed in parallel, one with test item radiolabelled in the phenyl moiety and the second with test them radiolabelled in the pyridyl moiety.

In the edible plant matrix (wheat grain) the TRR values amounted to 0.006 mg eq/kg (phenyl label) and to 0.012 mg eq/kg (pyridyl label), respectively. The highest TRR values in both experiments were detected in straw at 0.506 mg eq/kg (phenyl label) and 0.477 mg eq/kg (pyridyl label), respectively.

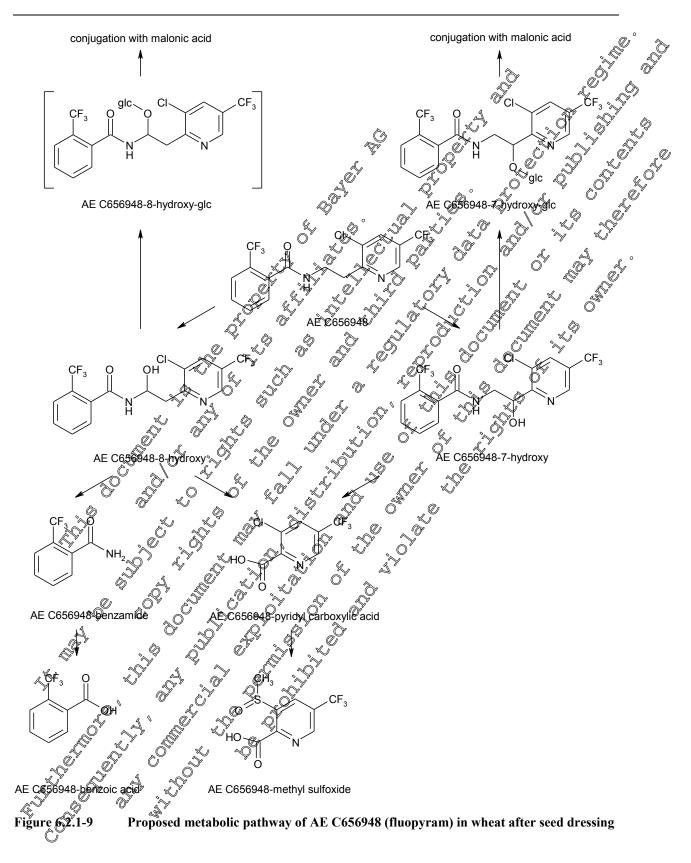
The metabolite patterns of the RACs of the present study were comparable to those obtained in the CRC studies. Parent compound was the main constituent in all RACs, accounting for more than 40% of the TRR in the secure atment study. In total nine metabolites were identified.



The following main metabolic routes were deduced:

.ongeneration of the second of Cleavage of the hydroxylated metabolites with and without additional oxidation
 On the basis of the nature and amount of metabolites found in forage, has straw and grains, pathway of fluopyram in wheat after seed treatment is proposed Figure 2.1-9.
 On the basis of the nature and amount of metabolites found in forage, has straw and grains, pathway of fluopyram in wheat after seed treatment is proposed Figure 2.1-9.
 On the basis of the nature and amount of metabolites found in forage, has straw and grains, pathway of fluopyram in wheat after seed treatment is proposed Figure 2.1-9.
 On the basis of the nature and amount of metabolites found in forage, has straw and grains, pathway of fluopyram in wheat after seed treatment is proposed Figure 2.1-9.
 On the basis of the nature and amount of metabolites found in forage, has straw and grains, pathway of fluopyram in wheat after seed treatment is proposed Figure 2.1-9.
 On the basis of the nature and amount of metabolites found in forage, has straw and grains, pathway of fluopyram in wheat after seed treatment is proposed Figure 2.1-9.
 On the basis of the nature and amount of metabolites found in forage, has straw and grains, the found in found







Assessment and conclusio	n by applicant:
The study is valid and accept	ptable.
Metabolism in paddy ric	n by applicant: ptable. e (foliar spray application) KCA 6.2.1/11 2018
Data Point:	KCA 6.2.1/11
Report Author:	
Report Year:	
Report Title:	Metabolism of [phenyl UL-14C ffluop) ram (ASC656948) in Gaddy rice after foliar treatment
Report No:	M17304953-2 2 ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~
Document No:	M-615284-01-10 , ~ 0 , ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~
Guideline(s) followed in study:	OECD Test Grideline No. 500, Commission Regulation (EUCNo. 289/2013) accordance with Regulation (EC) No. 1107/2009, OS EPA OCSPP, Test Guideline No. 860.1300; JAP FAMIC-ACIS Notification (2) Nousan 8147.
Deviations from current test guideline:	
Previous evaluation:	No, not previously submitted @
GLP/Officially recognised	Yes, conducted under GLP (Protocially becognised testing factories
Acceptability/Reliability:	$\begin{array}{cccccccccccccccccccccccccccccccccccc$

The metabolism of phenyl²UL-¹C]fluopyram formulated as an SC 400 was investigated in paddy rice following two forar spray applications. The applications were performed at BBCH 49 (flag leaf sheath open) and BBCH 65-¹D (between full flowering period and development of fruit - early milk). The single application rates were 118 and 420.7 g as ./ha, the total application rate was 239 g a.s./ha.

Executive Summar

The rice straw with panicles were harvested at maturity (BBCH 89-92), 30 days after the last treatment and dried. After drying, the rice panieles were separated into hulls and kernels. The straw, hulls and kernels were extracted at least three times with mixtures of acetonitrile/water, the concentrated extracts were analysed by HPLC and TLC and parent compound and metabolites identified. In total 96.9% (5.423 mg eq/kg), 91 % (4.8% mg eq/kg) and 93.6% (0.189 mg/kg) of the TRR was extracted from the rice straw, hulls and kernels respectively.

The TRR in padey rice straw and hulls were highest at 5.599 mg eq/kg and 5.362 mg eq/kg respectively due to the foliar application. Significantly lower residues were observed in the rice kernels with a concentration at 0.203 mg eq/kg.



Parent compound was the main component detected in all the matrices amounting to 76.3% (4.27) mg eq/kg) of the TRR in the rice straw, 86.5% of the TRR (4.636 mg eq/kg) in the hulls and 85.0% (0072 mg eq/kg) of the TRR in the kernels. Besides parent, three further metabolites were identified fluopyram 7 hydroxy, fluopyram-8 hydroxy and fluopyram-benzamide. All three were minor accounting for a maximum of 8.9% of the TRR or 0.496 mg eq/kg. The largest at 8.9% of the TRR was fluopyram-8 hydroxy and was seen in the rice straw. Up to eight additional minor metabolites (each $\leq 1\%$ of the TRR) were characterised based on the extraction procedure, partitioning behaviour and retention time. In total 92.8% of the TRR in the straw, 90.3% of the TRR in the hulls and 91.6% of the TRR in the series were identified.

The following two metabolic reactions occurred in the plants :

- hydroxylation of the ethyl linking group of the parent compound forming 7- and 8- hydroxy metabolites.
- hydrolytic cleavage of fluopyram-8-hydroxy feading to formation of fluopyram-benzamide

Based on these results, the metabolism of [phenyl-Ul Q^{14} C]fluopyrant in paddy roe after foliar treatment can be considered as well, understood and a metabolic pathway proposed. This metabolism study successfully fulfils all of the requirements of OECD test guideline 50 (2007)

A. Materials	Materials and Methods
A. Materials	
Chemical structure	CF3 CF3 CF3
Chemical structure	
Chemical structure	
	H C
Radia belled test material	*position of the radiolabel
	[phenyl_OL- ¹⁴ C]fluopyram
Specific radioactivity	5.15 ABq/mg
Radiochemical purity	
Radiochemical purity	KML 10175

2. Soils Monheim 4" (sandy oam from Germany), pH (CaCl₂) = 6.7, 72% sand, 18% silt and 10% clay, 1.1% organic carbot, cation exchange capacity (CEC) of 8.5 meq/100 g

3. Plant: Paddy rice, variety: "Balilla"



B. Study Design

1. Experimental conditions:

The paddy rice was cultivated under artificial temperature and light conditions in a greenhouse at the test facility. Plants were pre-grown in a Japanese nursey box. The pre-grown seedlings were transported into a plant container (surface of 0.5 m²) filled with a sandy from soil in eleven planting toles. Each planting O hole contained four seedlings. Water was then added to the plant container to a level of ca, 2 cm above the soil. Evaporated water was regularly renewed during cultivation until 12 days before harvest (the last irrigation was performed on the 20th March 2017). Hence, 88 plants were sprayed with phenye UL-¹⁴C]fluopyram formulated as an SC 400 with a kand putting sprayer. The envisinged use pattern at initiation of the study included two spray applications, each 1 log g a.s. that regulting is a maximum annual field rate of 220 g a.s./ha. The first field application was proposed at flag leaf sheath open growth stage BBCH 49; 10th February 2017) and the second application at between full flowering and front development - early milk (growth stage BBCH 65-73; 1st March 2017) The metabolism study simulated the envisaged use pattern according to agricultural practice and were based on the maximum proposed application rate. The time interval between the first and the second application was 39 days

Ô 0 All experiments were performed in the growthous with a day/night rhythm of 14/10 hours and an average temperature of 25 °C (day) and 20 °C (night) and a relative humidity of 80%

2. Sampling

Ľ

The rice plants were cucoff just above the soil surface at BBCH growth stage 89-92 (31st March 2017), 30 days after the last treatment and dried for 4 days After four days of drying in the greenhouse the grains were separated from the panicles, and the empty panicles added to the straw sample. The straw was cut into 1-2 cm lengths and an aliquot homogenised with liquid nitrogen in a highspeed blender. The rice grain was passed through a rice husker to remove the hulls and an alique of the hulls homogenised with liquid nitrogen using a polytron homogeniser. The husked grains (kerrels) were again homogenised with liquid nitrogen using a polytron homogeniser \measuredangle All samples stored at \le -18 °C until analysed.

C. Analytical Procedur

Straw, rise hulls and kernels were extracted and the extracts were analysed by HPLC and TLC.

1. Extraction and fractionation:

An aliquot of the hoppogen sed rice straw was soaked in acetonitrile/water (8:2, v/v) before being extracted using a high-speed blender. The extraction was repeated using acetonitrile/water (8:2, v/v) twice more and then finally work acetonitrile water (1:1, v/v). The suspensions were vacuum filtered and the three acetomitrile/water (\$2, v/) extracts combined and purified by SPE. The acetonitrile/water extract was passed through a pre-conditioned C18 solid phase extraction cartridge. The cartridge was then rinsed with an aliquer of acetonitrile and eluted with a mixture of methanol and THF. The resultant percolate and rinse



fractions were then mixed with the fourth extract (acetonitrile/water (1:1, v/v) subsequently concentrated by rotary evaporation and analysed by HPLC.

An aliquot of the homogenised <u>rice hulls</u> was treated in the same manner as the straw. The hulls were soaked in acetonitrile/water (8:2, v/v) before being extracted using a high-speed blender. The extraction was repeated using acetonitrile/water (8:2, v/v) twice more and then finally with acetonitrile/water (1,4, v/v). The suspensions were vacuum filtered and the three acetonitrile/water (8:2, v/v) extracts combined and purified by SPE. The acetonitrile/water extract was passed through a pre-conditioned C1s solid phase of extraction cartridge. The cartridge was then rinsed with an aliquot of acetonitrile and eluted with a mixture of methanol and THF. The resultant percolate and these fractions were then mixed with the fourth extract (acetonitrile/water (1:1, v/v) subsequently concentrated by fotary evaporation and analysed by HPLC

An aliquot of the homogenised <u>rice kernets</u> was soaked in actionitrile/water (8:2, \sqrt{v}) before being extracted using a high speed-blender. The extraction was repeated using acetonitrile/water (8:2, \sqrt{v}) three further times. The suspensions were vacuum filtered and the four acetonitrile/water (8:2, v/v) extracts combined and purified by SPE. The acetonitrile/water extract was passed through a pre-conditioned C18 solid phase extraction cartridge. The cartfidge was then rinsed with an aliquor of acetonitrile and eluted with a mixture of methanol and TotF. The resultant periodate and rinse fractions were concentrated by rotary evaporation and analysed by HPLC.

The radioactivity in liquid samples was determined by liquid scintillation counting (LSC). Solid samples were combusted. The O_2 produced by combustion was absorbed in a O_2 absorbent/ scintillation cocktail mixture and the radioactivity was measured by LSC.

The total radioactive residue (TRR) was determined by summation of the radioactivity of the combined extract(s) and of the remaining solids. The TRR was expressed in mga.s. equivalents per kg sample weight. Amounts of radioactive residues in the extracts were expressed as percentage of the TRR and also as mg a.s. equivalents per kg sample weight.

2. Identification and characterisation:

For elucidation of metabolism extracts and phases were analysed by HPLC and/or TLC with radio detection. Metabolites were either identified by LC/MS/MS of isolated peaks (in some cases supported by NMR) or by co-chromatography, with authentic reference compounds using two independent chromatographic methods with different selectivity (e.g. HPLC and TLC).

3. Storage stability;

All extraction experiments for metabolism investigations and the first HPLC analyses were performed within two months after sampling of the individual rice samples. The conventional extracts were analysed by HPLC or the day of the extraction. It is therefore concluded that the residues in the extracts were sufficiently stable during the experimental period of the study and that the chromatograms represented the metabolic pattern at harvest. All samples were stored at \leq -18 °C.



Determination of the extraction efficiency of the residue method

Validation of the residue analytical method 00984/M003 was performed in this study. Aliquots of rice straw and kernels were extracted by shaking with a mixture acetonitrile/water (8/2, y/y). The suspensions were vacuum filtered and the extracts purified by SPE, concentrated by rotary evaporation and analysed by HPLC. The resulting chromatograms were compared to the HPLC chromatograms from the corresponding sample extracts performed in this study and the extraction efficiency of the residue analytical method 00984/M003 calculated.

II. Results and Discussion

was investigated impaddy rice The metabolism of [phenyl-UL-14C]fluopyram formulated as following two foliar spray applications, alongle rates of 18 s/ha and a total rate of 239.0 g a.s./ha.

The TRRs in straw and hulls were relatively high amounting tos mg eg/kg (Table 6.2.1- 34). Significantly lower residues were observed in the ediple RAG (raw agricultural commodity), rice kernels (0.203 mg eq/kg) due to protection by the hufts.

1 able 6.2.1- 3	4: I RR values m pagety rice mat		t & phenyl- 🖓	2- ¹⁴ C]fluopyram
Matrix	Tyming and Application	🔊 Growth stage at		TRR
		, Onarvest "	(days)	(mg a.s. equiv./kg)
Straw	10toliar meatment at growth stage	57 BBCH 88-92	× 30	5.599
Hulls	2 nd foliai@reatmon at growth stage		30	5.362
Kernels	BBCH 65-73 5 with 118.3 gas./ha	BBCH 88 92	30	0.203

values were determined by summing up the radioactivity measured in the extract and in the PHI = pre-harvest interval, the TRK remaining solids

The straw, hulls and kernels were extracted at least three times with mixtures of acetonitrile/water (8/2;v/v), the concentrated extracts were analysed by HPCC and TLC and parent compound and metabolites were ŝ identified.

From rice straw, a portion of 96.9% of the TRR (5.423 mg eq/kg) was extractable with acetonitrile/water (Table 62.1-35) and 3 1% of the TRR (0.176 mg eq/kg) remained in the post extraction solids. From rice hulls, 97.1% of the TRR (4.888 mg eq/kg) was extractable with acetonitrile/water, 8.9% of the TRR (0.475 mg eq/kg) remained in the post extraction solids. Acetonitrile/water extracted 93.3% of the TRR (0.189 mg/kg) from the rice keepels leaving 6.7% of the TRR (0.014 mg eq/kg) in the post extraction solids (PES).



Virtually no radioactivity was lost during concentration of the extracts <0.1% (0.002 mg eq/kg). Only a small amount of radioactivity <0.2% (0.012 mg eq/kg) of the TRR was detected in the methanol/HF eluates of the SPE purification procedures from the rice straw and hulls.

apı	olication of [ph	enyl-UL- ¹⁴ C]fl	luopyram 🔊	、 、	\$, ×°
	stra	aw	(tru	ills 🖉	ker	nels 🔊	
TRR $[mg/kg] =$	5.5	99	5.3	62	02	203 🔊 🖌	
	% of TRR	mg a.s. equiv./kg	% of TRR	mg a(s. equiv/kg	°% of TOR	Ong a.s	
Acetonitrile/water extract	96.9	5.423	^{91,1}	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	93.3 C	, 0 ² 289	
Concentrate used for quantitation of metabolites	96.9	5.423	91.1 91.1	Q.88 Č	9393	\$ 0.1 \$ 9 \$	Ŷ
Not analysed fraction (methanol / THF)	0.2	0,012	× 91.1 0 × 0 × 0 × 7 × 7 × 7 × 7 × 7 × 7 × 7 × 7	0.006 0.006 0.002			
Not analysed fraction (condensate)	-	V	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		, . , .	
Not analysed fraction (distillate)	<0.1			5 0.00 <u>2</u>		°∼ý -	
Total extracted	96.9	5.423	£ 91.1	4.88	≥93.3 O	0.189	
Post extraction solids (PES)	96.9 3.1	6 2176	8,9	0.405	6.7	0.014	
Accountability	× 100 0	\$ 5.599 ^{°°}	0100.0 °	\$5.362	100.0	0.203	1
			5°, 5°		- Contraction of the second se		_

Table 6.2.1-35:	Distribution of radioactivity in the extracts of the paddy application of [phenyl-UL- ¹⁴ C]fluopyram	y rice <u>m</u> atrices	after foliar	spr
	application of [phenyl-UL- ¹⁴ C]fluopyram	sto "	°~~ °.	Ğ,

The radioactive residues in the acetonitrile/water extract from the participation of the form the form the participation of the form the acetonitrile/water extract from the participation of the form the form the form the participation of the form the participation of the form the form the form of the for

In the rice hull 86.5% of the PRR (4,636 mg/eq/kg) was parent compound. As with the rice straw the three minor metabolites huopycam-7, hydroxy, fluopyram-8 hydroxy and fluopyram-benzamide were all identified with each accounting for $\leq 22\%$ (5).120 ng/eq/kg) of the TRR. Five additional very minor metabolites each at $\leq 02\%$ (≤ 0.010 mg/eq/kg) of the TRR were characterised based on the extraction procedure, partitioning behaviour and retention tone. In total 90.3% (4.845 mg/eq/kg) of the TRR in the rice straw was identified and 0.8% (0.045 mg/eq/kg) of the TRR characterised based on the extraction and chromatographic behaviour.

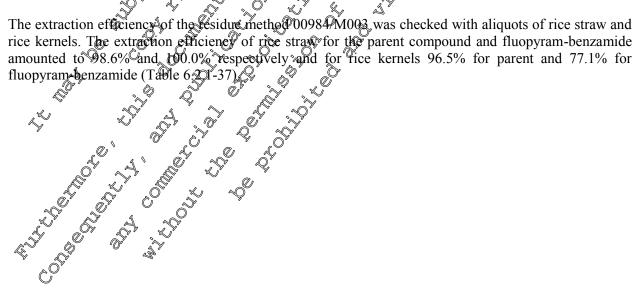
In the edible RAC rice kernels, parent compound was the main component amounting to 85.0% (0.172 mg eq/kg) of the TRR. Besides parent the three metabolites fluopyram-7 hydroxy, fluopyram-8 hydroxy and fluopyram-benzamide were all identified each accounting for $\leq 4.8\%$ (≤ 0.010 mg eq/kg) of the TRR. In total 91 % (0.86 mg/eq/kg) of the TRR in the kernels was identified. Only two minor peaks accounting for $\leq 1.0\%$ (0.002 mg eq/kg) of the TRR were characterised based on the extraction and chromatographic behaviour.



Fable 6.2.1-36: Distribution of parent					paddy rice	matrices
after foliar spray app				am á)	
TDD [ma/la] =		aw 599		362 Ø	ker 0.2	
TRR [mg/kg] =						
Compound	% of	mg a.s.	% of	mg≏a s.	% of ô	mg@.s. equiv./kg
	TRR	equiv./kg	> TRR	equiv./kg	TRR	equiv./kg
Acetonitrile/water extract	760	¥	065			
AE C656948 (fluopyram)	76.3	4.278	86.5	¥ 4.636	\$5.0 5	0.172
fluopyram-benzamide (M25)	6.6	0.368	2.2	0.120	o [∞] 4.8 Q̃	0.010
fluopyram-7-hydroxy (M08)	2.0	Ø: f 11	0.9	@.047		@.002_C
fluopyram-8-hydroxy (M18)	8.9	∞0.496	0.8	©0.042	<u>9</u> .7	0.000
Total identified	93.8 🖔	5.250	్ష స్త్రి0.3 🔨	4,845	91.6	0,186
Unknown 1	0.1	.0 07 (~0- <i>i</i>	1.0	0.002
Unknown 2	0.3	, @0.015 Ø	0Q	0.008	Ke	~0.001°
Unknown 5	Q.5 ~	× 0.029×	≫0.1 <i>⊨</i>	0.004		, -O ^V
Unknown 6	0.3 °	0,0216 、	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Í ,~~	~ - ₄ , `	, SF
Unknown 5	₩ 0. Q	0.051	0.%	õ.010 🦉		Ő -
Unknown 6	003 [×]	∿>0.014€)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	S - S	, Q ^e	-
Unknown 7	b - 6	<i>₽</i> ≫	A)0.1	0.003	N - W	-
Unknown 8	🔊 0.5 🔊	0.027	0.2	19910	O _ Š	-
Sum of unknowns (characterised by HPLC)	2,8	0.159		\$ 0.036 ⁰	. .7	0.003
Not analysed fractions (total)	6 0.3	0,015	0.1	0.007	Q -	-
- not analysed fraction (methanol (FHF))	0.2	012	0.1	×0.006	-	-
- not analysed fraction (Condensate)	-	2 - 📎	× (-	-
- not analysed fraction (distillate)	<u>∼</u> 0.1 ~	0.002	<0.1 0	0.002	-	-
Total characterised O (HPLC and not malysed)	× 3.1×	2 0,1 73	0,8	% .043	1.7	0.003
Total extracted	6.9	5.423,	.9M.1	4.888	93.3	0.189
Unextractable (PES)	3.1	0,476	0 8.9 0	0.475	6.7	0.014
Accountability	100.0	5.599	100,0	5.362	100.0	0.203
Peak assignments (M3, 5, 60, 8, 9, 10, 11 and	(4) were not as			5.502	100.0	0.205

Peak assignments (M3, 5, 60, 11 and 14) were not assigned in this study

j.





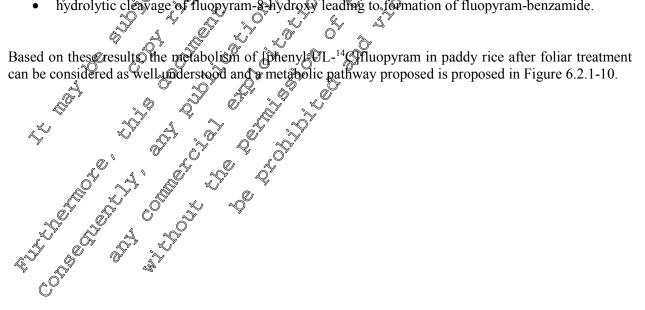
		Rice straw]	Rice kernels	Š ^V (
	Metabolism method	Residue method	Extraction efficiency	Metabolism method	Residue method	Extraction efficiency
	%TRR	%TRR	[%]	%TRR 🕰	%TRR	
Total extracted	96.9	94.1	Ĉ	93.3	88.0 🔊	
Unextracted (PES)	3.1	5.9	- The second sec	6, D [¥]	12.0	
TRR	100.0	100.0	L	168.0	1000	$\gamma \sim$
AE C656948 (fluopyram)	76.3	75.2	_₄ [®] 98.6	\$85.0	\$2.0 4	Q 965 g
fluopyram-benzamide	6.6	6.6	<u>م</u> 100.0	[™] 4.8⊘°	L 3.7 L	° 07.1 ,0°
TRR of relevant residues	82.9	81.8	98.7	× 89 ⁹ 8	× 85, D	© 95.4 °

Conclusion

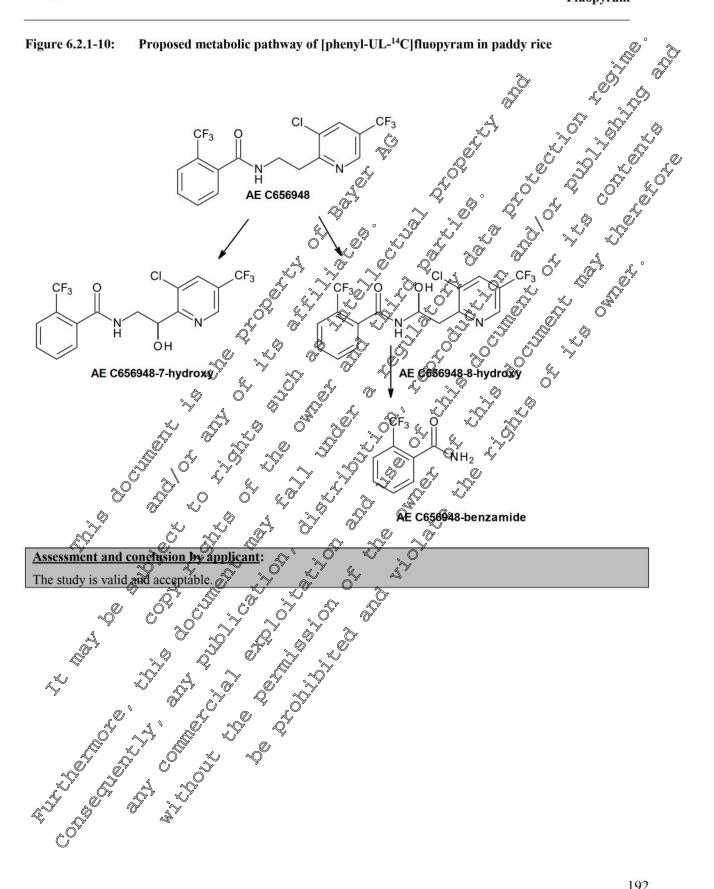
After foliar spray application of [phenyQring_UL-14C] Puopytam, the highest residues were in particular straw (5.599 mg eq/kg) and hulls (5.362 mg eq/kg) and matuly consisted of parefr compound, amounting to 76.3% and 86.5% of the TRR respectively due to the direct exposure from Foliar Deatment. The TRR found in the edible RAC kernels amounted to 0.203 mg eg/kg and again consisted of mainly parent compound at 85.0% of the TRR. Three further identified metabolities fluopyram-Phydroxy, fluopyram-8 hydroxy and fluopyram-benzamide were all minor accounting for Mess than 8,9% of the TRR. Up to eight additional unknown metabolites were characterised by HPLC but represented 1% each of the TRR in all plant parts.

Two metabolic reactions occurred in the plants Ś

- hydroxylation of the etho linking group of the parent compound forming 7- and 8- hydroxy metabolites. Ø
- fluopyram-&hydro leading to formation of fluopyram-benzamide. age`of hydrolytic clean









	° ô
Data Point:	KCA 6.2.1/12
Report Author:	
Report Year:	
Report Title:	Metabolism of [pyridyl-2,6-14C]fluopyram (AE C656948) in paddy rice after toliar
Report No:	M17304952-1
Document No:	<u>M-615282-01-1</u>
Guideline(s) followed in	M-615282-01-1 OECD Test Guideline No. 50 accordance with Regulation (EUCNo. 283/2013 m accordance with Regulation (EUCNo. 283/2013 m (C) (C) (C) (C) (C) (C) (C) (C) (C) (C)
study:	accordance with Regulation (EC) No. 1107/2009; US EPA OCSPP (Jest Guideline)
	No. 860.1300; JAP FAMIC-ACIS Notification 12 Nousan 8147
Deviations from current	none O' O' K K K K K
test guideline:	
Previous evaluation:	No, not previously submitted Yes, conducted under GLP/QfHcially recognized testing facilities
GLP/Officially recognised	Yes, conducted under OLP/Officially recognized testing facilities
testing facilities:	
Acceptability/Reliability:	Yes yes a a b' O' by sy the
A .	* A Executive Sammary

The metabolism of pyride 2,6-40 fluopyram formulated as an SC 400 was investigated in paddy rice following two folder spray applications. The applications were performed at BBCH 49 (flag leaf sheath open) and BBCH 65-75 (between full flowering period and development of fruit - early milk). The single application rates were 123.3 and 126.3 g a.s./ha. the total application rate was 249.6 g a.s./ha.

The rice straw with panicles were harvested at maturity (BBCH 89-92), 30 days after the last treatment and dried. After drying the rice panicles were separated into fulls and kernels. The straw, hulls and kernels were extracted at least three ones with minutes of acetonitrile/vater, the concentrated extracts were analysed by HPLC and FLC and parent compound and metabolites identified. In total 93.9% (4.344 mg eq/kg), 88.5% (3.819 mg eq/kg) and 92.7% (0.242 mg/kg) of the TRR was extracted from the rice straw, hulls and kernels and kernels are specified.

The TRRs in paddy rice praw and hulk were bighest at 4.626 mg eq/kg and 4.316 mg eq/kg respectively due to the fobrar application. Significantly lower residues were observed in the rice kernels at a concentration of 0.261 mg eq/kg.

Parent compound was the pain component detected in all the matrices amounting to 76.2% (3.525 mg eq/kg) of the TRR in the rice straw, 86.3% of the TRR (3.724 mg eq/kg) in the hulls and 88.3% (0.230 mg eq/kg) of the TRR in the kernels. Besides parent three further metabolites were identified :fluopyram-7 hydroxo fluopyram-8 hydroxy and fluopyram-pyridyl-carboxylic acid. All three accounted for \leq 9.8% of



the TRR or ≤ 0.455 mg eq/kg in rice straw, $\leq 1\%$ TRR and ≤ 0.05 mg eq/kg in hull and $\leq 5\%$ TRR (≤ 0.01 mg eq/kg) in kernel. The largest at 9.8% of the TRR was fluopyram-8 hydroxy and was seen in the rice spaw. Up to eleven additional minor metabolites (each $\leq 1\%$ of the TRR) were characterised based on the extraction procedure partitioning behavior extraction procedure, partitioning behaviour and retention time. In total 89.6% of the TRR in the straw 88.2% of the TRR in the hulls and 92.7% of the TRR in the kernels was identified.

The following two metabolic reactions occurred in the plants

- .0 •
- hydroxylation of the ethyl linking group of the parent compound forming 7- and 8- hydroxy metabolites. cleavage of fluopyram-7-hydroxy followed by oxidation leading to formation of formation of fluopyram-pyridyl-carboxylic acid. • ô^y A

Based on these results, the metabolism of [pydyl-26⁴⁴C]buopyram in paddy rise afterfoliar azatment can be considered as well understeed and a metabolic pathway proposed. This enetabolism study successfully fulfils all the requirements of DECD test gradeline 501 (2007).



I. Materials and Methods

A. Materials	
1. Test Material:	
Chemical structure	CF ₃ CI CF ₅ CF
Radiolabelled test material	[pyridyl-2,6, C]flippyram ~ ~ ~
Specific radioactivity	3×64 MBeymg ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
Radiochemical purity	
Batch	KMK 10174 5 5 5 5 5

2. Soil: "Monheim 4" (sandy loan from Germany), ph (Cach) = 60° , 72% and 8% silt and 10% clay, 2. Soil: "Monheim 4" (sandy loan from Germañy), pbr (CaGt2) = 60, 72% sand 18% 1.1% organic carbon, cation exchange capacity (CEC) of 8.5 med/100 g
3. Plant: Paddy rice, vaniety: "Balilla"
B. Study Design 1. Experimental conditions: The paddy rice was contivated under artificial temperature and light conditions in a green set of the paddy rice was contivated under artificial temperature and light conditions in a green set of the paddy rice was contivated under artificial temperature and light conditions in a green set of the paddy rice was contivated under artificial temperature and light conditions in a green set of the paddy rice was contivated under artificial temperature and light conditions in a green set of the paddy rice was contivated under artificial temperature and light conditions in a green set of the paddy rice was contivated under artificial temperature and light conditions in a green set of the paddy rice was contived to the paddy rice was contined to the paddy rice

The paddy rice was contivated under artificial temperature and light conditions in a greenhouse at the test facility. Plants were pre-grown in a Japanese nutsey box. The pre-grown seedlings were transplanted into a plant container (surface of 0, 5m²) filled with a sandy loan soil in eleven planting holes. Each planting hole contained four sectings Water was then added to the plant container to a level of ca. 2 cm above the soil. Evaporated water was regularly repowed during cultivation until 11 days before harvest (the last irrigation was performed on the 20th March 2017), Hence, 88 plants were sprayed with [pyridyl-2,6-¹⁴C]fluogyram formulated as an SC 400 with a hand pump sprayer. The envisaged use pattern at initiation of the study included two spray applications, each 110 g a.s./ha, resulting in a maximum annual field rate of 220 g a.s./ha. The first field application was proposed at flag leaf sheath open (growth stage BBCH 49; 9th February 2017) and the second application at between full flowering and fruit development - early milk (growth stage BBCH 65-73; 28th February 2017). The metabolism study simulated the envisaged use pattern according to agricultural practice and were based on the maximum proposed application rate. The time interval between the first and the second application was 19 days.

All experiments were performed in the greenhouse with a day/night rhythm of 14/10 hours and an average temperature of 25°C (day) and 20°C (night) and a relative humidity of 80%.



2. Sampling

The rice plants were cut off just above the soil surface at BBCH growth stage 89-92 (30th March 2017), 50 days after the last treatment and dried for 4 days. After four days of drying in the greenhouse the grafting were separated from the panicles, and the empty panicles added to the straw sample. The straw was at into a 1-2 cm lengths and an aliquot homogenised with liquid nitrogen in a highspeed blender. The rice grain was passed through a rice husker to remove the hulls and an aliquot of the hulls homogeneities don'th light nitrogen using a polytron homogeniser. The husked grains (kernels) were again homogenised with bouid O nitrogen using a polytron homogeniser. All samples stored at \leq -18 °Quntil analysed.

C. Analytical Procedures

tewere analysed by HPLC and Th Straw, rice hulls and kernels were extracted, and the .a.

1. Extraction and fractionation:

An aliquot of the homogenised <u>rice straw</u> was soaked in metonin $(8:2, \sqrt{v})$ before being extracted using a high-speed blender. The extraction was repeated using acetom tile/water (& Q, v/y) twice more and then finally with acetonitrile water (1:1,). The suspensions were vacuum filtered and the four acetonitrile/water (8:2, v/y)@extraco combined and purfied by SPE The combined acetonitrile/water extract was passed through a pre-conditioned CAS solid phase extraction cartindge. The cartridge was then rinsed with an aliquot of acetonic ile and eluted with a mixture of methanol and THE The resultant percolate and rinse fractions were then combined subsequently concentrated by rotary evaporation and analysed by HPLC.

An aliquot of the homogenised rice hulls was treated in a similar manner to the straw. The hulls were soaked in acetonithe/water (8:2, v/v) before being extracted using a high-speed blender. The extraction was repeated using acetonitate/water (8:2%/v) twice more and then finally with acetonitrile/water (1:1, v/v). The suspensions were vacuum filtered and the three acetonitrie water (8:2, v/v) extracts combined and purified by SPE. The acetonitrite water extragt was passed through a pre-conditioned C18 solid phase extraction cartridge. The cartridge was then rinsed with an adjust of acetonitrile and eluted with a mixture of methanol and THF. The resultant percolate and finse fractions were then mixed with the fourth extract (acetonitrile/water (1.1, v/v) subsequently concentrated by rotary evaporation and analysed by HPLC.

An aliquot of the homogenised rice kernels was soaked in acetonitrile/water (8:2, v/v) before being extracted using a high-speed blender. The extraction was repeated using acetonitrile/water (8:2, v/v) three further times. The suspensions were vacuum filtered and the four acetonitrile/water (8:2, v/v) extracts combined and purified by SPE. The acetorstrile/water extract was passed through a pre-conditioned C18 solid phase extraction cathidge. The cathridge was then rinsed with an aliquot of acetonitrile and eluted with a month a month of and HF. The resultant percolate and rinse fractions were concentrated by rotary

evaporation and analysed by PIPLC.



The radioactivity in liquid samples was determined by liquid scintillation counting (LSC). Solid samples were combusted. The CO_2 produced by combustion was absorbed in a CO_2 absorbent/ scintillation coefficient was measured by LSC.

The total radioactive residue (TRR) was determined by summation of the radioactivity of the combined a extract(s) and of the remaining solids. The TRR was expressed in mg a.s. equivalents per kg sample weight. Amounts of radioactive residues in the extracts were expressed as percentage of the TBR and also as a set of all also

2. Identification and characterisation:

For elucidation of metabolism, extracts and phases were analysed by HPLC and/or TLC with radio detection. Metabolites were identified by isolation of peaks followed by co-chromatography with authentic reference compounds using two independent chromatographic methods with different selectivity (e.g. HPLC and TLC).

3. Storage stability:

All extraction experiments for metabolism provestigations and the first HPLC analyses were performed within two months after sampling of the individual rice samples. The conventional extracts were analysed by HPLC on the day of the extraction of the day after. It is therefore concluded that the residues in the extracts were sufficiently stable during the experimental period of the study and that the chromatograms represented the metabolic pattern at Darvest All samples were at \underline{O} -18 \underline{O} .

O'II. Results and Discussion

The metabolism of [pyrdyl-2 G^{14} C] for one for the set of 123.3 and 126.3 g a.s./ha and a total rate of 249.6 g a.s./ha.

The TRR values in straw and hulls were high amounting to 4.626 mg eq/kg and 4.316 mg eq/kg (Table 6.2.1-38) Significantly lower residues were observed in the edible RAC (raw agricultural commodity), rice kernels (0.261 mg eq/kg), due to protection from the hulls.

6.2.1-38) Significantly lower residues are observed in the kernels (0.261 mg eq/kg), due to protection from the hulls.



Matrix	Timing and Application	Growth stage at harvest	PHI (days)	TRR
Straw	1 st foliar treatment at growth stage BBCH 49,	BBCH 88-92	30	4.626 ×
Hulls	123.3 g a.s./ha 2^{nd} foliar treatment at growth stage	BBCH \$8-92	2000	£4.316
Kernels	2 nd foliar treatment at growth stage BBCH 65-73 with 126.3 g a.s./ha	BBCH 88-92	3 0°	

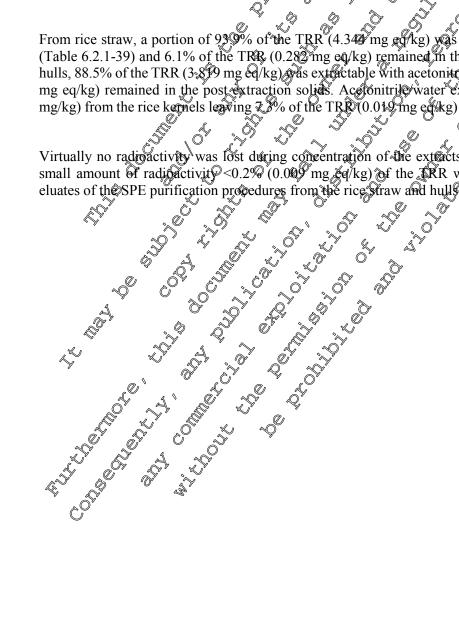
Table 6 2 1-38	TRR values in paddy rice matrices after application of [pyridyl-2,6- ¹⁴ C]fluopyram	
1 abic 0.2.1-30.	1 KK values in pauly file matrices after application of [pyridy1-2,0-1] [nupyrain	

PHI = pre-harvest interval, * the TRR values were determined by summing up the radioactivity measured in the extract and in the remaining solids

The straw, hulls and kernels were extracted by least three times with mixtures of acetonitrile/water (8 the concentrated extracts were analysed by HPLC and FLC and parcht compound and metabolites were identified.

From rice straw, a portion of 939% of the TRR (4.348 mg corkg) was extractable with acetonitrile/water (Table 6.2.1-39) and 6.1% of the TRR (0.282 mg eq/kg) remained in the post extraction solids. From rice hulls, 88.5% of the TRR (3,819 mg eq/kg) was extractable with acetonitole/water, 11.5% of the TRR (0.497 mg eq/kg) remained in the post extraction solids. Acefonitril@water extracted 92,7% of the TRR (0.242 mg/kg) from the rice kernels leaving 7.3% of the TRR (0.019 mg eg/kg) in the postextraction solids (PES).

Virtually no radioactives was lost during concentration of the extracts \$3% (0.013 mg eq/kg). Only a small amount of radioactivity <0.2% (0.009 mg eq/kg) of the TRR was detected in the methanol/THF eluates of the SPE purification procedures from the rice straw and hulls?





	stra	aw	hu	lls	ker	
TRR [mg/kg] =	4.6	26	4.3	16	0.2	261 🔧 🐧
	% of TRR	mg a.s. equiv./kg	% of TRR	mg a.s. equiv./kg	of TRR	ovg a.s.
Acetonitrile/water extract	93.9	4.344	88.5	3.819	92.7	
Concentrate used for quantitation of metabolites	93.4	4.321	\$88.3 \$	3.813	23.7 C	\$ 0.242 \$ 0.242
Not analysed fraction (methanol / THF)	0.2	0.009		[~] 0.0064´		×× - √×
Not analysed fraction (condensate)	<0.1	0.001		ð A	Č ⁹ -Č	
Not analysed fraction (distillate)	0.3	Q.013	×0.1 ×	× 0,003 ×		
Total extracted	93.9	k 4,344 j	885	3.8190	\$92.7 چې	
Post extraction solids (PES)	6.1	\$\vec{v}{0.282}	ð 1.5 "	00197	0 79 §	0.019
Accountability	100.0	4,626	× 1000	4.316	<u>0.0010</u>	0.261

Table 6.2.1-39: Distribution of radioactivity in the extracts of the paddy rice matrices after foliar spray

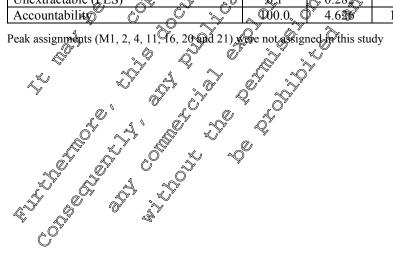
The radioactive residues in the aceton trile/water extract from the paddy five straw (Table 6.2.1-40), mainly consisted of parent sompound amounting to 76.2% (3.523 mg cg/kg) of the TRR. Besides parent a further three metabolites were identified as fluopyram-7 hydroxy, fluopyram-8 hydroxy and fluopyram-pyridylcarboxylic acie All were minor accounting for less than ≤9.8% of the TRR. Ten additional minor metabolites (each < 0% of the TRR) were characterised based on the extraction procedure, partitioning behaviour and retention the. In total 89,5% (4)42 mgeq/kg) of the FRR in the rice straw was identified and 4.3% (0.1201 m gra/kg) of the TRR characterised based on the extraction and chromatographic behaviour.

In the rice hull \$86.3% of the PRR (\$724 mg eq/kg was parent compound. As with the rice straw the three minor metabolites fluopyram-7 hydroxy fluopyram-8 hydroxy and fluopyram-pyridyl-carboxylic acid were all identified with each accounting for \$0.8% (\$0.033 mg eq/kg) of the TRR. One additional very minor metabolite at 2,1% (2005 mg eq/kg) of the TRR were characterised based on the extraction procedure, partitioning behaviour and retention time. In total 88.2% (3.808 mg eq/kg) of the TRR in the rice straw was identified and 0.3% (0.002 mg co/kg) of the TRR characterised based on the extraction and chromatographic behaviour.

In the edible RAC rice kernels parent compound was the main component amounting to 88.3% (0.230 mg eq/kg) of the JKR. Besides parent the three metabolites fluopyram-7 hydroxy, fluopyram-8 hydroxy and fluoryram-pyridyl carboxylic acid were all identified each accounting for <2.8% (<0.007 mg eq/kg) of the TRR. In total 92.⁴ (0,242 mg eq/kg) of the TRR in the kernels was identified and unextractable residues constituted 7.3% (0.019 mg eq/kg) of the TRR.



Table 6.2.1-40:Distribution of parenafter foliar spray app					paddy rice	matôjćes	10×
	•		, 10	- Or			
		aw			ker	<u> </u>	(Ĉo
TRR [mg/kg] =		526	Ϋ́Λ	816 🔊 🤊	<u>\$</u> 9.2		j j
Compound	% of TRR	mg a.s.	% of TRR	orging a.s.	‰of J¥R ≈	nig a.s. Dequiv	,©
Acetonitrile/water extract			C	\$1 <u>8</u>	× ~	2-1 <u>20-8</u>	Ô
AE C656948 (fluopyram)	76.2	3-525	86.3Q	" <i>3.</i> 924 "	88.3	230	¥
fluopyram-pyridyl-carboxylic acid	1.3	0.058	86.5% 10,4	0.019-Q	28	0.007	
(M43)		V		¥ 🔊			
fluopyram-7-hydroxy (M08)	2.3	0.005	x 0 8 x	0:033	0.9 %	0%002	
fluopyram-8-hydroxy (M18)	9.8	455		2031	0.7		
Total identified	89.6	~ 4.142	88.2	3.808	Q .7	0.242	
Unknown 1	0.3	0.018	<u>, 0</u> - , ,	× <u> </u>	× -		
Unknown 2	0.3	QQ16 2	Š <u> </u>	×?- 4	Ç _ K		
Unknown 3	D ^y ^x y	. ~		Q 005	i aş	© _	
Unknown 4	0.2	[~] 0.012 [~]	N- 8		<u> </u>	ð -	
Unknown 5	90.9	0.040	8.0		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	_	
Unknown 6		Ø 005 . (V _A	<u>ð</u> "(_	
Unknown 7	<u>í</u> Ś	c 0.012	, Ö ^ş	in - O	l a	_	
Unknown 7 Unknown 8	203	0.012	× ~	<u>, </u>	<u> </u>	_	
Unknown 9		0.020		~~ ~	<i>Q</i> -	-	
Unknown 10 🐇	0.6	\$€026 Ô	× (-	1 × ×	-	_	
Unknown 11	0.5	0.022	Õ- 4		_	-	
			0				
Sum of unknowns (characterised by TPLC) Not analysed fractions (total)	«پ» 3.9		© 0.1	0.005	-	-	
Not analysed fractions (total)	03	~~0.023 [~]	, 6 , 1	0.006	-	-	
- not analysed fraction (methanol / THF)	\$0.2 @	0.000	\$0.1	0.004	-	-	
- not analysed fraction (condensate		0%001	- x	-	-	-	
- not analysed fraction (distillated)	0.3	_0.013	′Q.Ŷ	0.003	-	- 1	
Total characterised		6 and					
(HPLC and not an speed)	6 ^{94.3}	0,201	0.3	0.012	-	-	
Total extracted 🔊 🔥 🖉	93,90	© 344	88.5	3.819	92.7	0.242	
Unextractable (PES)	1 %.Y	~ 0.282~°	11.5	0.497	7.3	0.019	
Accountability	\$ 000.0s. (¥ 4.6206	100.0	4.316	100.0	0.261	





III. Conclusions

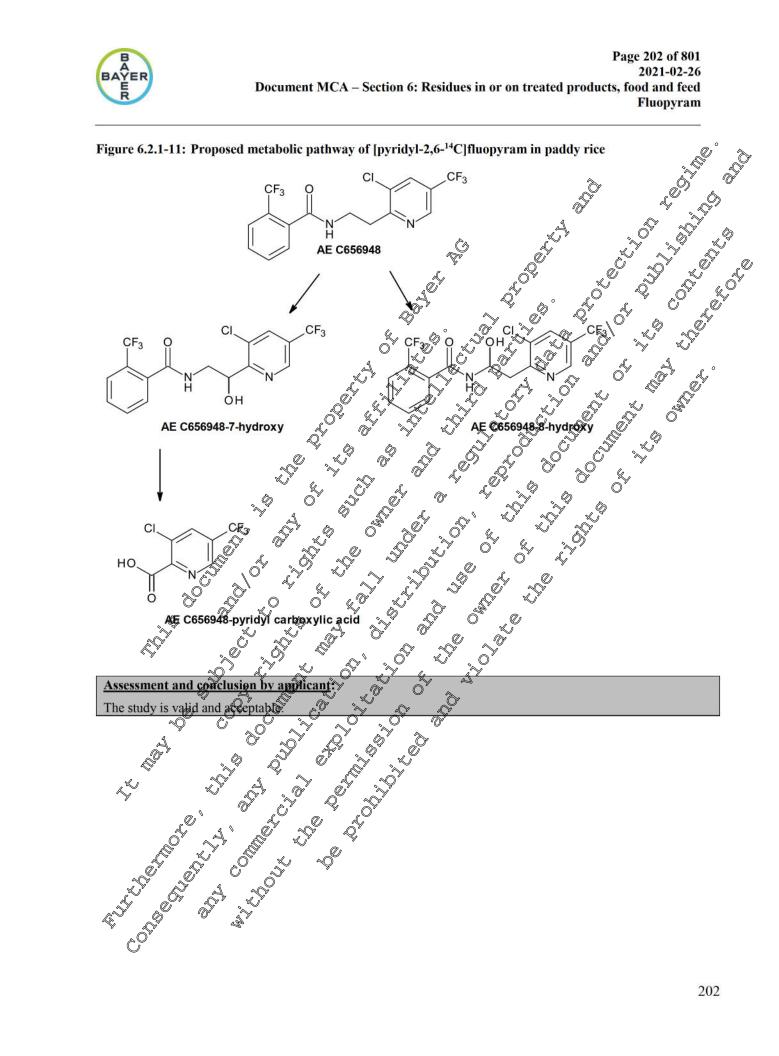
After foliar spray application of [pyridyl-2,6-14C]fluopyram, the highest residues were in paddy me straw (4.626 mg eq/kg) and hulls (4.316 mg eq/kg) and mainly consisted of parent compound, amounting to 76.2% and 86.3% of the TRR respectively due to the direct exposure from foliar treatment. The TRE found @ in the edible RAC kernels was relatively low and amounted to 261 mg eq/kg and again consisted of mainly parent compound at 88.3% of the TRR. Three further identified metabolites fluopyram-pyridy carboxy dc, fluopyram-7 hydroxy and fluopyram-8 hydroxy accounting for less than $\leq 9.8\%$ of the TRR. Ip to deven \odot additional unknown metabolites were characterised by NPLC but each represented 1% of the TRR in all plant parts.

Two metabolic reactions occurred in the plants:

- hydroxylation of the ethyl linking group of the parent compound forming 7- and 8- bydroxy metabolites. cleavage of fluopyram-7-hydroxy followed by exidation leading to formation of tormation of hydroxylation of the ethyl linking group metabolites. •
- •

Based on these results, the fretabolism of [pyrigh]-2,64 C]fluopyrant in paddy rice after foliar treatment can be considered as well understood and a metabolic pathway is proposed in Figare 6.2.1-11.







Data Point:	KCA 6.2.1/13
Report Author:	
Report Year:	
Report Title:	Metabolic and dynamic profiling for risk assessment of fluororam, a typical phenylamide fungicide widely applied in vegetable ecosystem
Report No:	<u>M-763231-01-1</u>
Document No:	<u>M-763231-01-1</u>
Guideline(s) followed in	not applicable
study:	
Deviations from current test guideline:	
Previous evaluation:	No, not previously submitted
GLP/Officially recognised	No, not conducted under GLP Officially recognised terming fachities
testing facilities:	
Acceptability/Reliability:	$Yes \qquad \qquad$

This is an article from the literature. Although it is not relevant for relevant for relevant supportive information.

🖉 ExecutiveSummary 🌜

Fluopyram, a typical phenylamide tungicide, was widely applied to protect fruit vegetables from fungal pathogens-responsible yield loss. A modified QuEChERS (Quick, Easy, Cheap, Effective, Rugged and Safe) extraction combined with GC-MS/MS analysis was developed to investigate fluopyram fate in the typical fruit vegetables including tomato, cucumber, pepper under the greenhouse environment. Fluopyram dissipated in accordance with the first-order rate dynamics equation with the maximum half-life of 5.7 d. Cleavage of fluopyram into fluopyram benzamide (2 trifluoremethyl benzamide in article) and subsequent formation of fluopyram-pyridyl-acetic acid (3-chloro-5-(trifluoremethyl) pyridine-2-acetic acid in article) and fluopyram-pyridyl-carboxylic acid (3-chloro-5-(trifluoremethyl) picolinic acid in article) was elucidated to be its ubiquitous metabolic pathway. Moreover the occurrence of fluopyram at the pre-harvest interval (PHI) of 7–2 between 0.0108 and 0.1603 mg/kg, and the Hazard Quotients (HQs) were calculated to be less than. Dindicating temporary safety on consumption of the fruit vegetables incurred with fluopyram, irrespective of the uncertain to ficity of the metabolites.

I Materials and Methods

Chemicals and reagents

Fluopyrame (purity 994%) was parchased from Dr. Ehrenstorfer (Augsburg, Germany). Fluopyrame Trifloxsytrobin SC (FLU+TFS, 500 g/L) used for field trial as well as acetonitrile (ACN, HPLC grade) ethyl acetate (EtOAc, GC grade) and other organic solvent, magnesium sulfate, sodium acetate and SA (primary secondary amine) were purchased from commercial suppliers.

Sol characteristics: 50% sand, 17% clay, 31% silt, 2% organic matter, pH 6.1, classified as sandy loam. Plants: Tomato (*Lycopersicon esculentum* cv. Dahongyihao), cucumber (*Cucumis sativus L.* cv.



Shandongmici) and pepper (*Capsicum annuum L*. cv. Qingjiaowang).

Study design and sample collection

In 2015, a field trial was conducted in fruit vegetables (tomato, cucumber and perper) in greenhouses m China (Institute of Pesticide and Environmental Toxicology, Zhejiang University, Jiangs) Province, China). For initial deposition, dynamics and metabolism, FLU+TFS SC was sprayed at rate of 62.4 ga.s./ha (2xGAP obtained from Institute for the Control of Agrochemicals, Minister of Agriculture, Chipa) when the first fruit on the main stem reached the typical size and form. Edible parts and soils, camples were taken at 2 h, 1, 3, 7, 14, 21 and 28 days after last application For monitoring of the occurrence, DU+TS SC was sprayed three times at a rate of 31.2 g a.s./ha (1xOAP) with an intervation 7 days. Mature edible part samples were collected at pre-harvest interval of 7, 14 and 21 days after the last application. Plant samples were stored in a freezer after quartering and homogenized into the sample vial. Soil samples were cleaned and screened. All field samples were stored in a Greezerat - 200°C unor analysis. All processes and operations in the supervised trials were carried out per Good Agrioultural Practices (GAPs) issued by the Institute for the Control of Agrochemicals, Ministry of Agriculture, China.

Sample extraction

The samples were analysed for fluopyram using a modified QuEChERSonethod. A homogenized vegetable sample (20 g or 10 g of soil sample) was mixed in a 250 mL-centrifuge bottle with 50 mL ACN and 10 mL deionized water. The mixture was shaken for 30 min and then centrating ated. Afterwards an aliquot of the extract (25 mL) was transferred int a 50-nd centrifuge tube. After the addition of 6 g magnesium sulfate and 1.5 g sodium acetate, each mixture was shaken vigorously for 1 mis and then centrifuged. The supernatant (25 mL) was concentrated. The resulting concentrates were re-dissolved with ethyl acetate (2 mL) and pipetted into 2 mL-clean op tube filled with 50 mg PSA and 150 mg magnesium sulfate. After shaking vigorously for 30 s the tube was centrifuged. After filt ation through a 0.22 µ m filter, the resulting filtrates were subjected to quantitative analysis of fluopyram

Quantification of fluopyram

Ś For quantification of flugpyram an Agient HP capillary column (Agient HP-5 MS) was installed in a GC-MS/MS (Agilent 700% C). MS/MS was operated \mathbb{O}^{n} electron ion dzation mode with a mass range of m/z50~500. Multiple reaction monitoring (MRM) transitions were 173.0 > 145.4 and 173.0 > 95.2. Series of dilutions of fluop@am in EtOAc spikedat the concentrations 0.001, 0.01, 0.1, 1 and 5 mg/kg in the matrices were used as the working solutions for quantification of the fluopyram using external standard method.

Validation was carried our using control matrix formato, cucumber and pepper fruits as well as control soil samples for tified with fluopyran at 0.007, 0.03 and 005 mg/kg with 5 replicates. Recovery was calculated for evaluation of the method performance. Spiked samples were left to stand for 60 min to allow pesticide absorption onto the sample adequately and then subjected to treatment and analysis under the same conditions as described above for reliability RSDR (intra-day precision) was measured by comparing standard deviation of the recoveries of five replicates in the same day, and RSDR (inter-day precision) was determined by analyzing spiked samples in three alternate days for reproducibility. Intra- and inter-day precisions tests were also done at 0.001 @.05 and 0.5 mg/kg with nine replicates on 3 different days.

Dynamics fitting.

The dynamics of buopyram in various samples was analysed by plotting the residue concentration against time via the first-order rate equation: $C_t = C_0 x e^{-kt}$. C_t and C_0 represent the concentrations of the residual fluop $\sqrt{2}$ and the day t and day 0 (2h), respectively, and k is the dissipation rate constant. The half-life (t_{1/2})



is defined as the time required for the pesticide residue level to fall to the half of the initial residual level of day 0 (i.e., C₀) and calculation was done using the following equation: $t_{1/2} = (\ln 2)/k$.

Track of fluopyram metabolism

Samples collected from multiple application trial were subjected to GC-MS/MS using the full scan mode. In the total ion chromatogram (TIC) peaks of interest were further isolated for characterization of the molecular structure. The parent ions of the tentative metabolites were selected and further subjected to MS/MS using daughter scan mode for characteristic daughter ion fragmentation. Finally, identification of the metabolites' structure was done by parent ion deconvolution and the daughter ion fragmentation assignment through the Agilent Mass-hunter Library DIST11.L database. The same analytical method as for fluopyram was used for extraction and purification of the metabolites. For each metabolite, a pair of quantitative ions were selected for quantification with the use of p-tert bitylphenol as an internal standard.

Dietary risk assessment.

For assessment of the dietary risk of floopyrany, the estimated daily intake (EDI) as a percentage of acceptable daily intake (ADI) for a 60-kp adult person is 0.01 mg/kg body weight (bw)/day for floopyram. EDI was calculated by multiplying the highest residue (HR) in each sample (mg/kg) with the average daily per capita consumption estimated for fruit vegetables (S8.291) g/day of China). The risk assessment of intakes compared to pesticide to recological data was conducted via calculation of the hazard quotient (HQ), where EDI was divided by the relevant $ADI/PQ = EDI/ADI \times 100\%$.

JI. Results and Discussion

Analytical approach performance

The matrix-matched carboration was done by the standard addition method in matrix extracts and the calibration curve of thoopyram was constructed by plotting analyte concentration against peak area. In the range of concentrations (from 1 to 3000 ng/kg), good linearity was achieved for the target compound with correlation coefficients higher than 0.99. The LOQ was 0.9 µg/kg in all matrixes. Using the modified QuEChERS, spiked recoveries for tomato, curumber, pepper and soil sample matrices at all spiked levels were obtained as 90.9–95.6%, 92.0–93.2% 89.0–95.4% and 88.3–95.1%, respectively with all RSD values < 20% (Table 6.24)-41 A), Besides, the intra-day and inter-day variability were lower than 10.7 and 13.5%, respectively, at all spiked level (Table 6.24)-41 BC. These data suggested the method established was of favorable performance and reliability.

< 20% (Table 6.23 -41 A), Besides, the intra-day and inter-day variability were lower than 10.7 and 13.5%, respectively, at all spiked level (Table 6.2.3, 41 B). These data suggested the method established was of favorable performance and reliability.



Table 6.2.1-41: Validation parameters of fluopyram (A). with various matrices and levels and (B). with intra-day and inter-day variability

٨	Toma	ito	Cucum	ber	Рерр	er	Soit		
Spiking level (mg/kg)	Recovery (%)	RSD (%)	Recovery (%)	RSD (%)	Recovery (%)	RSD (%)	Recovery	RSD (%)	6
0.001/0.005*	90.5 ± 7.8	8.6	92.0 ± 2.7	3.0	89.0±22	2.5	90c7±8.6		
0.01/0.05	95.6 ± 3.5	3.7	92.2 ± 2.3	2.5	89.5±2.4	2.6	8.5 ± 4.0	4.50	1 🛛
0.5/1	91.9 ± 4.3	4.7	93.2 ± 3.6	3.9	95.¥±4.3	4.5	95.1±2.2	×3	^ [

*0.001/0.005 expresses the fortified level of three vegetables/the fortified 4Q of soil (n = 5)

D	Spiking 0.001/0.0	05* mg/kg	Spiking 0.01/0	.05 mg/kg	Spiking 0.5	/I'mg/kg	
RSD _R (%)	Intra-day ^a	Inter-day ^b	Into-daya	Inter-day ^b	Intra-date	in the day	\sim \sim
Tomato	5.9	9.7	<u>م 6.1</u>	0.2	0 ⁷ 40 ⁰	8.5	
Cucumber	4.6	8.5	\$`.\$ <u>\$</u>	13.5	A.0 Ô	7.9	
Pepper	6.2	11.9	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	27	O ^V 7.2	1 <i>@ V</i> 🔿	
Soil	5.3	10,6	3.6%	× 8.8 0		\$ 5.1 () 5.1 ()	

*0.001/0.005 expresses the fortified level of three α egetables/the fortified level of soil a n = 3 Ω n

Initial deposition and dynamics of fluopyram

In edible parts samples collected from greenhouse plants after the foliar application, initial deposits of fluopyram followed the decreasing order of pepper > tomato cucumber. The initial deposit of fluopyram was 1.913 mg/kg in perper, while the initial deposits on tomato and oucumber were 1.391 mg/kg and 1.172 mg/kg, respectively. Compared with the equiple part of vegetables, almost 2-fold lower initial deposits of fluopyram were observed on the related greenhouse off, which were 0.637, 0.738 and 0.872 mg/kg in tomato soil, cucumber soil and pepper soil. The dynamics cubies demonstrated that the residual fluopyram dissipated rapidly within 7 days (Agure 6.2.1-12). Hatf-lives of fluopyram were similar in the three vegetables (368 d in pepper, 3.9 doin cucumber and 4.4 T in tomato, Table 6.2.1-42). In soils, fluopyram declined constantly with half-lives of 42, 5.7 and 4.3 d for tonato, occumber and pepper, respectively.

Table 6.2.1-42: Dynamic equations, correlation coefficients and half-lives of fluopyram in vegetables and soils.

C

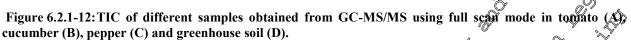
		St D X		
بە 1	Sample	Dynamic outation	Correlation coefficient (R ²)	Half-live(d)
A A A A A A A A A A A A A A A A A A A	Tomato	$C_t = 162e^{-0.158t}$		4.4
	Cucumber	$C_{t} = 1.165e^{-0.5t}$	0.8820	3.9
S S	Pepper	~ CO=2.368 0.181t	0.9056	3.8
	Tomato soil	$C_{t} = 3.696e^{-0.16}O$	0.9619	4.2
	Cucumber soil	C 0.814e 21t	0.8789	5.7
	Perper soil		0.8964	4.3
, d'		ST T		

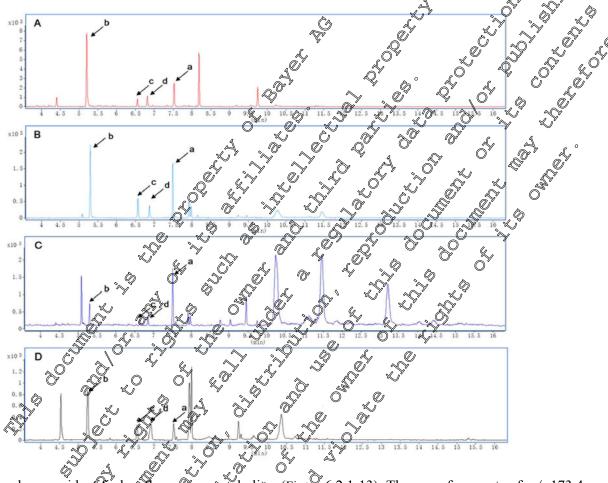
Metabolic pathway of fluopyram

Using fullscan mode of GC-MS/MS, a wide array of peaks was observed in the different samples (see figure below). Several peaks not observed in the control group, increased regularly along with the decline



of fluopyram. These relevant peaks were further selected and subjected to GC-MS/MS analysis per characteristic fragmentation and assigned by Agilent Mass-hunter Library NIST11.L database.





Three peaks were identified as fluopyram metabolites (Figure 6.2.1-13). The mass fragments of m/z 173.4 and 145.4 existed in both of peak a and b, indicating that they had identical functional groups (Figure 6.2.1-13, A, B), suggesting peak b originated from peak a Carallel to the absence of m/z 396.6 and m/z 207.3 peaks a peak at m/z 1893 emerged (Figure 6.2.1-13B), which showed the loss of a moiety of m/z 207.3 from m/z 396.6. A cleavage of fluopyram into a trifluoromethyl benzamide molecule (peak b) and a trifluoromethyl pyridine containing molecule occurred. Peak b was further identified as fluopyram-benzamide via the characteristic fragmentation mentioned above and database deconvolution (Figure 6.2.1-13B). Interestingly, the trifluoromethyl pyridine-containing molecule speculated as 2-(3-chloro-5-(trifluoromethyl)pyridin-2 fluopyram pyridine-carboxylic acid (Figure 6.2.1-13C) and fluopyram-pyridine-acetic acid Figure 6.2.1-13D) seemed to be degradation products of TPE.

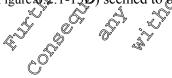
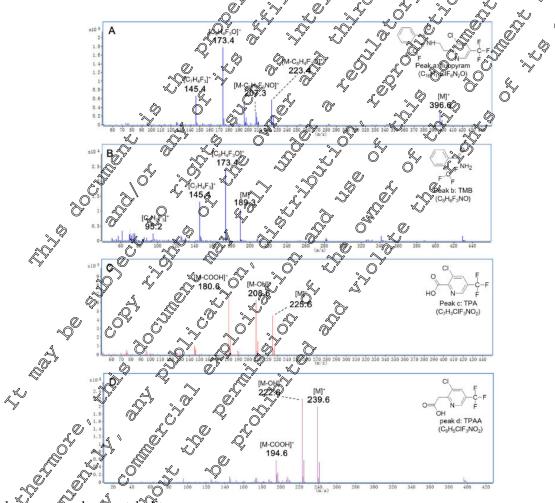




Figure 6.2.1-13: Fragmentations of fluopyram (A) and three metabolites fluopyram-benzamide (B), fluopyram-pyridine-carboxylic acid (C) and fluopyram-pyridine-acetic acid (D)

Based on the qualitative and quantitative analyses mentioned above, it was deduced that the parent molecule was split into TMB and potentially into TPE in the initial step of fluopyram metabolic pathway. Interestingly, we found that fluopyram was degraded in the sterilized soil with a 40-fold higher http://ife.com/oregime.com/or



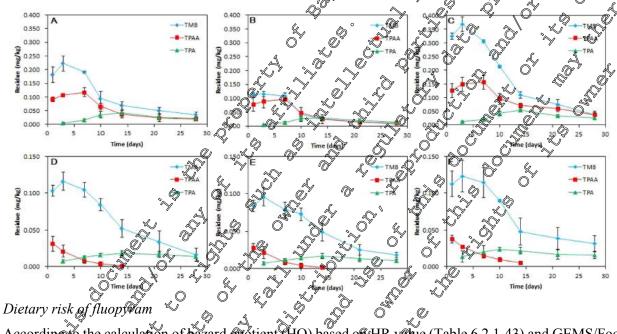
acid were secondary metabolites.

For the further elucidation of the metabolic pathway of fluopyram, the distribution and formation of these metabolities was also quantitatively analysed in plant and soil samples. fluopyram-benzamide began to occur at 1 d and then gradually dissipated from 3 d to 28 d in both plant and soil samples, and finally stayed



at level of 0.008 - 0.036 mg/kg (Figure 6.2.1-14). Similar to fluopyram-benzamide, the dynamics of fluopyram-pyridine-acetic acid showed an increasing tendency from 1d to 7 d in all vegetables followed by a constant decline until 28 d. In the soils, fluopyram-pyridine-acetic acid exhibited a constant decline curve and became undetectable (< 0.001 mg/kg) at 14 d. Highly associated with fluopyram-pyridine-acetic acid significantly declined within 14 d, followed by a slight decline stage and finally stayed at a relatively stable level until 28 d.

Figure 6.2.1-14: Distribution and formation dynamics of fluopyram metabolites in the fruit vegetable ecosystem in tomato (A), cucumber (B), pepper (C), tomato soil (D), cucumber soil (P) and pepper of soil (F). Values are means ± standard deviations (shown by extor bars) (n = 9).



According to the calculation of hazard protient (HQ) based of HR value (Table 6.2.1-43) and GEMS/Food consumption database fruit vegetable consumption in China), HQs in three fruit vegetables were all lower than 1, indicating safety of the fruit vegetable incurred with residues of this fungicide to the consumers by daily consumption. However, it was found that the calible parts of three vegetables were incurred with fluopyram-benzamide. Buopyram-pyfidine carboxylic acid and fluopyram-pyridine-acetic acid at trace level. It still to the unclear whether the three metabolites of fluopyram should be considered in the dietary risk assessment due to the unknown tox foological effect of these metabolites.

		Q & fluoryram in edible parts of the three fruit vegetables.
Table 6.2.1-43:	Ocentrence, HR and H	O 🕼 fluoity am in edible parts of the three fruit vegetables
	000000000000000000000000000000000000000	

	Celon		uronce (mg	(/kg)	HR	
Sample	* ¥	Ŷ\$HI7d∧	PHI 14 d	PHI 21 d	(mg/kg)	HQ
	\$8-10B	0.07	0.0331	0.0058	0.0769	0.4483
O Seumber	8-102	0.0571	0.0303	0.0043	0.0571	0.3328
Pepper	~C~10B	0.1603	0.0861	0.0108	0.1603	0.9344

* Code of Federa Regulations Group 8–10B and 8–10C indicate the fruit vegetable group.



III. Conclusions

In this study, an effective and sensitive analytical method using a modified QuECHERS extraction with GC-MS/MS for the detection of fluopyram in three fruit vegetables (tomato, eucumber, pepper) and relevant soils was developed and validated. After a single application at 62.4 g a s./ha, fluopyram dissipated rapidly in the vegetable greenhouse ecosystem in accordance with the first order rate dynamics, with the maximum half-life as 5.7 d. Fluopyram was split into a primary metabolite fluopyram benzamide and followed by formation of two secondary metabolites fluopyram-pyridine-acetic acti and fluopytam-pyridine-carboxylic acid along with the decline process. After the malti-application, the occurrence of fluopyram in tomato, cucumber and pepper at PHI 7–20° d ranged from 0.0108 to 0, 603 mg/kg, and all the related HQs were below 1. Taken together, a highly compatible fool to monitor fluopyram in plant-and environmental origin is provided.

3. Assessment and conclusion

Assessment and conclusion by applicant:

The first purpose of the publication was to describe and descuss the performance of a modified QuEChERs analytical method for fluopyram in food of plant origin and soil. Based on the provided validation results, the method is considered reliable, however, a full data package on valid methods for data generation and monitoring is already available and provided with the dossie?

The second purpose of the publication was the identification of passible metabolites of fluopyram in the matrices of tomato, cucumber and pepter fruits as well as in soil. Metabolites such as fluopyrambenzamide, fluopyram-portidine acetic acid and fluopyram pyridine-carboxylic acid have been identified. However, these metabolites have been already described in studies submitted in this AIR dossier and no new information is gained. Therefore, as such, the publication is relevant but do not affect risk assessment.

Data to address this point were presented in the dossier submitted for first inclusion in Annex and were deemed acceptable following evaluation and peer (eview at EU level (2013).

For details of data submitted previously please refer also to the Baseline dossier CA 6.2. For completeness, a summary of these previously submitted studies are included below.

the the first EU review process for inclusion on Annex I. (no new



Data Point:	KCA 6.2.2/01
Report Author:	2008
Report Year:	2008
Report Title:	Metabolism of [phenyl-UL-14C]AE C656948 in the laying ker
Report No:	MEF-06/329
Document No:	<u>M-297093-01-1</u>
Guideline(s) followed in	US EPA OPPTS 860.1300; Health Conda PMRA Rof, DACO 6.2; EV 91/444/EEC
study:	amended by 96/68/EC, Appendix F 🕅 🖉 🖉
Deviations from current	amended by 96/68/EC, Appendix F Deviation to OECD 503: 6 birds destead of 10. No impact, because sufficient amount of sample material was available for characterization and ident ocation of metabolites.
test guideline:	of sample material was available for characterization and identification
	metabolites.
Previous evaluation:	
	rev. 1 to Vol.3 of DAR \$7 Aug 2012 Deferences relie (on)
GLP/Officially recognised	Yes, conducted under OLP/Officially occognized testing facilities
testing facilities:	
Acceptability/Reliability:	Yes in the second secon

Executive Summar

The metabolism of [phenyl-UL-¹⁴C fluopytam was investigated in six faying hens, which where orally dosed for 14 consecutive days at a rate of 2.03 mg a.s./kg of body weight per day (equivalent to 26.42 mg a.s./kg feed/day). Sacrifice was made 24 h after the 14 administration. Radioactivity was measured in the excreta and eggs collected daffy, as well as in the kidney, liver eggs from the ovary and oviduct, skin without subcutaneous fat, muscle and fat at sacrifice. The collected eggs and the edible tissues and organs were analysed for parent compound and metabolites by extraction, chromatographic separation techniques and spectroscopic methods.

Until sacrifice, the excretion amounted to 82.67% of the totally administered radioactivity. An amount of 4.34% of the total dose was found in eggs. At sacrifice, the calculated or estimated total residue in the tissues and organs disserted from the body was approx. 783% of the total dose. More than half of this amount was detected in the moscle (4.94%) of the total dose.

The mean active substance equivalent concentrations in eggs increased from 0.462 mg/kg (day 1) to 3.90 Kmg/kg (day 1). A farther but slower increase was measured up to the test end, indication that a residue plateau-level was nearly reached.

At sacrifice, Kighest mean equivalent concentrations occurred in liver with 9.536 mg/kg and in kidney (5.759 mg/kg). The residue-level of eggs collected from the ovary and oviduct (5.771 mg/kg) was by a factor 1.6 higher compared to the laid eggs at the test end (3.901 mg/kg), indicating that the egg yolk was assumedly the preferential site for the excretion. These values were followed in decreasing order by the mean concentrations determined in the muscle (3.290 mg/kg), the skin (2.533 mg/kg) and the subcutaneous fat (1.696 mg/kg).



The radioactive residues were extracted with high efficiencies (92-99%) from eggs and edible organ for tissues with acetonitrile/water mixtures and identification was achieved by co-chromatograph reference compounds.

In all edible matrices fluopyram-benzamide (M25) was the major metabolite representing 68,6% of the TRR (1.126 mg eq/kg to 8.737 mg eq/kg). Other metabolites identified were flappyram-Z-olefin (M03), fluopyram-E-olefin (M02) and fluopyram-benzoic acid (M33), Duopyram-Z-olefin was identified in all edible matrices and ranged from 0.2% to 25.9% of the TRR (0.010 mg eq/kg to 0.425 mg Qq/k fluopyram-E-olefin was detected only in fat (2.3%)TRR or 0.037 mg ga/kg) and liver (0.3% TRR or 0.028 mg eq/kg). fluopyram-benzoic acid was detected only in liver (0.2% TRPor 0.024 mg kg/kg)

were deduced by the contract of the contract o The parent compound fluopyram was detected as minor componen the TRR or 0.024 mg/kg to 0.042 mg/kg).

Based on the identified metabolites, the following metabolic routes

- cleavage of the aliphatic chain as pajor brochengeal reaction
- hydroxylation of the alignatic chain followed by elimbration
- hydrolysis of the benzamideto the corresponding benzoic acid , Q

. Materials	I. Materials and Methods
Test Material:	
Materials	N-{2}[3-chloro-5-(trifluoromethyl)pyridin-2-yl]ethyl}-2- (trifluoromethyl)Denzamide
CAS Name	N-{2}[3-chloro-5-(trifluoromethyl)pyridin-2-yl]ethyl}-2- (trifluoromethyl)benzamide Benzamide, N-[2-[3-chloro-5-(trifluoromethyl)-2- pyridinyl]ethyl]-2- (trifluoromethyl)- (9CI) SE C656948 Fluopyram Fluopyram Code
Code name	©Ê C656948
Common name	Fluegyram
Empirical formula	6N2O
CXS Number 🔍 🖓 🖓	658066-35-4
Molar mass @	396.72 g/mol
Empirical formula	CF_3 CF_3 CF_3 $*$ position of the ¹⁴ C radiolabel
	[phenyl-UL- ¹⁴ C]AE C656948



Batch number	BECH 1920
Original specific radioactivity	$\frac{1.93 \text{ MBq/mg}}{= 52.1 \ \mu\text{Ci/mg} = 20.67 \ \text{Ci/mol}} = \frac{1.16}{52.1 \ \mu\text{Ci/mg} = 20.67 \ \text{Ci/mol}}$
Radiochemical purity	> 99% by radio-TLC
	> 99% by radio-HPLC
	The radiochemical purity deck was performed before dilution with the authentic fon-radiolabelled test compored.
Chemical purity	99% (HPQC) × 0° 0° 0°
Specific radioactivity after radiodilution used for the study	
Stability of test compound	The administration suspensions were freshly prepared on the day before their use and ach suspension was applied for
Ś	three to fear dosages. The radiolabelled parent compound
Q	was proved to be stable in the 0.5% aqueous tragacanth suspension for at least four days at 4 °C as shown by radio-
	HPLC analysis.
	The exaluation of the chromatogram revealed a
	\sim
Test Animals	
Species	Hen (Gallus gallus gamesticus)
Breed O O	
Breed Breeding facility Sex, pippber	
Sex, patenber	Six female laying frens
Mean body weight	J ² .53 kg at test start (1 43 – 1.64 kg)
	1.649kg at test end (1.52 – 1.75 kg)
Age of or of o	24 weeloold at x periment start
Acclimatization	18 days before administration, the egg production was recorded
Identification	Individual cages, wing tags
Housing	Each 1 bird per stainless steel metabolism cage, approx. 20– 25 °C, 40–58% rel. humidity, 16/8 hours light/dark cycle
Feed and water	Commercial pulverized hen feed, "Union Legemehl" (LS 211) at 200 g per day per animal, supplemented with eggshells and crushed marine shells
2 0 0 <u>1</u> 2	Tap water <i>ad libitum</i>
Health status	Acceptable



B. Study Design

Preparation of the dosing mixtures and administration:

The stock solution was prepared by dissolving the solid ratiolabelled tege compound gertified specific radioactivity: 1.93 MBq/mg) in 25 mL acetonitrile and radioassayed. The radioactivity concentration was determined to be 32.7 MBq/mL, corresponding to 16.9 mg compound/mL based on the pecific radioactivity.

Four administration suspensions were prepared on the day before their use and each suspension was applied for three to four dosages. Definite volumes of [phenyl-VL-14Cl uopyam stock solution in acetonitrile were taken to prepare the administration suspensions (suspensions 1-2.5.106 mL, corresponding to 86.4 mg fluopyram; suspensions 3-4: 4.149 mL, corresponding to 70.2 mg fluopyram). The solvent was repoved by a nitrogen stream. Definite volumes of 0.5% aqueous Tragacanth (432 mL for suspensions)-2 and 35.1 mL for suspensions 3-4) were added and the samples were stigred constantly until coministration. The radioactivity of the suspensions was calibrated by giquid scintillation counting and the animals were dosed related to their individual body weights at test start. The administration volume was 1 mL/kg bw, corresponding to a treatment rate of 2,03 mg/kg bw/per day. In relation to a mean body weight of 1.53 kg, the laying hens received a total mean dose of 43,47 mg per animal.

The oral administration proceeding was carried out with a knop cannula attached to glass syringe. Directly after dosage, the act of swallowing was sustained by a gentle massage of the throat in direction of the crop.

The radiolabelled parent compound was proved to be stable in the 0.5% aqueous tragacanth suspension for at least four days at +4 °C as shown by radio-HPLC analysis, and thus for the time from preparation of the administration suspension until dosing. The evaluation of the chromatogram revealed a radiochemical purity of > 99% in tragacanth suspension. The identity of the test compound was confirmed by LC-MS/MS (ionisation by electron-spray ionization)

Collection and processing of eggs and excretion

The eggs were collected each day (day 1-14) numbers and weight of eggs were recorded for all hens. For sampling, the egg-shells were discarded, and the white and yolk were thoroughly mixed. An aliquot sample of each eggmix way taken for the determination of total radioactivity by LSC. Two pools of eggs (day 1 to 6 and day 7 to 14) were prepared and stored at about -18 °C until extraction for metabolite analysis. One sample of the combined eggenix was taken for radioactivity measurement.

The faecal urine excreta were collected individually as quantitatively as possible at room temperature in intervals of 24 hours until sacrifice. All fractions were homogenised after adding water, before the total



weights were recorded. The total radioactivity was determined by combustion. The ${}^{14}CO_2$ absorbed was measured by liquid scintillation counting.

Sacrifice and collection of organs and tissues

The treated laying hens were weighed at the end of the test. They were sacrificed ca. 24 hours after the las dose. The animals were anaesthetised using carbon dioxide gas, sacrificed by decapitation, and exsanguinated. Immediately after sacrifice, the following organs and tissues were dissected liver without C bile bladder, kidneys, leg muscle, breast muscle, skin without subcutaneous fat, subcutaneous fat, eggs from the ovary and oviduct, and the bile bladder.

All tissues were individually weighed, and live? kidneys, muscle samples as well as the eggs dissected from the ovary and oviduct were thoroughly homogen and in Balf-frozen state. One aliquot of each resulting homogenized tissue was weighed, combusted and radiosssayed by lightid scintillation counting (LSC). Aliquots of the skin without fat were weighted, solubilised with tissue solubiliser and taken for radioactivity measurement by LSC. The two types of muscle (leg and breast) of all laying henswere combined, as well as their livers and fat samples and thoroughly homogenized.

Samples from the organs and other fiquid samples were kept frozen at about -18 at all times until Samples from the organs and other inquitesamples were kept frozen ar about -18 °C at an times thin extraction. During the analytical work, the samples were stored either at approx. +4°C in a refrigerator or at approx. -18 °C in a freezer.

four times with acetonitrile/water (4/1; v/v) using a Composite samples were conventionally extracted Polytron homogeneser.

The combined acetometrile/water expracts were partified by SPE using RP18 cartridge. Flow-through ("sample passage") and rinse solutions of the extracts with acetonitrile/water (4:1, v/v) were combined and, as they contained the main portion of radioactivity, were concentrated and used for HPLC analysis. The methanol/dichloromethane (19, v/v) eluate and the dried RP18 material were assayed for radioactivity by LSG Aliquots of the solid phase were submitted to combustion for determination of radioactivity.

Analytical methods:

The radioactivity of all Aquid samples was measured using a liquid scintillation spectrometer after mixing a known amount of each sample with scintillation fluid. Solid samples were combusted using an oxidizer. The resulting ¹⁴CQ was trapped in Carbosorb E or Oxysolve C400. The TRR in the samples was calculated by summing up the radioactivity measured in different extracts and remaining solids after solvent extraction. The TRR was expressed in mg a.s. equivalents per kg sample weight. Amounts of radioactive



residues in the extracts were expressed as percentage of the TRR and also as mg a.s. equivalents per bg sample weight.

Aliquots of all acetonitrile/water extracts were analysed by HPLC. Four metabolites as well as parent compound were identified by HPLC and TLC co-chromatography with reference compounds.

The HPLC was conducted using a reversed-phase column (RP18-endcapped, 250 x 4.6 mm) that was operated with a gradient mixture of water + 25% (∞) aqueous ammonia + fortoic acid (1000/1.54/0.8; v/v/v) and acetonitrile + methanol (1/1; v/v). The HPLC system was equipped with a radiodetector and a UV detector with variable wavelengths. The LOQ was derived from the average background level and the specific radioactivity of the radiolabelled test compound.

TLC was performed on HPTLC silica 60F254 plates, 20x20 cm, using two different mobile solvent systems (dichloromethane/ethyl acetate (3:1; $\sqrt[6]{v}$) or dichloromethane). Non-radioactive standards were visualized using UV light. Radioactive zone were detected by radioluminography.

Storage stability

Samples from the organs and other liquid samples were kept frozen at about -18. Oduring the entire study. During the analytical work, extracts of tissues and eggs were stored either at approx. +4 °C in a refrigerator or at approx. -18 °C in a freezer. The samples of eggs, muscle liver and fat were analysed 27–33 days, 84 days, 124 days and 130 days after sample conjection respectively. *e.* within a maximum of *ca*. 4 months after sample collection.

A second CTPLC analysic was conducted at later intervals (eggs: 4,405 months, liver: 1 month, muscle: 2.5 months, fat: 10 months). Comparing the metabolite patterns, no significant change could be observed regarding the qualitative distribution. Overall, the radioactive residues in all extracts were found to be stable under storage conditions

H. Results and Discussion

The metabolism in laying hens of [phenyl-UL C]fluopyram administrated at a daily dose of 26.42 mg/kg in the feed corresponding to a daily intake of 2.03 mg/kg body weight for 14 consecutive days was investigated

Until sacrifice 24 hours after the last dose, the mean excretion amounted on average to 82.67% of the radioactivity totally administered (Table 6.2.2-1). The time course of the excretion was characterised by a relatively constant rate starting at day 2 until test end (Table 6.2.2- 2). Only 4.34% of the dose totally administered was measured in the eggs produced within the whole test period. At sacrifice, 24 h after the



last administration, the total residue in the tissues and organs dissected from the body was calculated and estimated to about 7.83% of the total dose. Based on these values, the recovery amounted to 94.83% (Table 6.2.2-1).

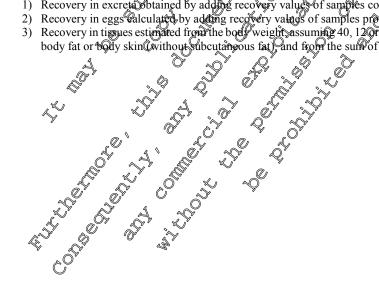
The total radioactive residues were determined in eggs and excreta produced from the work dose sacrifice and in edible tissues and organs at sacrifice. The highest mean active substance equivalent concentrations were measured in the liver (9.536 mg/kg, corresponding @ 0.86% of the total dose) and the eggs dissected from the ovary and oviduct (5.771 mg/kg, corresponding to 0.73% of the total dose) These values were followed in decreasing order by the mean concentrations determined in the kidney (5.759 mg/kg), the muscle (3.290 mg/kg), the skirk (2.533 mg/kg) and the fat (1.696 mg/kg). For details see Table 6.2.2-4. The mean radioactive residue in the total body skin appounted to about 0.38%, in the total body fat to about 0.76%, and in the body prosclest@about@4.94% of the dose totally arministered. The calculation of these values was based on the experimentally confirmed assurption that total body Skin (without subcutaneous fat), fat, and muscle account for 4%, 12%, and 40% of the body weight, respectively (Table 6.2.2-1).

Recovery of adioactivity following or al administration of [phenybuL-196] fluopyram at a Table 6.2.2-1: daily dose rate of 2.03 mg/kg body weight for 14 consecutive days

Matrix	Recovery of radioactivity (%) of the totally administrated radioactivity)
Excreta ¹⁾	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
Tissues ³⁾	
Recovery	94.80

1) Recovery in excreta obtained by adding recovery values of samples collected within the observation period of 14 days

Recovery in eggs calculated by adding recovery values of samples produced within the observation period of 14 days
 Recovery in tigges estimated from the body weight assuming 40, 120r 4% of the body weight for total body muscle, dissectible body fat or body skin (without subcutaneous fat) and from the sum of percentage values of the other organs prepared.





e 6.2.2- 2: 1	Time course of total i ⁴ C]fluopyram at a da	radioactivity in excreta fo aily dose rate of 2.03 mg/k	llowing oral administration of [phenyl-Up-° sg body weight for 14 consecutive days
Matrix	Time after the first dosage (day)	Administration number	(% of totally administrated radioactivity)
	0	1 🖏	
	1	2	Q 4.25 X X
	2	3	1 0 ⁵ √ 89 0 ⁵ [€]
	3	\$ \$	14.53 15.53 15
	4	0 [×] 5 0 ² 4	2093 ~ W
	5		Q 25.80 y 25.00 y
Excreta	6		0 31405 C
	7		1.85 fr O
	8 🖓		
			2 2 43.95 x 9 2 2 3 0 0.08 x 9
	0 ¹⁰ 0 ¹⁰	5 5 5 12 k	56 61 ⁰
	11 4		
			× × × × × × × × × × × × × × × × × × ×
	\$ 0 ⁹ 13 50 ⁹		10.20
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			82.67

The equivalent concentration of radioactivity in the eggs showed an increase from 0.462 mg/kg obtained

The equivalent concentration of radioactivity in the eggs showed an increase from 0.462 mg/kg obtained on day 2 (24 hours after the first dosage) of 3.904 mg/kg at satisfice (14 days after the first dosage). For details see Table 62.2-3. A further but stower increase was measured up to the test end, indication that a residue plateau level was nearly reached.



able 6.2.2- 3: T	Time course of total ⁴ C]fluopyram at a d	radioactivity in eggs follov aily dose rate of 2.03 mg/k	ving oral administration of [phenyl-UL-@° cg body weight for 14 consecutive days
Matrix	Time after the first dosage (days)	Administration number	(mg a.s. equiv./kg)
	0	1 🖉	
	1	2	
	2	3 2	1.017 ° 50° \$
	3	40	→ Q 91.6520 Q Q Q
	4	O ^V 5 C [°] L	
	5	× .60 ~ 0	2.445 × 2.445
	6		
Eggs	7	× × 8~ ~	243 ° O'
	8 2		2 2 3.22 × 2
	9		
		S M O	Q383 Q383 Q3565
		12 × 12	*********
			0 [°] & 3.802
	² ^y 10 ^y <del>2</del> ^y <del>13</del> <del>2</del> <del>y</del> <del>13</del> <del>2</del>		3.827
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			3.901
g a.s. equiv./kg: mg par	r@nt equivalents per kg	matrix	
E.G.			No. and the second seco
			× 0
Ę			
~~			
A.			
<u></u>			
mg a.s. equiv./kg: mg partit equivalents per kg matrix			
, O N			
		<u>v</u>	
)	
	A J JA		
	E Contraction of the second se		
Ô			



Table 6.2.2- 4: Distribution of residues in eggs, tissues and organs of laying hens following oral administration of [phenyl-UL-¹⁴C]fluopyram at a daily dose rate of 2.03 mg/kg body weight for 14 consecutive days

weight for 14 consecu		
Matrix	Interval (day)	TRR (mg a.s. equiv./kg)
Liver (composite)	14 🖉	9.536 × ×
Kidney	14	8 5.75
Eggs (composite)	14 2	
Eggs from ovary/oviduct	ko '	~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~
Muscle, leg		2 2 3 20 · · · · · · · · · · · · · · · · · ·
Muscle, breast	A 146 0	2 2 3 281 4 A
Composite muscle (leg and breast)	$\sqrt{34}$	3.290 S Q
Skin without subcutaneous fat		
Subcutaneous fat (composite)		
mg a.s. equiv./kg: mg parent equivalents per kg r	native of the second se	

In composite egg pool (day 1–6), 98.8% of the radioactivity (1.791 mg/kg) was extracted with solvent extraction (acetonitrile/water). Following solid phase extraction purification, the main radioactivity was contained in the combined sample passage and acetonitrile/water risks solution ("purified acetonitrile/water extract", 98.8% of the 5RR, 0790 mg/kg) and, after the concentration step, the concentrated acetonitrile/water extract contained 97.7% of the 5RR (1.770 mg/kg). In total, 98.9% of the TRR (1.791 mg/kg) was extracted whereas 1.1% of the 5RR (0.020 mg/kg) remained non-extractable in solids (Table 6.2.265).

In composite egg pool (day 7–14) 98.6% of the radioactivity (8.530 mg/kg) was extracted with solvent extraction (acetomirile/water). Following solid phase extraction purification, the main radioactivity was contained in the purified acetomirile/water extract (98 %) of the TRR, 3.527 mg/kg) and, after the concentration step, the concentrated acetomirile/water extract contained 98.2% of the TRR (3.515 mg/kg). In total, 98 6% of the TRR (3.530 mg/kg) was extracted, whereas 1.4% of the TRR (0.051 mg/kg) remained non-extractable in solid (Table 6.2.2-6)

In muscle, the major part of the radioactive residues (99.6% of the TRR, 3.265 mg/kg) was extracted with acetonitrile/water. After folid phase extraction purification, the main radioactivity was contained in the purified acetonitrile/water extract (99.5% of the TRR, 3.265 mg/kg). After the concentration step, the radioactivity on the concentrated extract amounted to 99.1% of the TRR (3.249 mg/kg). In total, 99.6% of the TRR (3.265 mg/kg) was extracted whereas only 0.4% of the TRR (0.015 mg/kg) remained non-extracted in solids (Table 6.2-7)

In fat, the radioactive residues extractable with acetonitrile/water amounted to 99.4% of the TRR (1.63 mg/kg) and, after clean-up procedure by solid phase extraction, to 99.3% of the TRR (purified



acetonitrile/water extract, 1.630 mg/kg). After the concentration step the radioactivity in the concentrated extract amounted to 99.1% of the TRR (3.249 mg/kg). In total, 99.4% of TRR (1.631 mg/kg) was extracted and only 0.6% of the TRR (0.010 mg/kg) remained non-extractable in solids (Table 0.2.2-8).

RŖ 🎘 In liver, the radioactive residues extractable with acetonitrile/water amounted to 93.6% of the (8.861 mg/kg) and, after clean-up procedure by solid phase extraction, 10, 93.5% of the TRR purified acetonitrile/water extract, 8.850 mg/kg). After the concentration step the radioactivity of the concentrated extract amounted to 93.0% of the TRR (8.805 mg/kg) In total, 93.6% of the TRO (8.86 mg/kg) extracted and 6.4% of the TRR (0.605 mg/kg) remained non extractable in solids (Table 6 2-9

Ô

Table 6.2.2- 5:	Extraction of radioactive residues from the den's egg pool (day 1-6) after dosing of	
	Extraction of radioactive residues from the pen's egg pool (day 1-6) after dosing of [phenyl-UL-14C]fluopyram at a daily dose rate of 203 mg/kg body weight for 14	, o
	appropriative days	· .

& .

consecutive days	â x			
l l l l l l l l l l l l l l l l l l l	St Ly . A			(day⊈≃6) Õ
TRR, mg eq/kg				3146 9
Fraction	. 4 ³ 6 ³		TRIO (mg às equiv./kg
Solvent extract ¹⁾	~~~~~	* 📎	§ 98.9 &	ا1.791 🐇
Purification via RP18		<i>©</i>	⁴ ³	N N
Purified acetonitrile/water extract Concentration Concentrated acotonitrile/water e Distillate	Ý, S	$\langle \rangle$	\$ ⁹⁸ .8	1.790
Concentration	xtract, 5		ري ⁹⁸ 988 ¹ 97.7 مي ¹ 197.7	
Concentrated agotonitrile/water e	xtract	×,×	0້ _%97.7 _>>້	1.770
Distillate			1.1	0.020
Methanol/dichl&romethane eluste				0.001
Solids O O	× • • •		S ¥.1	0.020
PES ²)	J Å	S O	° _ © 1.1	0.020
			98.9	1.791
Accountability / Total ³³	Č, Č, Č [*]		⊙ [≫] 100.0	1.811
1) Solvent extraction was done with 4x with a	cetonitrile/water (4	· & v/v) &	9	

Solvent extraction was done with 4x youn ac

2) PES: post extraction solids = non-extractable radioactority.

2, 1 LS. post extractor solids = non-e Gractable Padioactority.



Extraction of radioactive residues from the hen's egg pool (7–14 days) after dosing of phenyl-UL-¹⁴C]fluopyram at a daily dose rate of 2.03 mg/kg body weight for 14 consecutive days Table 6.2.2- 6:

consecutive days	
	Egg poor (day 7–14)
TRR, mg eq/kg	3.581
Fraction	% TREV mgas. equi@kg
Solvent extract ¹⁾	9826 2.539 0
Purification via RP18	
Purified acetonitrile/water extract	Ø 98.5 Ø \$.527 Ø \$
Concentration	
Concentrated acetonitrile/water extract	2.515 °
Distillate O [*] O [*]	0.3 × 0.012 ×
Concentrated acetonitrile/water extract Distillate Methanol/dichloromethane eluate	
Solids	
PES^{2}	
Total extracted	986 3.530
Accountability / Total ³⁾	2,981
1) Solvent extraction was done with $4x$ (bith acetonitrile/voter (4:1, x/v).	
 PES: post extraction solids = non-stractable adioactivity. Sum of extracts and PES. 	
Fractions given in bold font were apalysed of radio PPLC.	

Extraction of radioactive residues from the hear's muscle after dosing of [phenyl-UL-Table 6.2.2- 7: O⁴C]fluopyram at a daily dose rate of 2.03 mg/kg body weight for 14 consecutive days

	Muscle (c	omposite)
TRR, mg ea kg		280
Fraction	% TRR	mg a.s. equiv./kg
Solvent extract ¹⁾	99.6	3.265
Solvent extract ¹⁾ Purification via RP18 Purified acetomtrile/water extract Concentrated acetomtrile/water extract Distillate Methanol/dichloromethane elitate Solitis PEES2	99.5	3.265
Concentrated aceto Otrile/water excact	99.1	3.249
Concentrated acetomtrile/water extract Distrilate Methanol/dichloromethane eltiate	0.5	0.016
Methanol/dichloropathane eluate	n.q.	n.q.
Solitis V A O V	1.1	0.020
	0.4	0.015
Total extracted A Q	99.6	3.265
Total extracted A A A A A A A A A A A A A A A A A A A	100.0	3.280

1) Solvent extraction was done with $\frac{1}{2}x$ with acctonitrile/water (4:1, v/v).

PES post extraction solids = no-extractable radioactivity.
 Sum of extracts and PES.
 Fractions give in **boly** from were analysed by radio-HPLC. n.q.: not quantified



Table 6.2.2-8: Extraction of radioactive residues from the hen's fat after dosing of [phenyl-UL-¹⁴C]fluopyram at a daily dose rate of 2.03 mg/kg body weight for 14 consecutive days Ì

	Fat (composite)
TRR, mg eq/kg	01.641
Fraction	% TRR mg a@ equiv Kg
Solvent extract ¹⁾	994 × 1.631×
Purification via RP18	
Purified acetonitrile/water extract	99.3 Q.630 S
Concentration	
Concentrated acetonitrile/water extract	
Distillate	n.q. 2 2 n.q. 2
Methanol/dichloromethane eluate	
Distillate Methanol/dichloromethane eluate	
PES ²⁾	0.010
Total extracted	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
Accountability / Total ³)	× × × × × × × × × × × × × × × × × × ×
1) Conventional extraction was done with 4x with actonit ac/water	k:1, v/0, 0 0 0 0
2) PES: post extraction solids = non-extractable radioactivity.	

3) Sum of extracts and PES.

Fractions given in **bold** font were analysed by radio-HPLC. n for not quantified

Extraction afradioactive residues from the hen's diver after dosing of [phenyl-UL-Table 6.2.2- 9: ¹⁴ (Aluopyram at a daily dose rate of 2.93 mg/kg body weight for 14 consecutive days

	Liver (co	omposite)
TRR, mg eq/kg \sim \sim \sim \sim \sim \sim \sim		66
Fraction	Ø% TRR	mg a.s. equiv./kg
Solvent extract ¹⁾ Purification via RP4 Purified acetonitrio water extract	93.6	8.861
Purification via RP1	Ň	
Purified acetonitrio water extract	93.5	8.855
Concentration A Q V V O O		
Concentration	93.0	8.805
Distillator Control of	0.5	0.050
Methanel/dichloromethane elunde	n.q.	n.q.
Solids	6.4	0.605
PES ² A A	6.4	0.605
Concentrated acetonitrile water extract Distillate Methanel/dichloromethane eluate Solids	93.6	8.861
Accountability @otal ³	100.0	9.466

1) Conventional extraction was one with 4x with a setonitrile/water (4:1, v/v).
 2) PES: postextraction solids in non-extractable adioactivity.
 3) Sum of extracts and PES
 Fraction priven in Gold font were analysed by radio-HPLC. n.q.: not quantified



For elucidation of metabolism, all acetonitrile/water extracts were analysed by HPLC with radiodetection. Metabolites were identified by co-chromatography with authentic reference compounds using HPL and TLC co-chromatographic methods.

The parent compound fluopyram was detected as minor component only in e^{2} s and fat (0.2) the TRR or 0.024 mg/kg to 0.042 mg/kg). A total of four metabolites was identified. The identification rate was high (93.0–99.3% of the TRR).

In egg, the major metabolite was fluopyram-benzamide (M25), representing 95,8% and 96.3% of the FRR (1.735 and 3.447 mg eq/kg) for the pool day 1-Qand the pool day 7-14, respectively. fluopyram-Z-olefin (M03) was detected at a lower level (0.5% or 0,010 rog eq/kg and 102% of the TRR or 0,044 mg eq/kg for pool day 1-6 and pool day 7-14, respectively). In total 97.7% and 98.2% of the BRR was identified for egg pool day 1-6 (Table 6.2.2-10) and egg pool day 7-14 (Table 6.2.2-19, respectivels

of the TRE or 3.233 mg eq/kg). In muscle, fluopyram-benzamide @ras the only major component (985 TRR or 0015 mg eq/kg). In total fluopyram-Z-olefin (M03) was the sole other metabolite detected (6,5% 99.1% of the TRR was identified (Table 6.3.2-12)

In fat, fluopyram-bencamide (M25) was the major component with 68.6% of the TRR (1.126 mg eq/kg), followed by both flowpyran Z-oleun (MQ3) (25.9% of the TRR or 0.425 mg eg/kg) and fluopyram-E-olefin (M02) (2.3% of the TRR or 0.037 mg/kg). In total 99,3% of the TRR was dentified (Table 6.2.2-13).

In liver, Noopyram-benzamide (M25) was the major component with 92.3% of the TRR (8.737 mg eq/kg), followed by fluopyram-E-otern (M02) (0.3% TR® or 0.028 mg@eq/kg), fluopyram-benzoic acid (M33) (0.3% TRR or 0.02 mg eq/kg) and fluopyram Z-oleffin (M02) (0.2% TRR or 0.016 mg eq/kg). In total



 Table 6.2.2-10:
 Summary of identification and characterization of radioactive residues in the hen's egg pool (day 1–6) after dosing of [phenyl-UL-¹⁴C] fluopyram at a daily dose rate of 2.03 mg/kg body weight for 14 consecutive days

	ve days
	Egg pool (day 1-6) L&M Mg a.st equiv kg Mg a.st equiv k
TRR [mg eq/kg] =	1.57
Compound	% of TRR / mg a.sequiv 2
Acetonitrile/water extract	
AE C656948, fluopyram	
fluopyram-benzoic acid (M33)	
fluopyram-benzamide (M25)	\$ 95.8 \$ 1.735
fluopyram- <i>E</i> -olefin (M02)	
fluopyram-Z-olefin (M03)	Q
AE C000946, huopyram fluopyram-benzoic acid (M33) fluopyram-benzamide (M25) fluopyram-E-olefin (M02) fluopyram-Z-olefin (M03) Total identified in conventional extract Analysed extract(s) Volatiles in distillates	1.4 mg a.s. equiv Ag 0 0.026 0 0.026 0 0.001
Analysed extract(s) Q Q Volatiles in distillates Q Q	D D <thd< th=""> <thd< th=""> <thd< th=""> <thd< th=""></thd<></thd<></thd<></thd<>
Volatiles in distillates	
Extracts not analysed	@ 0M ~~ 0.001
Total extractable	0:1 0:01 0:98.9 0:01 0:020 0.020
Unextractable residues (Solids)	
Accountability / Total	2000.0 1.811
Analysed extract(s)	



 Table 6.2.2-11:
 Summary of identification and characterization of radioactive residues in the hen's egg pool (day 7–14) after dosing of [phenyl-UL-¹⁴C]fluopyram at a daily dose rate of 2.03 mg/kg body weight for 14 consecutive days

mg/kg body weight for 14 consecutiv	ve days
	Egg pool (dav7–14)
TRR [mg/kg] =	3,581 0 6
Compound	Wo of TRR mg a.st Equiv Age
Acetonitrile/water extract	
AE C656948, fluopyram	3.581 % of TRR mg a.se equiv Ag 0.7 0.7 0.024 0.024 0.024 0.024 0.044 0.044 0.044 0.044 0.044 0.044 0.044 0.044 0.044 0.044 0.05 0.044 0.05 0.044 0.05
fluopyram-benzoic acid (M33)	
fluopyram-benzoic acid (M33) fluopyram-benzamide (M25)	2° 5°96.3 5° 3.447
fluopyram- <i>E</i> -olefin (M02)	
fluopyram-Z-olefin (M03)	2 <u>41.2</u> <u>4</u> <u>5</u> <u>6</u>
fluopyram-benzoic acid (M33) fluopyram-benzamide (M25) fluopyram- <i>E</i> -olefin (M02) fluopyram- <i>Z</i> -olefin (M03) Total identified in conventional extract	0.7 0.024 0.024 0.024 0.0412 0.044 0.0412 0.044 0.044 0.0412 0.044 0.044 0.0412 0.044 0.0412 0.044 0.0412 0.0412 0.0412 0.041 0.044 0.0412 0.0412 0.041 0.044 0.0412 0.041 0.044 0.0412 0.041 $0.$
Analysed extract(s) Q Q Volatiles in distillates Q Q	<u>98.2</u> <u>5</u> <u>5</u> <u>5</u> <u>5</u> <u>5</u> <u>5</u> <u>5</u> <u>5</u> <u>5</u> <u>5</u>
fluopyram-benzamide (M25) fluopyram- <i>E</i> -olefin (M02) fluopyram- <i>Z</i> -olefin (M03) Total identified in conventional extract Analysed extract(s) Volatiles in distillates	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
Volatiles in distillates Volatiles Extracts not analysed Volatiles Total extractable Volatiles	0.32 0.012 0.003 0.003 0.003 0.003 0.003 0.003 0.003 0.0012 0.003 0.003 0.003 0.0012
Total extractable	$\frac{6}{2}$ $\frac{6}$
Unextractable residues solids)	<u> </u>
Accountability / Total	2000.0 3.581
Volatiles in distillates	



after dosing of [phenyl-UL- ¹⁴ C] fluo	acterization of radioactive residues in hen's muscle ° pyram at a daily dose rate of 2.03 mg/kg body weight
for 14 consecutive days	
	Muscle
TRR [mg/kg] =	$\frac{1}{2}$
Compound	
Acetonitrile/water extract	
AE C656948, fluopyram	\$% of TRR mg a.sc equiv Rg \$ \$ <
fluopyram-benzoic acid (M33)	
fluopyram-benzamide (M25)	2 5 98.6 fr at 3.233 to
fluopyram- <i>E</i> -olefin (M02)	
fluopyram-Z-olefin (M03)	
fluopyram-E-olefin (M02) fluopyram-Z-olefin (M03) Total identified in conventional extract	99.4 5 32749
Analysed extract(s)	<u>3.249</u>
Volatiles in distillates	
Extracts not analysed	
Total extractable	2 99.6 ² 3.265
Unextractable residues (Solids)	
Accountability / Total Accountability / Total	2000.0 3.280
Analysed extract(s)	



dosing of [phenyl-UL- ¹⁴ C] fluopyrar	acterization of radioactive residues in hen's fat after ° n at a daily dose rate of 2.03 mg/kg body weight for a
three consecutive days	
	Fat The set of the set
TRR [mg/kg] =	
Compound	% of TRR mg a.se equivale
Acetonitrile/water extract	
AE C656948, fluopyram	$\begin{array}{c c c c c c c c c c c c c c c c c c c $
fluopyram-benzoic acid (M33)	
fluopyram-benzoic acid (M33) fluopyram-benzamide (M25)	
fluopyram- <i>E</i> -olefin (M02)	2.5 $0.004268.6$ $1.1262.3$ 0.037 $1.1260.0037$ 0.042
fluopyram-Z-olefin (M03)	25.9 5 ⁻⁷ 5 ⁻⁰ 0.425 5 ⁻⁷
fluopyram-benzamide (M25) fluopyram- <i>E</i> -olefin (M02) fluopyram- <i>Z</i> -olefin (M03) Total identified in conventional extract	
Analysed extract(s)	<u> </u>
Volatiles in distillates	
Extracts not analysed	0 0.1 0 0.001
Total extractable	2 99.4 V 2 1.631
Unextractable residues Solids)	<u>, , , , , , , , , , , , , , , , , , , </u>
Accountability / Total , and the second	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
Analysed extract(s)	



 Table 6.2.2- 14:
 Summary of identification and characterization of radioactive residues in hen's liver after dosing of [phenyl-UL-¹⁴C] fluopyram at a daily dose rate of 2.03 mg/kg body weight for three consecutive days

for three consecutive days	
	Liver
TRR [mg/kg] =	9466 0 6
Compound	
Acetonitrile/water extract	
AE C656948, fluopyram	
fluopyram-benzoic acid (M33) fluopyram-benzamide (M25) fluopyram- <i>E</i> -olefin (M02) fluopyram- <i>Z</i> -olefin (M03) Total identified in conventional extract	0.024 0.
fluopyram-benzamide (M25)	
fluopyram- <i>E</i> -olefin (M02)	92.3 92.5 92.5
fluopyram-Z -olefin (M03)	
Total identified in conventional extract	→ → 0.2 → → → → 0.0k6 → → → → → → → → → → → → → → → → → → →
Analysed extract(s)	
Volatiles in distillates	Y 93.0 X 83805 Y 0.5 Y 0.006
Extracts not analysed	
L'I otol outro otobio	3 - 6 - 3 - 3 - 3 - 3 - 3 - 3 - 3 - 3 -
Unextractable residues folids)	
Accountability / Total	
Accountability / Toby	
	nclusion

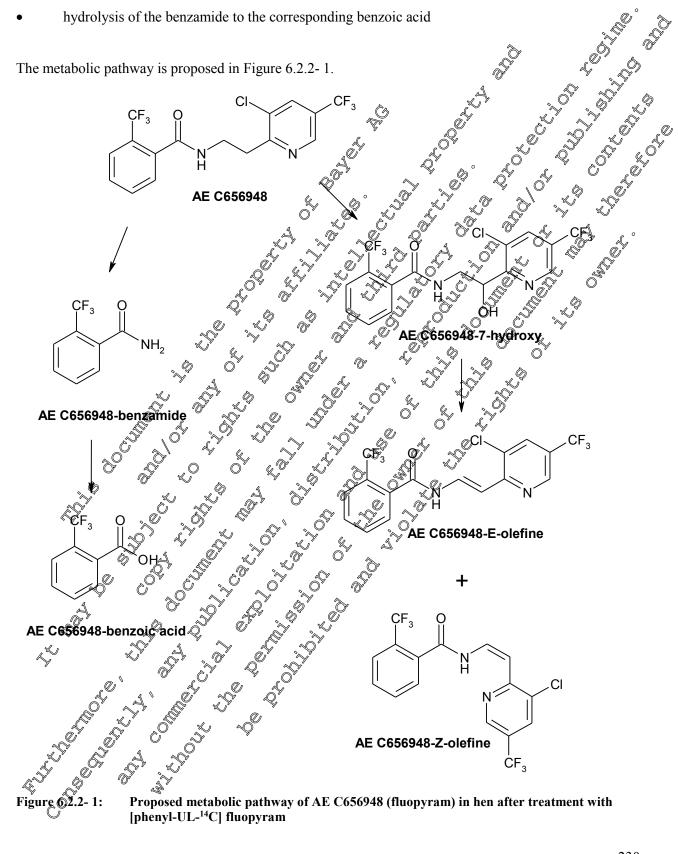
Six laying hens were dosed of ally for 14 consecutive days with phenyl-UL-¹⁴C]fluopyram at a daily dose of 2.03 mg/kg of body weight and sacrificed 24 hours after the last dose.

Laying hens extensively metabolised AE 536594 and the major compound in all edible matrices was metabolite AE C565948-benzamide (M23), representing 68.6% to 98.6% of the TRR. Other metabolites identified were fluopyram-Z-olofin(M03), fluopyram E-olefin (M02) and fluopyram-benzoic acid (M33). fluopyram-Z-olefin was identified in all exticle matrices and ranged from 0.2% to 25.9% of the TRR. fluopyram-E-olefin was detected only in that (2.3% TRR) and liver (0.3% TRR). fluopyram-benzoic acid was detected only in liver (0.3% TRR). The parent compound fluopyram was detected as minor component only in egg pools and fat (0.7% to 2.5% of the TRR).

Based of the identified metabolites, the following metabolic routes were deduced:

- cleavage of the aliphatic chain as major biochemical reaction
- Jydroxylation of the aliphatic chain followed by elimination







Proposed metabolic pathway of AE C656948 (fluopyram) in hen after treatment with [phenyl-UL-14C] fluopyram



Assessment and conclusion	n by applicant:
The study is valid and acce	ptable.
	n by applicant: ptable. KCA 6.2.2/02 Metabolism of [pp:rtly1-2.6714C1A] C655948 in Ale laying then MEF-06/405
Data Point:	KCA 6.2.2/02 & 6° 5° 6° 6° 5° 5°
Report Author:	
Report Year:	2008 <u>A</u>
Report Title:	Metabolism of [pr) dyl-2 6/14ClAP C656948 in the laying hen
Report No:	MEF-06/405 @ ' ' ' ' ' ' ' ' '
Document No:	M-298190-06 & & & & &
Guideline(s) followed in	US EPA OF TS 800.1300, Yealth Qanada, MR A Sef.: DACO 6,2 EU 91/414/EEC
study:	amended by 96/68/EC, append F 2 6 5 5
Deviations from current	Deviation to OPCD 500? 6 birds instead of 10 who impact, because sufficient amount
test guideline:	of scripple material cost available for marace vizition and id@tification of metabolit
Previous evaluation:	ves, evaluated and accored rev. KT Vol 3 of DAS B7 Ageust 2002 (references whed our
GLP/Officially recognis	Yer conducted under GLP Officially recognised testing far ties
testing facilities:	
Acceptability/Reliability:	Ofes N V N N N
	KCA 6.2.2/02 2008 Metabolism of [pr]rfdyl-2 (*14CA)? C63x948 in Ale laying hen MEF-06/405 M-298190-05 US EPA Q4PTS 8/01300; Mealth Qanade, IMRA Secf.: D5CO 6 GEU 91/414/EEC amended by 96/86/EC, append F Deviation to Q5CD 50% 6 birds instee of 10 No interf, begatise sufficient amount of sciple material cos available for inarce zation and identification of metabolities yes, evaluated and accorded rev. 1/b Vol3 of DA/BB7 Accust 2022 (references refield on Proceeding and the string factories of the strin
The metabolism of Byric	1 6-14 Offlues Pam was investigated in six laving hens, which where orally

The metabolism of pyrid 2,6-14 fluory ram was investigated in six laying hens, which where orally dosed for 14 consecutive days at a rate of 2,92 mg A.s./kg of body weight per day (corresponding to 25.96 mg a.s./kg feed day). Sacrifice was brade 24 h after the 14th administration. Radioactivity was measured in the excrete and eggs collected daily, as well as in the kidney, liver, eggs from the ovary and oviduct, skin without substance or fat, fouscle and fat at sacrifice. The collected eggs and the edible tissues and organs were analysed for parent comported and metabolites by extraction, chromatographic separation techniques and spectroscope methods.

The overall recovery (sum or radioactivity in the excreta, eggs as well as organs and tissues) was 95.6% of the total administered dose. The residual balance of only 4.4% at sacrifice may be still present in the gastrointesting tract. Until sacrifice, the excretion amounted to 94.71% of the totally administered radioactivity. An amount of 0.36% of the total dose was found in eggs. At sacrifice, the calculated or estimated total



residue in the tissues and organs dissected from the body was approx. 0.48% of the total dose. About half of this amount was detected in the fat (0.22%).

The mean TRRs in eggs increased from 0.047 mg eq/kg (day 1) to 0.321 mg eq/kg (day 8) and slowly decreased to 0.262 mg eq/kg (day 14). This showed that a residue plateau-level was clearly reached.

At sacrifice, highest mean equivalent concentrations occurred eggs dissected from the form and ovident (0.831 mg eq/kg) and was by a factor 3 higher compared to the laid eggs at the test end (0.262 mg eq/kg), indicating that the egg yolk was assumedly the preferential site for the secretion. These values were followed in decreasing order by the mean concentrations determined in the fiver (0.538 mg eq/kg), subcutaneous fat (0.498 mg eq/kg), the kidney (0.242 mg eq/kg), skin without subcutaneous fat (0.152 mg eq/kg) and total body muscle (0.048 mg eq/kg). The radioactive residues were extracted with efficiencies of 32.3-99.2% from eggs and edible organs or rissues with acetonit the water mixtures and *n*-heptane, and identification was achieved by co-chromatography with reference compounds.

For elucidation of parent compound and metabolites, eggs organs and tesues is well as excreta were extracted with acetonitrile/water mixtures. Fat was extracted with a heptatic. After purification and concentration steps, the resulting extracts of eggs muscle, fat and excreta represented between ca. 28% and 95% of the total radioactive residue (TRR). To increase the extraction efficiency an alternative approach was applied to the two egg pools and the liver pool Aliquots of these were extracted by enzymatic digestion using proteolytic enzymes. The resulting efficiency was slightly higher to that of the conventional extraction. To solubilize even more of the radioactive residues the extracted solids of the eggs (from day 7 to 14) after conventional extraction and the solids of the biver after enzymatic digestion were additionally extracted with microwave at increased temperature. With this procedure, the radioactivity remaining in the final solids was below 0.05 mg/kg. Thus a total extraction efficience of approx. 99% and 90% of the TRR was achieved for the oggs (7.14 days) and the liver respectively.

AE C565948 was extensively metabolised, but was still the major compound in egg pool 1–6 days (14.7– 17.9% of the TRR) and represented 1%–12% in the other matrices excluding liver. fluopyram-Z-olefin was the main metabolite in egg pool 7–14 days, muscle and fat and accounted for 15.4% to 70.5% of the TRR, and was also found at 4.1% in egg pool 4–6 days and at 1.9%–3.1% of the TRR in liver. fluopyram-*E*-olefin was the major metabolite in liver (11.8% -13.9% of the TRR) and represented 1.0% to 12.4% of the TRR in the other matrices. Further detected metabolites were fluopyram-7-hydroxy (M08) found in eggs, liver and excreta (0.8–5.8% of the dose) and fluopyram-pyridyl-acetic acid found in eggs and liver (1.3–6.4% of the TRR).

Ś

Based on the identified metabolites, the following metabolic routes were deduced:

- A hydroxylation of the aliphatic chain followed by elimination
- Kidative cleavage of the aliphatic chain



I. Materials and Methods A. Materials 1. Test Material: **IUPAC** Name *N*-{2-[3-chloro-5-(trifluoromethyl), pyridin-2-yl]ethyl (trifluoromethyl)benzamide CAS Name N-[2-[2; chloro-5-(trif@ioromethy] Benzamide. pyridinyl]eth@1-2-(trifluoromethyl)- (9CI) AE C656948 Code name Fluony Common name Empirical formula CAS Number Molar mass Chemical structure positions of radiolabel Radiolabelled test material C656948 BECH 1939 Batch number 0 Original specific radioactive $MBq/mg \approx 1.16 \times 10^8 dpm/mg$ 1 uCi/mg = 20.67 Ci/molRadiochemical (TLC) for BECH 1976 98% (HPLC); > 99% (TLC) for BECH 1939 99% (HPLC) for BECH 1976 and BECH 1939 Chemical purit Stability of Pest compound The administration suspensions were freshly prepared on the day before their use and each suspension was applied for three to four dosages. The radiolabelled parent compound was proved to be stable in the 0.5% aqueous tragacanth suspension for at least four days at +4 °C as shown by radio-HROC analysis. The evaluation of the chromatogram revealed а radiochemical purity of > 98% in tragacanth suspension.



2. Test Animals

Test Animals	
Species	Hen (Gallus gallus domesticus)
Breed	Hen (Gallus gallus domesticus) Image: Comparison of the second
Breeding facility	Six female laving bens
Sex, number	Six female laying hens
Mean body weight	Six female laying thens 1.53 kg at test start (1.46–1.6 P kg) 1.62 kg at test end (1.57–1.67 kg)
Age	ca. 20 week old at experiment start
Acclimatization	8 days L C A A A
Identification	Individual cage cards and wing tags 5
Housing	Each bird per standess steel merabolism cage approx 8-
	30°C, 53-80% rel? humarity, 16/8 hours light dark cycle
Feed and water	Commercial polverized hen fred, "Legement" (REG-Lm) at
Feed and water	200 g per day per animal supplemented with eggshells and
No.	\sim crushed marine shells $\sqrt{2}$
, ý , Ô	Tap water ad libitum
Health status	Acceptable ST
Study Design	
	V N S G L O

B. Study Design

Preparation of the dosing mixtures and administration:

The stock solution was prepared by dissolving both batches of the solid radiolabelled test compound (certified specific radioactivity: 0.93 MBq/mg) n 50 mL acetonitrile and radioassayed. The radioactivity concentration was determined to be 1.66 MBq/mL, corresponding to 7.56 mg compound/mL based on the specific radioactivity.

Four administration suspensions were prepared on the day before their use and each suspension was applied for three to four dosages. Definite volumes of [pyridyI-2,6-¹⁴C]fluopyram stock solution in acetonitrile were taken to prepare the administration suspensions tsuspensions 1–2: 12.381 mL, corresponding to 93.6 mg fluopyram; suspensions 4: 9286 mL, corresponding to 70.2 mg fluopyram). The solvent was removed by a nitrogen stream. Definite volumes of 9.5% aqueous Tragacanth (46.8 mL for suspensions 1–2 and 35.1 mL for suspensions 34) were added and the samples were stirred constantly until administration. The radioactivity of the suspensions was calibrated by liquid scintillation counting. The administration volume was 1 mL/kg bw, corresponding to a treatment rate of 2.02 mg a.s./kg bw per day. In relation to a mean body weight of 1.55 kg, the laying hens received a total mean dose of 43.24 mg per animal.

The oral administration procedure was carried out with a knob cannula attached to a glass syringe. Directly after to sage, the act of swallowing was sustained by a gentle massage of the throat in direction of the crop.



The radiolabelled parent compound was proved to be stable in the 0.5% aqueous tragacanth suspension for at least four days at +4 °C as shown by radio-HPLC analysis, and thus for the time from preparation of the administration suspension until dosing. The evaluation of the chromatogram revealed a radiochemical purity of > 98% in tragacanth suspension. The identity of the test compound was confirmed by LC/MS and ω LC-MS/MS.

Sampling: <u>Collection and processing of eggs and excreta</u> The eggs were collected each day (day 1–14), number and weight of eggs were tecorded for at hense For sampling, the egg-shells were discarded, and the white and yolk were thoroughly mixed. An alignet for the day of each egg mix was taken for the determination of tool radioactivity by LSC. Two bools of eggs day 1 to 6 and day 7 to 14) were prepared, thoroughly homogenized and stored arabout 38 °C ontil extraction for metabolite analysis. One sample of the combined egg-mx was taken for radioactivit@measurement.

The faecal-urine excreta were collected individually as quantitatively as possible at room temperature in intervals of 24 hours until sacrifice All fractions were homogenised after adding water, before the total weights were recorded. The total adioactivity was determined by combustion?

Sacrifice and collection of Organs and tissues

The treated laying here were weighed and sacrificed ca 24 hours after the last dose. The animals were anaesthetised using carbon dioxide gas, sacrificed by decapitation and essanguinated. The following organs and tissues were dissected: liver without galf bladder, kidneys, heg and breast muscle, skin without subcutaneous fat, subcutaneous fat, eggs from the mary and ovident, and the gall bladder.

All tissues were individually weighed, and liver, kidneys, muscle samples as well as the eggs dissected from the ovary and ovidect were thoroughly homogenized in Talf-frozen state. One aliquot of each resulting homogenized orssue was weighed, combusted and radioassayed by liquid scintillation counting (LSC). Aliquots of the skin without fat were weighted, solubilized with tissue solubiliser and taken for radioactivity measurement by LSC. The gal bladders were punctured for the collection of the bile fluid that was stored at ≤ -18 °C for the (optional) metabolite analysis. The two types of muscle (leg and breast) of all laying hens were combined, as well as their livers and lat samples and thoroughly homogenized.

Samples from the organs and other liquid samples were divided into equal portions and kept frozen at about -18 °C at all times until extraction. During the analytical work, the samples were stored either at approx. Cipra refogerator or at approx. -18 °C in a freezer.



C. Analytical Procedures

Extraction and fractionation:

Aliquot samples from egg, combined muscle, liver and excreta pools were conventionally extracted times with acetonitrile/water (4/1; v/v) using a Polytron homogeniser. The resulting extracts and solids were separated by filtration or centrifugation.

The combined acetonitrile/water extracts were purified by SPE using BP18 cartridge The effuent whick contained the major part of the applied radioactivity were concentrated using a rotative evaporator. The solids after extraction of the egg pool day 7-14 were further extracted twice with acetopitrile/water (1/1; v/s) and with acetonitrile/1N hydrochloric acid (1/1; v) with microwave assistance at increased temperature (approx. +120 °C) for solubilisation of remaining radioactivity.

The distillate from the concentration of the excreta extract was applied on a reversed phase SPE-cartridge. The effluent was then collected and the cartridge was exited 5 times with a small volume comethod. The second and third methanol eluate were combined and concentrated prior to HPL Schromatography.

An aliquot of the fat pool was extracted twice with a mixture of acetomutrile/water (442, v/v) and *n*-heptane. After each extraction the acetory trile/water and the n-heptane phases were separated. The acetonitrile/water extracts were combined and subjected to a glean-up step using a reversed phase SPE-cartridge. The effluent which contained the major part of the applied adioactivity was concentrated using a rotary evaporator, yielding the fat acetopitrile extract. The n neptane extracts were combined and partitioned against acetonitrile. The acetonitrile phase was concentrated, yielding the fat heptane extract.

Aliquots of the two egg pools and the liver pool were enzymatically digested by the proteolytic enzyme subtilisin Carlsberg (type VIII) and subsequently with taxtaric acid. The extracts were separated from the solids by centrifugation and the remaining solids were extracted successively three times with acetonitrile water (4/1; v/y) using a Polytron homogeniser. The resulting extracts and solids were separated by centribugation. All adividual extracts were combined and subjected to a clean-up step using a reversed phase SPE-cartridge The offluents which contained the major part of the applied radioactivity were concentrated using a rotaty evaperator. The source extraction of the liver pool were further extracted twice with acetonitrile water (1); v/g with microwave assistance at increased temperature (approx. +120 °C) for solubilisation of remaining radioactivity vity C

Analytical methods

The radioactivity of all aquid samples was measured using a liquid scintillation counter after mixing a known amount of each sample with scintillation fluid. Solid samples were combusted using an oxidizer. The resulting $^{4}CO_{2}$ was trapped in an alkaline scintillation cocktail. The TRR in the samples was calculated by summing up the radioactivity measured in different extracts and remaining solids after solvent extraction. The TRR was expressed in mg a.s. equivalents per kg sample weight (mg eq/kg). Amounts of radioactive series and also as mg a.s. equivalents per kg sample weight (ng eq/kg).



Aliquots of all acetonitrile/water and n-heptane extracts were analysed by HPLC. Four metabolites as well as parent compound were identified by HPLC co-chromatography with reference compounds.

The HPLC was conducted using a reversed-phase column using a reversed phase column and a buffered acetonitrile/water gradient. The HPLC system was equipped with a radiodetector and a UV detector with variable wavelengths. The LOQ was derived from the verage back found level and the specific radioactivity of the radiolabelled test compound.

Storage stability: Samples from the organs and other liquid samples were kept ftozen apabous 38 °C puring the entire study. During the analytical work, extracts of tissues and eggs were stored either at approx. +4 Q in a terrigerator or at approx. -18 °C in a freezer. All solvent extraction experiments and first HPLC analyses of the extracts from eggs, muscle, fat, liver and excrete were performed within ca. 6 months after sacrifice of the mens.

The conventional extract of egg poor day 1-6 was analysed again 1 year later, the muscle extract ca. 10 months later, the fat extract ca. 5 months later. Nosignificant change was observed in the metabolic profiles. Overall, the radioactive residues in all extracts were found to be stable under storage conditions.

Recollts and Discossion

The metabolism in laving hers of [pyridy]-2,6 fluopyram administrated at a daily dose of 25.96 mg eq/kg in the feed copesponding to a daily witake of 2.02 for eq/kg body weight for 14 consecutive days was investigated.

Until sacrifice 24 fours after the dast dose, the mean excretion amounted on average to 94.71% of the radioactivity totally administered (Table 6.2.2-95). The time course of the excretion was characterised by a relatively constant role starting at day 1 until test and (Table 6.2.2-16). Only 0.36% of the dose totally administered was measured in the eggs produced within the whole test period. At sacrifice, 24 h after the last administration, the total residue in the tissues and organs dissected from the body was calculated and estimated to about 0.48% of the total dose. Based on these values, the recovery amounted to 95.55% (Table 6.2.2-15).

The total radioactive residues were determined in eggs and excreta produced from the first dose until sacrifice and in edible Ossues and organs at sacrifice. The highest mean active substance equivalent concentrations were measured in the eggs dissected from the ovary and oviduct (0.831 mg eq/kg) and liver (0.532 mg eokg). These values were followed in decreasing order by the mean concentrations determined in the suboutaneous fat (0.498 mg eq/kg), the kidney (0.242 mg eq/kg), skin without subcutaneous fat (0.152 mg eq/kg) and total body muscle (0.048 mg eq/kg). For details see Table 6.2.2-18).



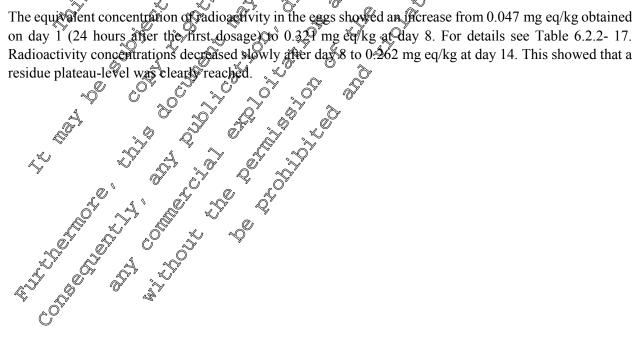
Recovery of radioactivity following oral administration of [pyridyl & 6-14C] fluopyram at a Table 6.2.2-15: Í. daily dose rate of 2.02 mg eq/kg body weight for 14 consecutive days Ó

ua	ny dose rate of 2.02 mg eq/kg body weight for 14 consecutive days
Matrix	Recovery of radioactivity (% of the totally administrated radioactivity) 94.71 0.36 0.50 km c 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	(% of the totally administrated radioactivity)
Excreta ¹⁾	<u>94.71</u> Q Q Q Q Q
Eggs ²⁾	
Totally excreted	95.01 95.01 3
Tissues ³⁾	94.71 94.71 95.010
Recovery	A 05.55 0 0 A A
P. Recovery in eggs calculated in the second sec	Handed by adding recovery values of samples produced within the observation period of 14 days inated by adding recovery values of samples produced within the observation period of 14 days inated from the body weight and the observation period of 14 days without subcutaneous fail, and from the sum of period by each for the body weight for the inated from the values in the report of the body weight and the period of the body weight for the body weight for the the body weight and the period of the body weight for the body weight for the body weight for the body weight for the the body weight and the period of the body weight for the body wei
	238



Matrix	Time after the first dosage (day)	Administration number	TRR (mg a.s. equiv./kg)
	0		
	1	2	
	2	3	
	3	A Contraction of the second se	25.212 25.212
	4	0 ⁴⁵ 0 2	
	5	A . 60° . C	Q. 0 13.177 A
	6		→ → → → → → → → → → → → → → → → → → →
Excreta	7		2.189 S O
	8 Q		× × 11.67 ×
	9 10 %	10 ° 10 °	
			L . 12.41 P
	×11	\$ 12 fr	11,294
	S B L		\$ \$ \$ \$ \$ \$ \$ 2.277
	\$ \$\sum_13 \sum_13	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	O″ ♣⁄ 12.506
	≥ 14 ⁵ &		² ² 11.889

The equivalent concentration of adioactivity in the eggs showed an increase from 0.047 mg eq/kg obtained





Eggs	0 1 2 3 4 5 6 7		0.040° 5° 5° 0.0093 ° 5° 0.0093 ° 5° 0.1540° 6° 0.223 5° 0.223 5° 0.223 5°
	2 3 4 5 6		0.040° 2° 2° 0.040° 2° 2° 2° 2° 0.093 2° 0° 0°
	3 4 5 6	40	
	4 5 6		
	5 6		
	6		
		ê in di	
	7		
		8 6 8 6	
	8 Q		
	9, °, °, 10 %,		
	10 %		مَنْ 0.293 [°]
	×11 A	\$ 12 K	2 ⁵⁴ 02289
j.	/ 1 8		<u>لَمْ الْمَ الْمُ</u>
	~13 °	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.262
	<u>, 145 %</u>	N N N	0.262
la l	× à		
			0 7
			<i>u</i>
, a si a s	" ₆ 5° . 0°		
0 Çr	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		
	AX		
Ó ^r "A`		Q ⁴	
	Š ⁱ v ~		
	, Nor i		



Table 6.2.2- 18: Distribution of residues in eggs, tissues and organs of laying hens following oral administration of [pyridyl-2,6-14C]fluopyram at a daily dose rate of 2.02 mg eq/kg body weight for 14 consecutive days

weight for 14 consecu		
Matrix	Interval (day)	TRR (mg a.s. equiv./kg)
Liver (composite)	14 🖉	0.538 × × ×
Kidney	14	
Eggs from ovary/oviduct	14 JUV	
Muscle, leg *	KO T	
Muscle, breast *		
Total body muscle	A 14 0	6 6 0048 K A
Skin without subcutaneous fat	J JA N	5 A 6 0.152 C V
Subcutaneous fat (composite)		
Total body fat	°° ằ¥ [×] ∿ [×]	
mg a.s. equiv./kg: mg parent equivalents per kg r	nafræx og og og	
* sample		

In the composite egg, pool (easy 1–6) with <u>conventional extraction</u> \$3.6% of the radioactivity (0.084 mg eq/kg) was extracted with solvent extraction (acetoritrile/water). Following solid phase extraction purification, most of the radioactivity was contained in the combined sample passage and acetonitrile/water inse solution ("purified acetonitrile/water extract" (49.9% or 0.078 mg eq/kg) and, after the concentration step, the concentrated acetonitrile/water extract contained 47.8% of the TRR (0.075 mg eq/kg). In total, 53.6% of the TRR (0.084 mg eq/kg) vas extracted, whereas 46.4% of the TRR (0.072 mg eq/kg) remained non-extractable in onics (Table 6.2.2-19).

In composite egg port (day 4-6) with <u>enzymatic freatment</u>, 69.7% of the radioactivity (0.109 mg eq/kg) was extracted with solvent extraction (actionitie/water). Following solid phase extraction purification, most of the radioactivity was contained in the combined sample and acetonitrile/water rinse solution ("purified acetonitrile/water extract", 65.9% or 6103 mg eq/kg) and, after the concentration step, the concentrated acetonitrile/water extract", 65.9% or 6103 mg eq/kg) and, after the concentration step, the concentrated acetonitrile/water extract container 57.7% of the TRR (0.090 mg eq/kg). In total, 69.7% of the TRR (0.047 mg eq/kg) remained non-extractable in solids (Pable 6.2.2-19). With this procedure, the radioactivity remaining in the final solids was therefore below 0.05 mg/kg.

In the composite egg pool (day 7–14) with <u>conventional extraction</u>, 47.8% of the radioactivity (0.137 mg/eq/kg) was extracted with solvent extraction (acetonitrile/water). Following solid phase extraction purification, the main radioactivity was contained in the purified acetonitrile/water extract (39.9% of the TRR 0.114 mg/eq/kg) and, after the concentration step, the concentrated acetonitrile/water extract contained 38.0% of the TRR (0.109 mg/eq/kg).



After further extraction of the solids with acetonitrile/water (1/1, v/v) using a microwave and temperature gradient, the microwave extracts contained further 51.2% of the radioactivity (0.146 mg eq/kg) and only (0.003 mg eq/kg) remained in the solids.

In total, 99.0% of the TRR (0.283 mg eq/kg) was extracted, whereas 1.0% of the TRR (0.003 mg eq/kg) remained non-extractable in solids (Table 6.2.2-20)

In the composite egg pool (day 7–14) with enzymatic treatment, 64.1% of the radioactivity (0.183 mg eq/kg) was extracted with solvent extraction (acetonitrile vater). Following solid phase extraction purification, the main radioactivity was contained in the purified acetonitrile vater extract (63.7% of the TRR, 0.182 mg eq/kg) and, after the concentration step, the concentrated acetonitrile/water extract contained 55.5% of the TRR (0.159 mg eq/kg). In total, 64.1% of the TRR (0.183 mg eq/kg) was extracted, whereas 35.9% of the TRR (0.103 mg eq/kg) remained not extractable in solids (Table 6.2.2-20).

In muscle, the major part of the radioactive residues (59/3% of the TRR, 0.029 mg of/kg) was extracted with acetonitrile/water. After solid phase extraction purification, the main radioactivity was contained in the purified acetonitrile/water extract (58,3% of the TRR 0.029 mg eq/kg). After the first concentration step, the radioactivity in the concentrated extract amounted to 55.7% of the TRR (0.027 mg eq/kg) and to 54.6% of the TRR (0.027 mg eq/kg) in the second concentration step. In tetal, 59.3% of the TRR (0.029 mg eq/kg) was extracted, whereas 40.7% of the TRR (0.020 mg eq/kg) remained non-extractable in solids (Table 6.2.2-21).

In fat, the radioactive residues extractable with acotonitrite/water amounted to 71.1% of the TRR (0.353 mg eq/kg) and, after clean-up procedure by solid phase extraction to 70.8% of the TRR (purified acetonitrile/water extract, 0.351 mg eq/kg). After the concentration step the radioactivity in the concentrater extract amounted to 69.6% of the ORR (0.345 mg eq/kg).

The radioactive residues extractable with *n* beptane amounted to 28,1% of the TRR (0.139 mg eq/kg) and, after partition against acetonitrile to 25,5% of the TRR (0.124 mg eq/kg) in the acetonitrile phase. After the concentration step the radioactivity in the concentrated extract amounted to 25.5% of the TRR (0.127 mg eq/kg).

In total, 94,2% of TRR (0.492 mg eq/sg) was extracted and only 0.8% of the TRR (0.004 mg eq/kg) remained non-extractable in solids (Table 6.2.2-22).

In liver with <u>conventional extraction</u>, 32.3% of the radioactivity (0.172 mg eq/kg) was extracted with solvent extraction (acctonit (e/water)). Following solid phase extraction purification, the main radioactivity was contained in the purified acetonitril (water extract (28.9% of the TRR, 0.154 mg eq/kg) and, after the concentration step, the concentrated acetonitrile/water extract contained 28.2% of the TRR (0.150 mg eq/kg).

In total, 32,3% of the TRR (0.172 mg eq/kg) was extracted, whereas 67.7% of the TRR (0.360 mg eq/kg) remained non-extractable in solids (Table 6.2.2-23).



In liver with <u>enzymatic treatment</u>, 82.9% of the radioactivity (0.441 mg eq/kg) was extracted with solvent of extraction (acetonitrile/water). Following solid phase extraction purification, the main radioactivity was contained in the purified acetonitrile/water extract (75.9% of the TRR, 0.404 mg eq/kg) and, after the concentration step, the concentrated acetonitrile/water extract contained 67.3% of the TRR (0.358 mg eq/kg).

After further extraction of the solids with acetonitrile/water (1/1, v/v) using a microwave and temperature gradient, the microwave extract contained further 7.4% of the radioactivity (0.039 mg eq/kg) and 9.7% (0.052 mg eq/kg) remained in the solids.

In total, 90.3% of the TRR (0.480 mg eq/kg) was extracted, whereas 97% of the TRR (0.052 mg eq/kg) remained non-extractable in solids (Table 6.2.2-20).

).

 Table 6.2.2- 19:
 Extraction of radioactive residues from the hen's rgg pool (day 56) after dosing of [pyridyl-2,6-14C] fluopyram at a daily dose rate of 2.02 mg eq/kg body weight for 14 consecutive day

consecutive days			° 20 k	
		~Egg pool	(day 1-6) ^O	
	Convention	al extraction	Enzymati	c treatment
TRR, mg eq/kg		<u>کې د 0.1</u>	56	
Fraction	TRIS T	mg a.so ©equiy./kg	∕°∕° TRR	mg a.s. equiv./kg
Solvent extract ¹	× <u>5</u> 3% ~	× 00084 ~~	69.7	0.109
Purification Ha RP 8 20 0 40	49.85 [°]	00084 00084 0 0.078		
Purified acetonitrile/water extract?	49. %	~	65.9	0.103
Concentration				
Concentrated acetonitele/water extract	, 0 47.8 ≪ ^y	_م 00.075	57.7	0.090
Distillate	× 2.1×	رورورور ک ^۲ 0.003	8.2	0.013
Concentrated acetonitie/water extract	P 3.9 📎	0.006	-	-
Solid phase \mathcal{O} \mathcal{O} \mathcal{O} \mathcal{O}	<u> </u>	-	3.8	0.006
Solids	× 46.4	0.072	30.3	0.047
PES ²⁾	464	0.072	30.3	0.047
Total extracted	\$\$3.6	0.084	69.7	0.109
Accountability / Total	100.0	0.156	100.0	0.156

1) Solvent extraction was done with 43 with acconitric water (4/1, v/v).

PES: post extraction solids = not extractable radioactivity.
 Sum of extracts and PES. Q.

5) Sum of extracts and PES. Fractions given m bold font were analysed by radio-HPLC.



[pyridyl-2,6-¹⁴C]fluopyram at a daily dose rate of 2.02 mg eq/kg body weight for 14 consecutive days Table 6.2.2- 20: S.

consecutive augs			Q°		
		Egg pool	(day 7) 14)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
	Conventional		Enzymatic	treatment	Ŷ
TRR, mg eq/kg			86 ×		1
Fraction	% TRR	mg a.s. equiv. Akg	% TRR	ng a.s. ⊘equiy∰g	Ô
Solvent extract ¹⁾	47 8	0.1377	° 64/1 L	00/83	1
Purification via RP18			~~ \O*	S O	
Purified acetonitrile/water extract	\$ 39.9 €	\$0.11 4 €	_₹ 63.20	°, [™] , [™] 0.1,8, [™]	
Concentration			¢ 7 1	2	
Concentrated acetonitrile/water extract	>38.0	0.109	55.5 O	30.159	
Distillate	1.9	0.006	°~ ^{0°} 6.2≪	0.018	
Concentrated Methanol/dichloromethan	28	x 800x0 X		0.606	
Solid phase	* <u>`~</u> ` ~`	~~-~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	\$0.4 °	0.001	
Solids	\$ 52.2°	× 0.149	گ ² 35.9	[≪] 0.103	
Microwave solvent extraction $\frac{2}{\sqrt{3}}$				· ¥	
Microwave extract	51.2	0.146 0		-	
Solids	1.0	0.002	°~°° - ©	-	
PES ³⁾	1.07	> 0.003 🔬	\$ 35,9	0.103	
Total extracted	9 .0 ×	0×283 🔬	\$ \$4.1	0.183	
Accountability / Total	~100.05°	0.2860	<i>√</i> y″100.0	0.286	

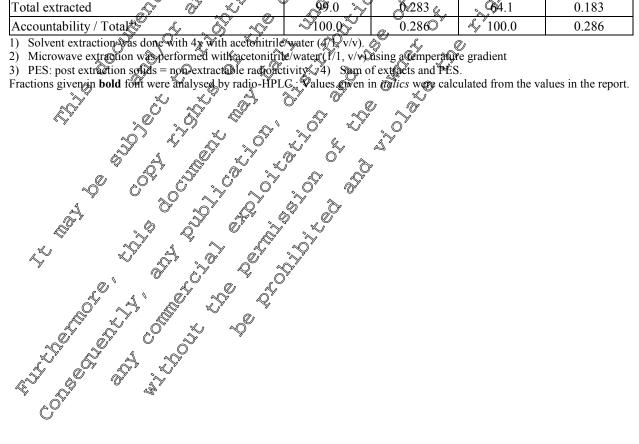
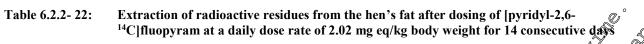




Table 6.2.2- 21:Extraction of radioactive residues from the hen's muscle after dosing of [pyridyl-2,6- or section of a daily dose rate of 2.02 mg eq/kg body weight for 14 consecutive days14C]fluopyram at a daily dose rate of 2.02 mg eq/kg body weight for 14 consecutive days

Chuopyrain at a dairy dose rate of 2.02 mg	
	Muscle composite)
TRR, mg eq/kg	0.049
Fraction	% TRR mg a@ equiv kg
Solvent extract ¹⁾	595 2 0.0297
Purification via RP18	
Purification via RP18 Purified acetonitrile/water extract Concentration and repeated purification via RP18 Concentrated acetonitrile/water extract 1	58.3 0.029 5
Concentration and repeated purification via RP18	
Concentrated acetonitrile/water extract 1	59.7 × 0 0.027
Concentration	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
Concentrated acetonitrile/water extract 2	
Distillate	$\begin{array}{c} 0.023 \\ 0.001 \\ 0.8 \\ 0.8 \\ 0.001 \\ 0.000 \\ 0.0$
Concentrated Methanol/dichloromethane eluate	
Distillate	
Concentration and repeated purification via RP18 Concentrated acetonitrile/water extract 1 Concentrated acetonitrile/water extract 2 Distillate Concentrated Methanol/dichloromethane eluate Distillate Solid phase Methanol/dichloromethane eluate	54.0 0.027 0.027 0.027 0.027 0.001 0.0020
Solid phase	
Methanol/dichloromethane eluate	
Solids ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	
PES ²	40.7 0.020
Total extracted	× 59.5× 0.029
Accountability / Total ³)	0.049
 Solvent extraction was done with 1x acconstruction of 2x with account intrile/ PES: post extraction volids Don-extra able adjoactivity 	water $(4/1 \mathbb{Q}^{1/2})$.
3) Sum of extracts and PES	
Fractions given in bold for were analysed boradio-HOLC.	
	Õ
	, T
	. 7
	۲. Ala and a second s
	~
Solid phase Methanol/dichloromethane eluate Solids PES ²⁾ Total extracted Accountability / Total ³⁾ 1) Solvent extraction we done with 1x accontrile and 2x with acetophrile/ 2) PES: post extraction solids = non-extractable adioactivity. 3) Sum of extracts and PES Fractions given in bold for were analysed by radio-HPLC.	
ζΨ.	





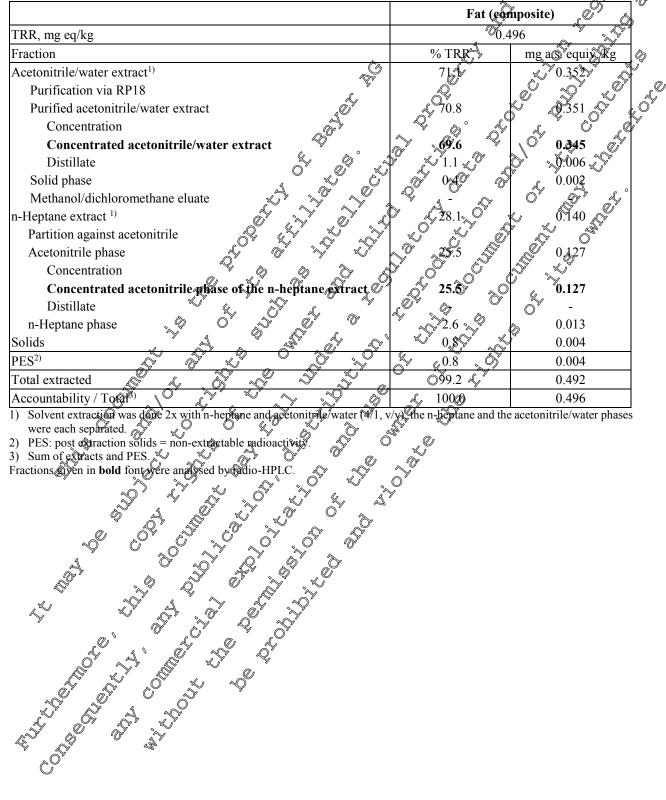




Table 6.2.2- 23:	Extraction of radioactive residues from the hen's liver after dosing of [pyridyl-2,6- ¹⁴ C]fluopyram at a daily dose rate of 2.02 mg eq/kg body weight for 14 consecutive days	
	C indepyram at a dany dose rate of 2.02 mg eq/kg body weight for 14 consecutive days	S

Conventional extraction Enzymatic treatment TRR, mg eq/kg 0.532 Fraction % TRR mg a.s. equiv /kg % TRR mg a.s. equiv /kg Solvent extract ¹⁷ 323 0.152 833 0.445 Purification via RP18 75.9 0.4042 0.452 833 0.445 Purified acetonitrile/water extract 28.9 0.154 75.9 0.4042 Concentrated acetonitrile/water extract 28.2 (0750 67.3 9.358 Solid phase 0.7 6.004 8.6 0.046 Concentrated Methanol/dichloromethang eluatt 67.7 0.061 0.7 0.062 Solids 67.7 0.366 57.1 0.052 0.91 Microwave solvent extraction ²¹ 7 0.366 9.4 0.039 Solids - - 9.7 0.052 PES ³ 67.7 0.366 9.4 0.039 Solids - 0.72 9.012 0.052 PES ³ 67.7	FRR, mg eq/kg 0.532 Fraction % TRR mg a.s. equiv./kg % TRR mg a.s. equiv./kg % TRR mg a.s. equiv./kg Solvent extract ¹⁾ 32,0 0.152 82,3 0.441 Purification via RP18 28.9 0.154 75.9 0.404 Purified acetonitrile/water extract 28.9 0.154 75.9 0.404 Concentration 28.2 0.004 1.4 0.007 Solid phase 0.7 0.004 1.4 0.007 Concentrated Methanol/dichloromethang eluate 27.7 0.044 0.007 Microwave solvent extraction ²⁾ 67.7 0.360 9.7 0.052 Microwave solvent extraction ²⁾ 67.7 0.360 9.7 0.052 PES ³⁾ 67.7 0.360 9.7 0.052 Total extracted 27.3 0.172 90.3 0.480 Accountability / Total ⁴ / ₂ 4.000 0.532 0.000 0.532 Solids 0.7 0.360 9.7 0.052 Ototal extracted 0.7 0.360 9.7 0.05			Liver (co	mposite)	SUN A
Fraction % TRR mg a.s. equiv./g % TRR mg a.s. equiv./g % TRR mg a.s. equiv./g Solvent extract ¹⁾ 32% 0.152 823 0.441 Purification via RP18 28.9 0.154 75.9 0.441 Purified acetonitrile/water extract 28.9 0.154 75.9 0.441 Concentrated acetonitrile/water extract 28.2 0.044 8.6 0.046 Solid phase 0.7 0.004 8.6 0.046 Concentrated Methanol/dichloromethang eluate 67.7 6.014 0.007 Microwave solvent extraction ²⁾ 67.7 0.360 9.7 0.052 PES ³ 67.7 0.360 9.7 0.052 Total extracted 22.3 0.172 50.3 0.480 Accountability / Total ⁴ 0.007 0.532 700.0 0.532	Fraction % TRR mg a.s. equiv./g % TRR mg a.s. equiv./g % TRR mg a.s. equiv./g Solvent extract ¹⁾ 32% 0.152 823 0.441 Purification via RP18 28.9 0.154 75.9 0.441 Purification via RP18 28.9 0.154 75.9 0.441 Purified acetonitrile/water extract 28.9 0.044 8.6 0.044 Concentrated acetonitrile/water extract 28.2 0.052 0.044 8.6 0.046 Solid phase 0.7 0.004 8.6 0.046 0.046 0.067 Solids 0.7 0.004 9.7 0.030 0.091 0.091 Microwave solvent extraction ²¹ 0.7 0.360 9.7 0.052 Microwave extract 0.04 0.067 0.052 0.052 Total extracted 0.03 0.7 0.360 9.7 0.052 Otids 0.00 0.532 700.0 0.532 0.00.0 0.532 Oblevent extracted 0.00 0.532 700.0 0.532 0.00.0 0.532 </th <th></th> <th>Conventiona</th> <th>l extraction</th> <th>Enzymatic</th> <th>treatment</th>		Conventiona	l extraction	Enzymatic	treatment
Production 70 TRC * equiv/kg 70 TRC * equiv/kg 70 TRC * equiv/kg Solvent extract ¹) 32% 0.152 823 0.44* Purification via RP18 28.9 0.154 75.9 0.404 Purified acetonitrile/water extract 28.9 0.154 75.9 0.404 Concentrated acetonitrile/water extract 28.2 0.004 8.6 0.046 Solid phase 0.7 0.004 8.6 0.046 Concentrated Methanol/dichloromethane eluate 2.7 6.014 6.7 0.030 Solids 67.7 0.366 9.7 0.052 Microwave solvent extraction ²⁾ 67.7 0.366 9.7 0.052 PES ³ 67.7 0.366 9.4 0.052 Total extracted 2.3 0.172 90.3 0.480 Accountability / Total ⁴ 0.014 0.02 0.532 900.0 0.532 Oblem extraction was done with 4x with actemptici/water (4/1 w/). 0.00 0.532 900.0 0.532 Oblem extraction was done with 4x with actemptici/water (4/1 w/). 0.00 0.532 900.0	Solvent extract ¹⁾ 32% 0.152 823 0.44% Purification via RP18 28.9 0.154 75.9 0.404 Purified acetonitrile/water extract 28.9 0.154 75.9 0.404 Concentrated acetonitrile/water extract 28.2 0.064 14 0.067 Distillate 0.7 0.004 14 0.067 Solids 0.7 0.004 14 0.007 Microwave solvent extract 27 0.014 67.7 0030 Solids - - 9.7 0.052 PES ³ - 67.7 0.369 9.4 0.052 Total extracted - 27.3 0.172 90.3 0.480 Accountability / Total ⁴ - - 9.7 0.052 Osolvent extraction was done with 4x with accepturile/water (4/1 w). - - 9.4 0.039 Solvent extraction was done with 4x with accepturile/water (4/1 w). - - 9.7 0.052 Other extraction was done with 4x with accepturile/water (4/1 w). - - - - -	TRR, mg eq/kg	<u>È</u> a		62 ×	O ^v O ^v
Purification via RP18 Purified acetonitrile/water extract Concentrated acetonitrile/water extract Distillate Solid phase Concentrated Methanol/dichloromethane eluate Solids Solids Solids Solids PES ³⁾ Total extracted Accountability / Total ⁴⁾ Solvent extraction ²⁾ Microwave solvent extraction ²⁾ Microwave extract Solids Concentrated Methanol/dichloromethane eluate Concentrated Methanol/dichloromethane eluate Concentrate Methanol/dichloromethane Concentrate Meth	Purification via RP18 Purified acetonitrile/water extract Concentrated acetonitrile/water extract Distillate Solid phase Concentrated Methanol/dichloromethane eluate Solids Microwave solvent extraction ²⁾ Microwave extract Distillate Solids Solids Concentrated Methanol/dichloromethane eluate Solids Microwave extract Distillate Solids Microwave extract Distillate Solids Solids PES ³⁾ Concentrated Methanol/dichloromethane eluate Concentrated Methanol/di	Fraction	% TRR	mg a.s. equiv./kg	% TRR	ng a.s.
Solid phase Solid phase Concentrated Methanol/dichloromethans eluate Solids Microwave solvent extraction ²⁾ Microwave extract Solids $PES^{3)}$ Total extracted Accountability / Total ⁴⁾ Solvent extraction we show with 4x wolf acetembrile/water (4/1, $\sqrt{1}$). Microwave extraction we show with 4x wolf acetembrile/water (4/1, $\sqrt{1}$).	Solid phase Concentrated Methanol/dichloromethane eluate Solids Microwave solvent extraction ²⁾ Microwave extract Solids $\frac{50}{12}$ 50		32.	0.142	82.5	Q 0.449 🛊
Solid phase Solid phase Concentrated Methanol/dichloromethans eluate Solids Microwave solvent extraction ²⁾ Microwave extract Solids $PES^{3)}$ Total extracted Accountability / Total ⁴⁾ Solvent extraction we show with 4x wolf acetembrile/water (4/1, $\sqrt{1}$). Microwave extraction we show with 4x wolf acetembrile/water (4/1, $\sqrt{1}$).	Solid phase Concentrated Methanol/dichloromethane eluate Solids Microwave solvent extraction ²⁾ Microwave extract Solids $\frac{50}{12}$ 50	Purification via RP18	CO'T			U Q
Solid phase Solid phase Concentrated Methanol/dichloromethans eluate Solids Microwave solvent extraction ²⁾ Microwave extract Solids $PES^{3)}$ Total extracted Accountability / Total ⁴⁾ Solvent extraction we show with 4x wolf acetembrile/water (4/1, $\sqrt{1}$). Microwave extraction we show with 4x wolf acetembrile/water (4/1, $\sqrt{1}$).	Solid phase Concentrated Methanol/dichloromethane eluate Solids Microwave solvent extraction ²⁾ Microwave extract Solids $\frac{50}{12}$ 50	Purified acetonitrile/water extract	28.9 。	0.154	75.9	\$0.404
Solid phase Concentrated Methanol/dichloromethans eluate Solids Microwave solvent extraction ²⁾ Microwave extract Solids $PES^{3)}$ Total extracted Accountability / Total ⁴⁾ Solvent extraction we with 4x work accentrile/water (4/1, $\sqrt{2}$). Microwave extraction we with 4x work accentrile/water (4/1, $\sqrt{2}$).	Solid phase Concentrated Methanol/dichloromethane eluate Solids Microwave solvent extraction ²⁾ Microwave extract Solids $\frac{50}{12}$ 50	Concentration	o ^y o ^g x	\sim \sim .		\sim \sim
Solid phase Concentrated Methanol/dichloromethans eluate Solids Microwave solvent extraction ²⁾ Microwave extract Solids $PES^{3)}$ Total extracted Accountability / Total ⁴⁾ Solvent extraction we with 4x work accentrile/water (4/1, $\sqrt{2}$). Microwave extraction we with 4x work accentrile/water (4/1, $\sqrt{2}$).	Solid phase Concentrated Methanol/dichloromethane eluate Solids Microwave solvent extraction ²⁾ Microwave extract Solids $\frac{50}{12}$ 50	Concentrated acetonitrile/water extract	28.2	0 2150 8	67 .3	0.358
Solid phase Concentrated Methanol/dichloromethane eluate Solids Microwave solvent extraction ²⁾ Microwave extract Solids $PES^{3)}$ Total extracted Accountability / Total ⁴⁾ Solvent extraction webdone with 4x wob acetembrile/water (4/1, v). Microwave extraction webdone with 4x wob acetembrile/water (4/1, v). Microwave extraction webdone with 4x wob acetembrile/water (4/1, v).	Solid phase Concentrated Methanol/dichloromethano eluate Solids Microwave solvent extraction ²⁾ Microwave extract Solids $PES^{3)}$ Concentrated Concentrated Methanol/dichloromethano eluate $Concentrated Methanol/dichloromethano eluate Concentrated Methanol/dichloromethano eluate Concentrate Methanol/dichloromethano Concentrate Methanol/dichloromethano Concentrate Methanol/dichloromethano Concentrate Methanol/dichloromethanol/dichl$		× 0.7	0.004	\$ 8.6 O	Q0.040
Solids Microwave solvent extraction ²) Microwave extract Solids PES^{3} Accountability / Total 4) Solvent extracted $Accountability / Total 4) Solvent extraction was done with 4x work acceedint ile/water (4/1, sy). Nicrowave extraction was done with 4x work acceedint ile/water (4/1, sy).$	Solids Microwave solvent extraction ²⁾ Microwave extract Solids $PES^{3)}$ Colored extracted Accountability / Total 4) $Colored extractedColored extracted$	Solid phase		ς 0.0 6 ¥΄ ΄		0.007
Solids Microwave solvent extraction ² Microwave extract Solids PES^{3} Accountability / Total 4 Solvent extracted $Accountability / Total 4 Solvent extraction we show with 4x work accountile/water (4/1, sy). Solvent extraction we show with 4x work accountile/water (4/1, sy). Solvent extraction we show with 4x work accountile/water (4/1, sy).$	Solids Microwave solvent extraction ² Microwave extract Solids $PES^{3)}$ Call extracted Accountability / Total 4) $Call extractedCall ex$	Concentrated Methanol/dichloromethane eluate		g g g 14 č	B .7 S	00030
Microwave solvent extraction 2° Microwave extract Solids PES 3° Accountability / Total 4° Solvent extracted Accountability / Total 4° Solvent extraction was done with $4x$ with acceptibility water $(4/1, \sqrt{1})$. Microwave extraction was done with $4x$ with acceptibility ($4/1, \sqrt{1}$).	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Solids Solids	×677×	~0.360 [~]	\$17.1\$	ي 0.091
Solids 4 $ 9.7$ 0.052 PES 3) 67.7 0.369 9.7 0.052 Total extracted 2.3 0.172 90.3 0.480 Accountability / Total 4) 2.3 0.052 0.052 1) Solvent extraction was done with 4x work accemptrile/water (4/1, $\sqrt{2}$) 0.532 0.000 0.052 0.052 0.052	Solids 4 $ 9.7$ 0.052 PES 3) 67.7 0.360 9.5 0.052 Total extracted 22.3 0.172 90.3 0.480 Accountability / Total 4) 0 0.532 0.000 0.532 Solvent extraction we done with 4x work acetopticile/water (4/1, sv). 0 0 0.532 Output was referenced as a substrained acetopticile/water (4/1, sv). 0 0	Microwave solvent extraction 2		Š, O		×,
Solids 4 $ 9.7$ 0.052 PES 3) 67.7 0.369 9.7 0.052 Total extracted 2.3 0.172 90.3 0.480 Accountability / Total 4) 2.3 0.052 0.052 1) Solvent extraction was done with 4x work accemptrile/water (4/1, $\sqrt{2}$) 0.532 0.000 0.052 0.052 0.052	Solids 4 $ 9.7$ 0.052 PES 3) 67.7 0.360 9.5 0.052 Total extracted 22.3 0.172 90.3 0.480 Accountability / Total 4) 0 0.532 0.000 0.532 Solvent extraction we done with 4x work acetopticile/water (4/1, sv). 0 0 0.532 Output was referenced as a substrained acetopticile/water (4/1, sv). 0 0	Microwave extract	Ĩ Â L		ř , Đặ 🔬	0.039
Total extracted $2/3$ 0.172 99.3 0.480 Accountability / Total ⁴) 0.000 0.532 000.0 0.532 1) Solvent extraction was done with 4x with acetomtrile/water (4/1, 5v). 0.172 0.172 $0.00.0$ 0.172 0.172 0.172 0.172 0.172 0.172 0.172 0.172 0.172 0.172 0.172 0.172 1) Solvent extraction was done with 4x with acetomtrile/water (4/1, 5v). 0.532 0.172 0.172 1) Microwaya extraction was done with 4x with acetomtrile/water (4/1, 5v). 0.532 0.172 0.172	Total extracted Z.3 0.172 09.3 0.480 Accountability / Total ⁴ A	Solids	× - »	L'- Q	9.7 O [¥]	0.052
Accountability / Total 4° 6°	Accountability / Total 4 6 6 $^{100.0}$ 6 $^$	$PES^{3})$	67.7		≥y 9.₽	0.052
1) Solvent extraction was done with 4x with acctementatile/water (4/1, 5v).) Solvent extraction was done with $4x \text{ why acccontrile/water } (4/1, sv). \bigcirc$	Total extracted	\$ <u>\$</u> \$2.3 \$	0.172	20 .3	0.480
1) Solvent extraction was done with 4x with acetemerile/water (4/1, 5v).) Solvent extraction was done with 4x with acetomerile/water (4/1, 5v).	Accountability / Total ⁴		0.532	> 200.0	0.532
		ractions given in bold food were analysed by radio-HPLC				



For structure elucidation, all acetonitrile/water extracts and *n*-heptane extracts were analysed by HPLC with radiodetection. Metabolites were identified by co-chromatography with authentic reference compounds.

In egg pool 1–6 days, the main compound was the parent amounting for 14.7% - 17.9% of the TRR (0.023 mg eq/kg - 0.028 mg eq/kg with conventional extraction and enzymatic treatment, respectively). The main metabolite in the conventionally extracted eggs was fluopyram-pyridyl-acetic acid (PAA, M4D), representing 6.4% of the TRR (0.010 mg eq/kg). The main metabolite with enzymatic treatment was fluopyram-7-hydroxy (M08) (5.8% of the TRR or 0.009 mg eq/kg), which also amounted to 3.9% of the TRR (0.006 mg eq/kg) in the conventionally extracted eggs. fluopyram-Z-olefin was found in equal amounts in eggs extracted conventionally and after enzymatic treatment (4.1% of the TRR or 0.006 mg eq/kg), while fluopyram-E-olefin was only found in low phounts in conventionally extracted eggs (1.0% of the TRR or 0.001 mg eq/kg). In total 27.8% (enzymatic) - 30.2% (conventional) of the TRR was identified for egg pool day 1–6 (Table 6.2.2, 24).

In egg pool 7–14 days, the parent compound amounted to 6.0% - 9.5% of the TRR f0.017 mg eq/kg to 0.027 mg eq/kg with conventional extraction and enzymatic treatment, respectively. The main compound was fluopyram-Z-olefin and amounted to 15% (0.004 mg eq/kg) 19.3% (0.055 mg eq/kg) of the TRR with conventional extraction and enzymatic treatment, respectively. fluopyram pyridyl-acetic acid (PAA, M40) was found only in conventionally extracted eggs at 3.7% of the TRR (0.011 mg eq/kg). fluopyram-7-hydroxy (M08) and fluopyram E-olefin were found in low amounts in egg pool 6 14 days at less than 2% of the TRR ($\leq 0.00\%$ mg eq/kg). In total, 26.9% (enzymatic) 32.2% (conventional) of the TRR was identified egg pool day 7–94 (Table 6.2.2+25).

Due to a high amount of matrix components and the low concentration of radioactivity, no HPLC profile of the microwave extracts could be recorded. However, a total extraction efficiency of approx. 99% and 90% of the TRR was achieved for the eggs (7-14 days). Though representing a higher amount of the TRR, the profile of the extract after enzymatic digestion showed nother regnificant amounts of further metabolites nor different amounts of metabolites compared to the profile of the conventional extract. This indicates, that the radioactivity released by microwave extraction from the solids did not consist of any further unknown metabolites.

In muscle, fluopyram-Z-oterin was the major component (33.0% of the TRR or 0.016 mg eq/kg). The only other components detected were fluopyram-Colefin at 3.9% (0.002 mg eq/kg) and the parent compound accounting for only & 0% (0.001 mg eq/kg) in total 37.9% of the TRR was identified (Table 6.2.2- 26).

In fat, the properties also the major component with 70.5% of the TRR (0.350 mg eq/kg), followed by both the pyram-*E*-olefin (12.4% of the TRR or 0.062 mg eq/kg) and the parent compound (12.2% of the TRR or 0.061 mg eq/kg). In total 95.2% of the TRR was identified (Table 6.2.2- 27).



In liver, fluopyram-*E*-olefin was the major component accounting for 11.8%-13.9% of the TRR (0.063 mg eq/kg–0.074 mg eq/kg, with conventional extraction and enzymatic treatment, respectively). In liver pool with enzymatic treatment, fluopyram-*Z*-olefin accounted for 3.1% of the TRR (0.017 mg eq/kg) and fluopyram-7-hydroxy (M08) accounted for 2.9% of the TRR (0.016 mg eq/kg). In liver pool with conventional extraction fluopyram-pyridyl-acetic acid (PAA, M40), fluopyram-7-hydroxy and fluopyram-*Z*-olefin accounted each for < 2% of the TRR ($\leq 0.01 \text{ mg eq/kg}$).

In total 15.7% -20.0% of the TRR was identified with conventional extraction and enzymatic treatment, respectively (Table 6.2.2-28).

Due to a high amount of matrix components and the fow concentration of radioactivity to HPLC profile of the microwave extracts could be recorded. However, at ôtal extraction efficiency of approx 90% of the TRR was achieved for liver.

Table 6.2.2- 24:	Summary of identification and characterization of radioactive residues in the hen's egg
	pool (day 1–6) after dosing of [pyridyl-2,6-14C] thropy an at a thilly dese rate of
	pool (day 1-6) after dosing of [pyridyl-2,6-14C] flatopyram at a daily dose rate of 2.02 mg eq/kg body weight for 4 consecutive days

S & S		Ligg pool	$(day 1-6) \bigcirc^{\vee}$	
$TRR [mg eq/kg] = \sqrt[5]{9} \sqrt[6]{9}$			<u>567 , Q</u>	
	Convention	al extraction	* Anzymatic	treatment
Compound	% of TRR	mg a.so equix/kg	% of TRR	mg a.s. equiv./kg
AE C656948, favopyram	4.7 6.4	¢.023 €	17.9	0.028
fluopyram-poridyl-acetic acid (M400)		0.010	-	-
fluopyram-paridyl-acetic acid (M40a) fluopyram-7-hydroxy (M08)		Q.906	5.8	0.009
fluopyram- <i>E</i> -olefin (M08) fluopyram- <i>E</i> -olefin (M02) fluopyram- <i>Z</i> -olefin (M03)		0.001	-	-
	× 1.0 × 4.0 ×	0.006	4.1	0.006
Total identified	<u> </u>	0.047	27.8	0.043
	6 17 6	0.028	29.9	0.047
Sum of unknowns Image: Constraint of the second secon	s,≦¥7.8	0.075	57.7	0.090
Volatiles in distillates	2.1	0.003	8.2	0.013
Microwave extracts	-	-	-	-
Extracts not analysed & P	3.7	0.006	3.8	0.006
Total extractable	53.6	0.084	69.7	0.109
Unexpectable residues (solids)	46.4	0.072	30.3	0.047
Accountability	100.0	0.156	100.0	0.156



 Table 6.2.2- 25:
 Summary of identification and characterization of radioactive residues in the hen's egg

 pool (day 7–14) after dosing of [pyridyl-2,6-¹⁴C] fluopyram at a daily dose rate of 2.02 mg eq/kg body weight for 14 consecutive days

	for 14 consecuti	ve uays	Ő		0
		Egg pool ((day 7214)		
$\Gamma RR [mg eq/kg] =$			286	5° 5°	Ċ,
	Convention	al extraction	Enzymatic	treathent	
Compound	% of TAR	mg a.s. equivQkg	% of TAR	mgas	
AE C656948, fluopyram	8 .0	0.017 . 0	9.5 0 1.6 0 4	0.027 (⁴	
fluopyram-pyridyl-acetic acid (M40)	0 0 0 0 0 0 0 0 0 0 0 0 0 0	0.010		N S	
fluopyram-7-hydroxy (M08)	\$~~ ⁰⁹ ~	00002 C		0.905 °	
fluopyram- <i>E</i> -olefin (M02)	1.0	0.003		0.005	
fluopyram-Z-olefin (M03)	\${* I	0.1644		0055	_
Fotal identified	26.9	≈ 0.077 °	<u>స</u> ి32.2 క్రి	\$ 0.092	_
Sum of unknowns	<u>0</u> 115	0.032	220	[™] 0.067	_
Analysed extract(s)	38.0	0.109, \$	55.5	0.159	_
Volatiles in distillates $\sqrt[3]{3}$	1.9¢ 0 1.9¢ 0 57.2 ¢	0.000	~~~ 6.2 ⁽²)	0.018	
Microwave extracts	\$ \$F.2 .	Q 146	í <u>, 3</u> 2	-	
Extracts not analysed	گ 7.9 گ	0.0230	<i>√</i> 2.4	0.007	_
Total extractable	99,0	0,283	64.1	0.183	_
Unextractable residues solids)	1.0	20.003	35.9	0.103	_
Accountability 🔬 🏑	5 100 D	0.286	100.0	0.286	
Analysed extract(s)					



 Table 6.2.2- 26:
 Summary of identification and characterization of radioactive residues in hen's muscle for after dosing of [pyridyl-2,6-14C] fluopyram at a daily dose rate of 2.02 mg eq/kg body weight for 14 consecutive days

weight for 14 consecutive c	Jays
	Muscle pool
TRR [mg/kg] =	
Compound	% of YRR mg a.s. equiv 7kg
AE C656948, fluopyram	$\begin{array}{c c} & & & & & & & & & & & & & & & & & & &$
fluopyram-pyridyl-acetic acid (M40)	
fluopyram-7-hydroxy (M08)	
fluopyram-E-olefin (M02)	
fluopyram-Z-olefin (M03)	3.9 3.3.0 0.002 0.016 0.016 0.016 0.010
Total identified	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
fluopyram-Z-olefin (M03) Total identified Sum of unknowns Analysed extract(s)	$\begin{array}{c} & & & & & & & & & & & & & & & & & & &$
Analysed extract(s)	
Volatiles in distillates	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
Microwave extracts	
Extracts not analysed	
Total extractable	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
Unextractable residents (solids)	<u>~</u> <u>~</u> <u>~</u> <u>~</u> <u>~</u> <u>~</u> <u>~</u> <u>~</u> <u>~</u> <u>0.020</u>
Accountability 0 0 4	0.020
Volatiles in distillates Microwave extracts Extracts not analysed Total extractable Unextractable resides (solies) Accountability Contraction of the solution of the sol	



dosing of [pyridyl-2,6- ¹⁴ C]	and characterization of radioactive residues in hen's fat after ° fluopyram at a daily dose rate of 2.02 mg eq/kg body weight
for 14 consecutive days	
	Fat pool
TRR [mg/kg] =	
Compound	% of TRR mg a sequiv the
AE C656948, fluopyram	
fluopyram-pyridyl-acetic acid (M40)	
fluopyram-7-hydroxy (M08)	
fluopyram-E-olefin (M02)	
fluopyram-Z-olefin (M03)	$\begin{array}{c} & & & & & & & & & & & & & & & & & & &$
Total identified	
Sum of unknowns	
Analysed extract(s)	<u>6</u> <u>6</u> <u>95.2</u> <u>6</u>
Analysed extract(s)	
Microwave extracts	Image: Second
Total extractable	99.2 × 6, 0.492
Unextractable residences (solids)	0.004
Accountability O	10 0 .0 0.496
Extracts not analysed	



 Table 6.2.2-28:
 Summary of identification and characterization of radioactive residues in hen's liver after dosing of [pyridyl-2,6-14C] fluopyram at a daily dose rate of 2.02 mg eq/kg body weight for 14 consecutive days

weight for 14 consecutive u	ays		Č,		0
		Liv	ver		
TRR [mg/kg] =		0.5	30 ¹ ,		Ô
	Convention	al extraction	Enzymatic	treatment	_(
Compound	% of TAR	mg a s equivQkg	% of TR	equi kg	
AE C656948, fluopyram		~~·~~	<u>^?`</u> ^^		
fluopyram-pyridyl-acetic acid (M40)		× 0.00			
fluopyram-7-hydroxy (M08)	\$, 0 8_C	00004 [©]	2.9	0 .016 °	
fluopyram- <i>E</i> -olefin (M02)	×11.8	0.063	2.9 ° [*] 13.9	0.074	
fluopyram-Z-olefin (M03)		0.000		00017	
Total identified	15.7	<u></u>	20.0	[©] 0.106	
Sum of unknowns	0 ² 12,5 ²	0.066	67.3 O	≫ 0.252	
Analysed extract(s)	28.2	0.150, 0	67.3	0.358	
Volatiles in distillates	0.7	0.00	× 8.6	0.046	
Microwave extracts		^y &- , ^x	^v 3.4	0.039	
Extracts not analysed	3.4	0.0180	× 7.0	0.037	
Total extractable	372 .		90.3	0.480	
Unextractable residues (solids)	67.7		9.7	0.052	
Accountability	5 ³ 1000	0.532	100.0	0.532	
		. 0			
	IL Conclusion	J. J			

Six laying hers were dosed orally for 14 consecutive days with [pyridyl-2,6-¹⁴C]fluopyram at a daily dose of 2.02 mg eq/kg of body weight and satisficed 24 hours after the last dose.

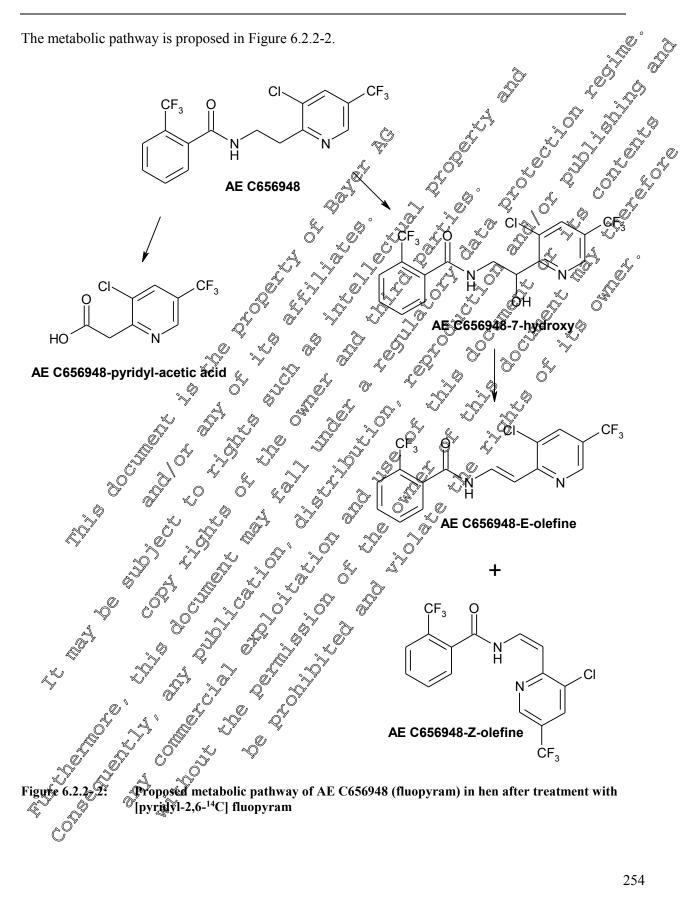
The major component and metabolite in eggs, muscle and fat was fluopyram-Z-olefin (up to 70.5% of the TRR). The other isomer fuppyram E-olefin was the major metabolite in liver (up to 13.9% of the TRR) and represented 1.0% to 32.4% of the TRR in the other matrices. Parent compound fluopyram was detected at up to 17.9% of the TRR. Further detected minor metabolites were fluopyram-7-hydroxy and fluopyram-pyridyl-acetic acid found in eggs and liver at up to 6.4% of the TRR.

Based on the dentified metabolites, the following metabolic routes were deduced:

- hydroxylation of the aliphatic chain followed by elimination
- stidative cleaving of the aliphatic chain



The metabolic pathway is proposed in Figure 6.2.2-2.





Assessment and conclusion	by applicant:
The study is valid and accep	table.
CA 6.2.3 Lactat	ing ruminants
Data to address this point deemed acceptable following	table. ing ruminants were presented in the dossier submitted for first inclusion in Annex and were of ng evaluation and peer review at EU level 2013). ed previously please refer also to the Baseline dossier CA 6.2 Por completeness, usly submitted studies are included below.
Ean datails of data submitta	d maximuch mlance material to the Dealting during (2) Or an the latera
a summary of these previou	a previously please refer also to the Baseline cossier CA 6.2 Por completeness,
a summary of these previou	during the first & D review process for inetasion on Armex I. On new
	during the first EV review process for inelasion of Annex 1.00 new
Data already evaluated	during the first EV review process for inclusion on Arnex I. to new
studies)	
<u>-</u>	
Data Point:	10 A 6.20 01 2 0 0 0 2 2 2 2
Report Author:	
Report Year:	
Report Title:	Metabolico of [ponyl-US/14C]AJ C65(948 in the lactating goat
Report No:	MEF-00919 5
Document No: C Guideline(s) for wed in	USEPA Revidue, Gremistry Test, Guideling OPPT& 860,1300
study:	Ature of the Restrue – Bants, Leestock
Study.	PMRA Ref.: DA CO & Metabolism in Lives wek
	EU Ouncil Grective 91/414/EEC Gended by the Commission Directive 96/68/EC
Deviations from current	
test guideline:	4' $3'$ $0'$ $4'$ $4'$
Previous evaluation	yes, Culuated and accepted O
CI P/Official Cooperation	rex 2 to V@3 of DAR B6 August 912 (references relied on)
GLP/Official Orecograd	Tess, conducted indeer one of the formed by recognised testing facilities
Acceptab@ry/Reliability	Yes Q'AT' Q' Q'
	Yes, conducted Oder GO/Offic@Ily recognised testing facilities
	Secutive Summary

The metabolism of [pheryl-UL-¹⁴C]flugpyram was investigated in one lactating goat, which was orally dosed for 5 consecutive days at a rate of 1.91 mg a.s./kg of body weight per day corresponding to 46.26 mg a.s./kg feed/day. The goat was sacrificed 24 h after the fifth administration. Radioactivity was measured in the exercta, milk and plasma collected at timed sampling intervals, as well as in the liver, kteney, puscle and fat a sacrifice. The milk, edible organs and tissues and excreta (urine and faeces) were



analysed for parent compound and metabolites by extraction, chromatographic separation techniques and spectroscopic methods.

Until sacrifice, the excretion amounted to 88.31% of the totally administered radioactivity. An amount of 0.56% of the total dose was found in milk. At sacrifice, the calculated total residue in the tissues and organs of dissected from the body was approximately 4.58% of the total dose. About half of this amount was detected in the muscle (2.31%).

The mean active substance equivalent concentrations in plasma increased from 0.989 mg eq/kg at 24 b to 0.720 mg eq/kg at 120 h. Also mean active substance equivalent of centrations in milk increased from 24 h to 120 h. This showed that a residue plateau-level was not yet reached.

At sacrifice, highest mean equivalent concentrations occurred in liver (8.379 mg eq/kg). These values were followed in decreasing order by the mean concentrations determined in the kidney (2.295 mg eq/kg), total body muscle (0.737 mg eq/kg) and total body fat (0.399 mg eq/kg). The radioactive residues were estracted with efficiencies of 91.8–99.5% from milk, edible organs or tissues and excrete with acetonitrile/water mixtures and n-heptane, and identification was achieved by LC-MS/MS, co-chromatography or comparison of profiles with those from the lagrating goat study with pyridy 22,6-14C]fluopyram

Fluopyram was extensively metabolised, but was still the major compound in taeces (13.18% of the dose) and represented 0.4%-18% of the TRR in the other neutrices except muscle. The label-specific metabolite fluopyram-benzamide (M25) was the main compound in mitk and edible organs and tissues, accounting for 49.1–97.6% of the TRR, but accounted for <5% of the dose in excreta. Fluopyram-Z-olefin (M03) was found in significant amounts in goat fat (13.1% of the PRR) and fluopyram-*E*-olefin (M02) was found at 8.6% of the TRR in fat Other minor metabolites accounted for < 5% of the TRR in milk and edible organs and tissues.

Further relevant metabolities were fluonyram-DOH-GA (isomer 1) and fluopyram-8-OH-GA (isomer 2) found in urine at amounts of 17.18% and 15.75% of the dose respectively. Furthermore, in faeces fluopyram-7-hydroxy accounted for 10.33% of the dose. Other minor metabolites accounted for < 5% of the dose in excreta

Based on the identified metabolites, the following metabolic routes were deduced:

• hydroxylation of the ethylene bridge of the molecule resulting in fluopyram-7-hydroxy, fluopyram-8-hydroxy, and a dihydroxy lated compound

- hydroxylation of the phenyl ring leading to fluopyram-phenol
- conjugation of the hodroxy and metabolites with glucuronic acid
- elimination of water from compounds hydroxylated in the ethylene bridge leading to fluopyram-Zofefin and E-olefin
- molecular cleavage of fluopyram-benzamide

a.

hydroxylation of thopyram-benzamide followed by conjugation with sulphate



I. Materials and Methods A. Materials 1. Test Material: **IUPAC** Name N-{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]etby (trifluoromethyl)benzamide N-[2-[& hloro-5-(trifteoromethyl) CAS Name Benzamide, pyridinyl]eth@-2-(trifluor@nethyl)- (9CI) AE C656948 Code name Fluopyram Common name Empirical formula C16H11ClF6N CAS Number 58066 Molar mass g/nao Chemical structure position of the ¹C **a**diolabel [phenyl-Radiolabelled test material 56948 2013 (padiolabelled) Batch number C633-Q4 (non radiola belled) Original specific radioactivity MBq/mg ♥ 13969 μCimg (HPLC) Ø <u>average</u> <u>average</u> <u>and</u> Radiochemical purity Ø 99.8% 99.8% (potentiometric titration) 1.98 MBq/mg = $1.188 \times 108 \text{ dpm/mg}$ 53.5 gci/mg 21.22 Ci/mol



Test Animals

Species	Goat (<i>Capra hircus</i>)
Breed	"Bunte deutsche Edelziege"
Breeding facility	
Sex, number	One female lactating goat
Body weight	One female lactating goat
Age	ca. 32 months old at experiment start
Acclimatization	8 days and an experiment start in a good of the start in
Housing	Statiness seen incrations cage, approx. 10–25 C, 40-25/04
Identification	Skin marking
Feed and water	Ruminant feed, hay apples (ad libitum)
	Tap water ad libitim
Health status	Acceptable
. Study Design	Acceptable

Preparation of the dosing mixtures and administration.

()

The radio action of MBq/mg) was radiodiluted with the non-radiolabelled test tem to a specific radioactionty of 1.98 MBq/mg. In total, five gelatine capsules containing 66 mg each of the radiodiluted solid test item were prepared immediately before the first administration and stored at -1 C. In relation to a Gody weight of 36 kg, this amount of radioactivity corresponded to an actual dose of 9.91 mg a.s./g body weight (bw). Based on the experimentally determined food consumption this corresponds to #6.26 mg a.s./kg feed/day.

The goat received daily one gelatine capsule administered orally using a capsule applicator. The administration was performed on two consecutive days in the morning after milking.

 \bigcirc

The radiolabelled parent compound was proved to be stable for at least eleven days at -18 °C as shown by radio-HPLC analysis, and thus for the time from preparation of the gelatine capsules until dosing. The evaluation of ψe chromatogram revealed a radiochemical purity of > 99%. The identity of the test compound was confirmed by LC-MS/MS.



Sampling:

Collection and processing of blood

Micro-samples of blood were taken from the ear veins at 0.25, 0.5, 1, 2, 3, 4, 6, 8, 24, 32, 48, 56, 76, 80, 96, 104 and 120 hours after starting the experiment. The blood was collected in heparinized capillaries which were centrifuged afterwards using a haematocrit centrifuge for separation of blood cells and plasma. The plasma samples were weighed and prepared for radioactivity measurement by LSC.

Collection and processing of milk

The goat was milked in the morning immediately prior to each administration, about 8 hours later in the afternoon, and directly before sacrifice (time schedute: 8, 24, 32, 48, 56, 92, 80, 96, 104, and 420 hours after the first administration). After weighing, one aliquot was taken from each sample for radioactivity measurement by LSC.

Collection and processing of urine

Urine samples were collected in plastic vessels as quantitatively as possible under dry ice cooling in intervals of 24 hours after each administration. The vessels were changed immediately before the next administration. The collection funnel was rinsed with deionised water into the same urine vessel of the respective collection period. After recording the total columes one aliquot was taken from each sample for radioactivity measurement by DSC.

Collection and processing of face

Faeces samples were collected as quantitatively as possible at foom temperature in intervals of 24 hours after each administration, i.e. intriediately before the next administration. The collecting grid was cleaned prior to each administration, by samples of the ripsing where were taken for radioactivity measurement. Each faeces fraction was homogenized after addition of water to get a wet paste before the total weight was recorded. One aligned of each wet sample was weighed and prepared for radioactivity measurement by combustion/LSC.

Sacrifice and collection of organs and tissues

For the collection of organs and tissues, the animal was sacrificed *ca*. 24 hours after the fifth administration, a time distance that is consistent with normal slaughtering practices. The animal was anaesthetised by an intravenous dose of about 40 ms eq/kg w Petrobarbital-Na (Narcoren®), exsanguinated by cannulating the jugular veine and sacrificed by intracardiac injection with ca. 10 mL of the sacrificing agent "T 61®". The following organs and tissues were dissected: muscle (round and loin), fat (omental and perirenal), liver without gat bladder, kidneys, and the gat bladder.

The organs or to sue samples were then transferred into tarred plastic vessels and after determination and recording of the individual weights, liver, kidneys, fat and muscle samples were passed several times through a princing machine in half-frozen state. One aliquot of each resulting tissue pulp was weighed and prepared for radioactivity measurement by combustion/LSC.



The gall bladder was punctured for the collection of the bile fluid that was stored in a freezer for the (optional) metabolite analysis.

C. Analytical Procedures

Extraction and fractionation:

Samples of milk and edible tissues were extracted three times with sectonitrile/water mixtures (2. 8/2 v/v). The combined extracts were applied to C18 SPE@artridges to remove the lipid fraction of the matrix The SPE percolate and the column wash with acetohitrile/water were combined and concentrated to the aqueous remainder for HPLC analysis. After the wash step, the SPE cartridge was eluted with dichloromethane/methanol to recover very lipophilic radioactivity, to present. All Guates were discarded since no significant amount of radioactivity was detected.

For muscle, liver, and kidney an additional solvent step was performed with acetopurile/water (14, v/v) under microwave assistance at 120 °C, The acetonitrite water extracts from microwave assisted extraction were concentrated to the aqueous remainder and then analysed by MPLC

An alternative extraction of muscle, diver, and kidney was conducted under the conditions of the residue analytical method developed for analysis of sample materials from a daily cox feeding study (denoted as "residue method"). The samples avere homogenised with acetonitrile/water (\$2; v/x) using a Polytron Typ PT 6000 homogenizer and then extracted twice in a microwave oven for 30 minut 120 °C. Extracts and solids were separated each time by centrifugation

The combined extracts were purified by SPE on C18 cartridges and then concentrated for HPLC profiling.

Analytical methods;

The radioactivity of all liquid samples was measured asing a liquid scintillation counter after mixing a known amount of each sample with contillation fluid. Solid samples were combusted using an oxidizer. The resulting ¹⁴CO₂ was trapped in an alkaline scint Hation cockta?. The TRR in the samples was calculated by summing up the radioactivity measured in different extracts and remaining solids after solvent extraction. The TRR was expressed in mg a.s. equivalents per kg sample weight. Amounts of radioactive residues in the extracto were expressed as percentage of the TRR and also as mg a.s. equivalents per kg sample weight.

Aliquots of all extracts were analysed by HPLO. Nine metabolites as well as parent compound were identified by LC-MS/MS HPLC co-chromatography and comparison of profiles with those from the lactating goat study with [pyridyl-2,6-14C]fluopyram.

was conducted using a reversed-phase column and a buffered acetonitrile/water gradient. The The HPLS HPLC System was equipped with a radiodetector and a UV detector with variable wavelengths. The LOQ was derived from the average background level and the specific radioactivity of the radiolabelled test compound



Storage stability

Extraction and first HPLC-analyses for quantification of extracts from morning milk, evening milk, milkscle, fat, liver and kidney were performed within 6 weeks after sacrifice of the goat.

A second extraction and analysis of muscle, liver, and kidney with the procedure of the residual analysical method was conducted between ca. 3-3.5 months after sacrifice. These second extractions how of very similar extraction rates as the extractions procedures for the fust quantification. The metabolic profiles were also very similar to profiles of the first analyses.

All experimental work in the study for extraction, guantification, and identification of residue completed within less than 4 months.

An additional experiment for solvent extraction of muscle under modified conditions was conducted a. 8 months after sacrifice. In this experiment only the balance for radioactivity was determined.

Extracts were measured by HPLC for quantification of residues within two to six day Dafter shart of the extraction, i.e. normally on the day when the sample preparation was completed.

samples vere therefore not required. Investigations on storage stability of radioactive residees in while

goat of phen UL - C]flugpyram ddmin strated at a daily dose of The metabolism in lactating 46.26 mg eq/kg in the feed corresponding to a daily wake of 9.91 mg eq/kg by for consecutive days was investigated.

I. Results and Discussion

Until sacrifice 24 hours after the last dose the mean excretion smounted on average to 88.31% of the radioactivity jotally administered (Table 6.2.3-1). The time course of the excretion was characterised by a relatively constant rate starting at day 4 until lest end (Table 6.2 3-2). Only 0.56% of the dose totally administered was measured in the milk secreted within the whole test period. At sacrifice, 24 h after the last administration, the total residue in the results and organs dissected from the body was calculated and estimated to about 4.58% of the total dose. Based on these values, the recovery amounted to 93.46% (Table 6.2.3-1)

The TRR-values in plasma, determined over the whole testing period in timed sampling intervals increased continuously antil the test end (Table 6.2.3-3). During the 8-hour period after each dosing, a significant increase was observed. In the following 16-hour time range until delivery of the next dose the TRR values increased or decreased only slightly. This indicated an ongoing absorption of the test item, a rapid distribution of the system cally bioavailable compound-related radioactivity within the body and a delayed excretion. Aplateau devel of plasma concentration was not reached during the observation period.

The rotal radioactive residues were determined in milk, faeces and urine produced from the first dose until sacrifice and in edible bissues and organs at sacrifice. The highest mean active substance equivalent concentrations were measured in liver (8.379mg eq/kg) and kidney (2.295 mg eq/kg). These values were



followed in decreasing order by total body muscle (0.737 mg eq/kg) and total body fat (0.399 mg eq/kg). For details see Table 6.2.3-5.

Table 6.2.3-1: Recovery of radioactivity following oral administration of [phenyl-UL-14C]fluopyram at a daily dose rate of 1.91 mg eq/kg body weight for 5 consecutive days

Matrix	Recovery of radioactivity (% of the totally administrated radioactivity)
Excreta ¹⁾	
Milk ²⁾	
Totally excreted	A & & & & & & & & & & & & & & & & & & &
Tissues	
Recovery	

Recovery in excreta obtained by adding recovery values of samples collected within the observation period of 5 days
 Recovery in milk calculated by adding recovery galues of samples produced within the observation period of 5 days

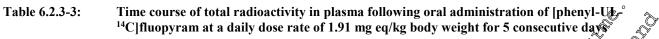
Values in *italics* were calculated from the values in the report

Table 6.2.3-2:Time course of total radioactivity in excreta following orak administration of [phenyl-UL-14Clfuopyram at a daily dose rate of 1.91 mg eq/kg body weight for 5 consecutive days

Matrix	Time after the birst dosage & Administration number (hours)	Excretion per day Excretion per day (Se of totally administrated radioactivity)
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		5.52 C
	8 8 4 x x	11.73
	72 × 5 [×] × 4	9.13
Urine		13.51
	O [*] O ² O Storifice o [*]	12.69
A		2.36
•		10.99
Faeces		7.71
		6.07
	Y Sacrifice	8.55
		·

The equivalent concentration of radioactivity in the milk showed an increase from 0.009 mg eq/kg (morning milk) or 0.029 mg eq/kg (evening milk) obtained on day 1 (24 hours after the first dosage) to 0.057 mg eq/kg (morning milk) or 0.105 mg eq/kg (evening milk) at day 5. For details see Table 6.2.3-4.





		[	
Matrix	Time after the first dosage (hours)	Administration number	[mg ed/kg plasma]
	0.25	Û V	
	0.5	, s	
	1	A.C.Y	$\begin{array}{c} & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & \\ & & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & &$
	2		
	3		$\begin{array}{c} 0.098 \\ \hline 0.098 \\ \hline 0.012 \\ \hline 0.012 \\ \hline 0.0107 \\$
	4		$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
	6		0.098
	8		\$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$
Plasma	24 🖓		
	32 5 5		2 348 k
	é ⁴⁸ é		0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.364 0.
	56 A 57 10 X	Strate Strate	
			0' \$ \$ 0.439
	0 ⁴ 80 5		0.577 0.629 0.716
			0.629 0.716
			0.720
			0.720
			Ý
Å,			
, C		4 Ö ^y	
		Q° Qr	
Ċ ^O .			



Ŵ

# Table 6.2.3-4:Time course of total radioactivity in milk following oral administration of [phenyl-UL- $\emptyset^\circ$ 14C]fluopyram at a daily dose rate of 1.91 mg eq/kg body weight for 5 consecutive days

Matrix	Time after the first dosage (hours)	Administration number	Secretion per period (%) of totally administrated radioactivity)
	8	1	
	24		
	32	2	Q ⁴ 2° QQ26 Q Q ⁴
	48		
Milk	56		
WIIIK	72		
	80		
	96		
	104 🖓		
	120		

 Table 6.2.3-5:
 Distribution of residues in the sues and organs of lactating goats following oral administration of pheny-UL-14 (Pluopyram at a daily dose rate of 1.91 mg eq/kg body weight for 5 consecutive days

	e e e e e e e e e e e e e e e e e e e
	S a
	TRR (mg a.s. equiv./kg)
Liver Liver Liver	8.379
Kidne Kidne	2.295
Total boost muscle 5 5 4 A	0.737
Total body dat	0.399
mg a.s. equiv./kg mg parent equivalents per kg matro	

In milk pool, 99.4–99.5% of the TRR (6227–6275 mg eq/kg) was extracted with solvent extraction (acetonitrile/water). Following degreasing by SPE, most of the radioactivity was contained in the percolate and wash (98.4–99.0% of the TRR or 0.224-0.273 mg eq/kg) and, after the concentration step, the aqueous remainder contained 96.8%–97.9% of the TRR (0.223-0.273 mg eq/kg). In total, 99.4–99.5% of the TRR (0.227-0.275 mg eq/kg) was extracted, whereas 0.5-0.6% of the TRR (0.001 mg eq/kg) remained non-extractable in solids (Table 6.2.2-6).

In soat muscle with conventional extraction, 67.7% of the TRR (0.499 mg eq/kg) was extracted with solvent extraction (acconitrile/water). Following degreasing by SPE, most of the radioactivity was



contained in the percolate and wash (67.5% of the TRR or 0.497 mg eq/kg) and, after the concentration step, the aqueous remainder contained all of the radioactivity.

After further extraction of the solids with acetonitrile/water (1/1; v/v) using a microwave at 120°C, the microwave extract contained further 31.7% of the radioactivity (0.234 mg eq/kg) After the concentration step, the aqueous remainder contained 31.4% of the radioactivity (0.231 mg eqAg).

In total, 99.4% of the TRR (0.733 mg eq/kg) was extracted, whereas 0.6% of the TRR (0.004 mg eq/kg) remained non-extractable in solids (Table 6.2.3-7).

In goat muscle extracted by residue method, 96.6% of the TRR (0.712 mg end kg) was extracted with solvent extraction (acetonitrile/water). Following degreasing by SPE, most of the radioactivity was contained in the percolate and wash (96.3% of the TRR or 0.700 mg end kg) and, after the concentration step, the aqueous remainder contained all of the radioactivity.

In total, 96.6% of the TRR (0.712 mg eq/kg) was extracted, whereas 37% of the TRR (0.025 mg eq/kg) remained non-extractable in solids (Table 6.2.3%).

In goat fat, 96.9% of the radioactivity (0.387 mg/q/kg) was extracted with actionit/le/water, while the nheptane phase contained only 2.3% of the TRR (0.009 mg er/kg). Following degreasing of the acetonitrile/water phase by SPE, most of the radioactivity was contained in the percolate and wash (96.7% of the TRR or 0.386 mg eq/kg) and, after the concentration step, the actions remainder contained all of the radioactivity.

In total, 99.2% of the TRR (0.396 mg eq/kg) was extracted, whereas 0.5% of the TRR (0.003 mg eq/kg) remained non-extractable in solids (Table 0.2.3-8).

In goat liver with conventional extraction, 76.6% of the TRR (6416 mg/eq/kg) was extracted with solvent extraction (acetonitrile/water). Following degreesing by SPE, most of the radioactivity was contained in the percolate and wash 76.5% of the TRR or 6.409 rug eq/kg) and after the concentration step, the aqueous remainder contained 70.2% of the TRR (6384 mg/eq/kg).

After further extraction of the solids with accontril@water (1/1; v/v) using a microwave at 120 °C, the microwave extract contained further (7.4%) of the TRR (1.456 mg eq/kg). After the concentration step, the aqueous remainder container 17.3% of the TRR (1.449 mg eq/kg).

In total, 94.0% of the TRR (7.872 mg eq/kg) was extracted, whereas 6.0% of the TRR (0.507 mg eq/kg) remained non-extractable in solids (Table 62.3-9).

In goat liver extracted by residue method, 93.6% of the TRR (7.846 mg eq/kg) was extracted with solvent extraction (acetonitrile water). Following regreasing by SPE, most of the radioactivity was contained in the percolate and wash (93.3% of the TRR or 7.814 mg eq/kg) and, after the concentration step, the aqueous remainder contained all of the radioactivity.

In total, 93.6% of the TRR 7.846 mg eq/kg) was extracted, whereas 6.4% of the TRR (0.533 mg eq/kg) reptained pon-extractable in solids (Table 6.2.3-9).



In goat kidney with conventional extraction, 68.6% of the TRR (1.573 mg eq/kg) was extracted with solvent extraction (acetonitrile/water). Following degreasing by SPE, all of the radioactivity was contained in the percolate and wash and, after the concentration step, the aqueous remainder contained 68.1% of the TRR (1.564 mg eq/kg).L

After further extraction of the solids with acetonitrile/water (1/1; v/v) using  $\Delta$ microwave at 20 % the microwave extract contained further 29.8% of the TRR (0.684 mg eq/kg). After the concentration step aqueous remainder contained 29.5% of the TRR (0.677 mg  $e_{\rm c}/kg$ ).

And a second with Second with



Table 6.2.3-6:Extraction of radioactive residues from the goat milk pool after dosing of [phenyl-UL-14C]fluopyram at a daily dose rate of 1.91 mg eq/kg body weight for 5 consecutive day

	a daily dose rate of 1.91 mg eq/kg body weight for 5 consecutive days				
		Milk			
	Mornir	-	Evenin		
RR, mg eq/kg	0.2	76	× 0.2		
raction	% TRR	mg a.s. equiv./kg	0.2 % TRR 99 99 98.4 9729 \$970.5	mg a.s.	
plvent extract ¹⁾	99.5 99.0 99.0 99.0 99.0	0.275	99	Q 0.25 \$	
Degreasing via SPE	99.0 99.0 96.8 2.2 2.2 0.6 2 4 0.6 2 5	0.274 0.273 0.273 0.273 0.267 0.006 0.006 0.002 0.002 0.001 0.001	99 <b>6</b> 98.4 9729 9729 50.5 1.0 26		
Percolate and wash	99.0 99.0 99.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.5 9.	Q ^{9.273}	98.4	\$0.224 °	
Concentration	Õ "Ø	× 4		$\sim \sim \sim$	
Aqueous remainder	96.8	, 0,267	× 970.9	0.223	
Distillate	× × 2.2 ×	≥ ^{0.006} ₹	\$0.5 U		
Eluate	مَ [*] % 0.6 €	0.002	× 1.0 ,	0.060 00001	
olids		0.601		× 0 <b>0</b> 01	
	0.0	<u>\$9.001</u>	<u></u>	<i>©</i> 0.001	
otal extracted	\$ 99.5 [°]	6 0.275	0.5 1.0 0.6 0.6 0.6 0.6 0.6 0.6 0.6 0	°∼ 0.227	
ccountability / Total ³ )	j 10 <b>020</b> "	0,22,6	189 <b>9</b> .0 &	0.228	
Solvent extraction was done with 3x with acetonic PES: post extraction solids = non-extractible ratio	$\frac{1}{\sqrt{2}}$ /water (4/1, v/x).				
Sum of extracts and PES.					
actions given in <b>bold</b> font were analysed by real-HPL			. S		
ball extracted	1000 /water (4/1, v/g). tivite 5. 5. 5. 5. 5. 5. 5. 5. 5. 5. 5. 5. 5. 5		2 V		

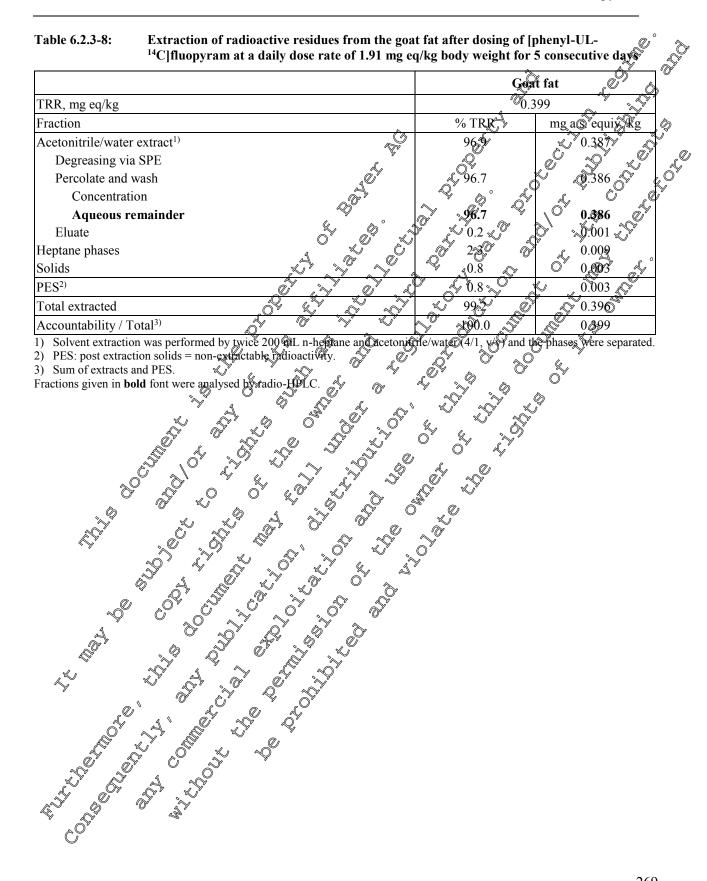


 Table 6.2.3-7:
 Extraction of radioactive residues from the goat muscle after dosing of [phenyl-UL 

 ¹⁴C]fluopyram at a daily dose rate of 1.91 mg eq/kg body weight for 5 consecutive days

,	Goat	muscle 2 0 A	
	Conventional autreation Desidue method		
TRR, mg eq/kg		730 Residue metriod	
	maas a		
Fraction	equiv./kg	/ True Squiv./kg	
Solvent extract ¹⁾	67.7 67.5 0.499 0.497 0.497 0.497 0.497 0.002 0.002 0.238 31.7 0.234 0.231 0.002 0.231 0.002 0.231	96 5 0.7 5 0 0 V	
Degreasing via SPE		96.3 96.3 96.3 96.3 96.3 96.3 96.3 96.3	
Percolate and wash	67.5° 09.497°	96.3 96.3 96.3 96.3	
Concentration			
Aqueous remainder Eluate		963 02710 0.3 00.002 0.03	
Aqueous remainder Eluate Solids 1 Microwave solvent extraction ²⁾ Microwave extract Concentration	S Yan a Y I want		
Microwave solvent extraction $^{2)}$			
Microwave extract	31.7 0,234		
Concentration			
Microwave extract Concentration Aqueous remainder	31.7 31.7 31.7 31.7 31.7 0.234 0.231 0.231 0.231 0.231 0.231		
Distillate	(0.3) $(0.025)$	- O [¥] -	
Distillate Solids 2			
PES ²⁾		0.025	
Total extracted	99.4 × 0.733 &	\$6.6 0.712	
Accountability / Tota	[∞] 100.0 [∞] 0.737 ⁰	100.0 0.737	
<ol> <li>Solvent extraction was done with 34 with acetonitril</li> <li>Microwave extraction was performed with sectonits</li> </ol>	e/water (40, v/v). le/water (1/1, v/v) at 120 C	Ž	
3) PES: post extraction solids = non-extractable radioa	ctivity 0 2		
4) Sum of extracts and PES.			
Fractions given in bold tont were analysed by facto-fir			
w SA S	, O ^Y		
	G		
Accountability / Total Accountability / Total 1) Solvent extraction was done with 34 with acetonitril 2) Microwave extraction solves = non-extractable radioa 3) PES: post extraction solves = non-extractable radioa 4) Sum of extracts and PES. Fractions given in <b>bold</b> font were analysed by radio-HP			
$\bigcirc$			







	lose rate of 1.91 mg eq/kg body weight for 5 consecutive days Goat liver				Ô
	Conventional extraction ⁽⁷⁾ Residue			method ~	ĺ
RR, mg eq/kg		8.3	<u> </u>	OV DV	Ô
raction	% TRR	mg a.s. equiv./kg	% TRR	mg a.s.	
olvent extract ¹⁾	76.6	6.416	93	Q 7.848 \$	Ô
Degreasing via SPE				Č,	,×
Percolate and wash	76.5 。	<b>6</b> .409 S	93.3 V ^O	\$7.814 ¢	
Concentration	o ^r Q				l
Aqueous remainder	76,2	<b>6 38</b> 4 6	° 9 <b>3</b> .3	2814	
Distillate	× ~~ 0.3 ~~	0.024	~~ ⁰ `		l
Eluate		مري 0.00 <b>8</b>		0.02	l
olids 1	227	ځ 1,963 کې		00333	1
Microwave solvent extraction $^{2)}$				, Q	l
Microwave solvent extraction 27 Q Microwave extract Concentration	Q 17.4 O	§ 1.450		~~ -	l
Concentration	, ^O			·	
Aqueous remainder 🖉 炎 🖉	ر 17.3 _م	J.449.	~ O [×]	-	l
Distillate	0.1	0.00	× - 0	-	
Solids 2		S 0.507 🔬	× ×	-	
$ES^{2}$	\$.0 ×	Ø:507 &	<u></u> ⊗ <b>6</b> .4	0.533	1
otal extracted	^{~~} 94.0~~	7.872 ⁰	93.6	7.846	l
ccountability / Total ⁴	> 100,0	§ 8 <b>3</b> 79	100.0	8.379	l
ccountability / Total ⁴ Solvent extraction was done with 3x with acetonitrile Microwave extraction solids = non-extractable fadioact Sum of extracts and PES c actions given in <b>bold</b> for evere and sed by radio-HRL	e/water (1/1, 4/v)	at bo °C			



		Goat l	kidney	ser os
	Convention	al extraction	Residue	method
TRR, mg eq/kg		2.2	95 ×	
Fraction	% TRR	mg a.s. equiv./kg	% TRR Č	ng a.s.
Solvent extract ¹⁾	68.6 [©] ″	1.575	97	Q 2.23 x
Degreasing via SPE	Con the second sec			Ŭ (
Percolate and wash	68.6	J.573 S	97.1	2.228 O
Concentration	or a			$\sim$ $\sim$
Aqueous remainder	68,1	0 1 <b>,56</b> 4 0	970.1 🔨	2228
Distillate	× ۲ میں ۲ میں ۲	0.009	~~ O`	Q'- 7
Eluate	( in the second se	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	× 0.4°	0.0 <b>09</b> 00059
Solids 1	3,1,4 ~	<u>م 22</u> ک	2 2 S	× 0 <b>0</b> 59
Microwave solvent extraction ²⁾		1 ~ ~		, Óg
Microwave extract	Q 29.8 Q	0.6840	0 - ²	- ``
Concentration			Ď ₂ 0 _{&amp;.}	"
Aqueous remainder 🕺 🐇 💧	29.5	0.677.	~ - O [¥]	-
Distillate		0.00	× - Q	-
Solids 2	\$ 16 ⁴	\$` 9.037 🔬		-
PES ²⁾	", ", ", ", ", ", ", ", ", ", ", ", ", "	Ø:037 &	°~2.6	0.059
Total extracted	<u>∿</u> *98.4	2.258 ⁰	· 97.4	2.236
Accountability / Total ⁴	100,0	2,2,995	100.0	2.295

2) Microwave extraction was performed with aceton trile/water (1/1)

å

3) PES: post extraction solids = non-extractable radioactivity.

4) Sum of extracts and PES.

Fractions given in **bold** fon @vere and ysed by vadio-HPLC

 $\bigcirc$ O For elucidation of metabolism all acconitrile water extract were analysed by HPLC with radiodetection. Metabolites were identified by LC-MS/MSOco-chomatography or comparison of profiles with those from the lactating goat study with [pytidy]-2,6 C]fluopyram, **N** 

In morning milk, the parent compound as counted for only 0.7% of the TRR (0.002 mg eq/kg). The main component was the label specific metabolite fluopyram-benzamide, amounting to 89.2% of the TRR (0.246 mg eq/kg). The second most abundant compound was fluopyram-benzamide-SA and accounted for 4.3% of the TRR (0.012 mg/kg) The metabolites fluopyram-7-OH-GA (isomer 1 and 2), fluopyram-7hydroxy and fluopyram 2 olefin were minor compounds and accounted each for < 2% of the TRR (< 0.005 mg eq. (s). In total, 96.3% of the TRR was identified in morning milk (Table 6.2.3-11).

Incevening milk, the parent compound accounted for only 1.7% of the TRR (0.004 mg eq/kg). The main component was the label specific metabolite fluopyram-benzamide, amounting to 88.4% of the TRR



(0.202 mg eq/kg). The second most abundant compound was fluopyram-benzamide-SA and accounted for 4.3% of the TRR (0.010 mg eq/kg). The metabolites fluopyram-7-OH-GA (isomer 1 and 2), fluopyram-7- whydroxy and fluopyram-Z-olefin were minor compounds and accounted each for < 2% of the TRR (< 0.005 mg eq/kg). In total, 96.8% of the TRR was identified in milk pool (Table 9.2.3-12).

In goat muscle, no parent compound was found. The label specific metholite fluopyram-benzamide accounted for the majority of the TRR and accounted for 97.6% of the TRR (0.719 ing eq. g). Other metabolites found were fluopyram-benzamide-SA, fluopyram-7-OH A (isomer 1) and fluopyram-7- hydroxy, which accounted each for < 1% of the TRR ( $\frac{1}{2}$  0.005 mg eq. g). In total, 98.9% of the TRR was identified in goat muscle (Table 6.2.3-13).

In goat fat, the parent compound accounted for 13% of the TRR (0.02 mg eq/kg). Again the major component was fluopyram-benzamide and accounted for 49.1% of the TRR (0.196 mg eq/kg). The second most abundant metabolite was fluopyram? Z-olefin (13.0% of the TRR or 0.952 mg eq/kg), followed by fluopyram-*E*-olefin (8.6% of the TRR of 0.034 mg eq/kg) and fluopyram-7 hydroxy (7.7% of the TRR or 0.031 mg eq/kg). In total, 96.7% of the TRR was identified in goat fat (Table 6.23-14)

In goat liver, the parent compound was identified in traces of 1% of the TRR 60.05 mg eq/kg). fluopyram-benzamide accounted for the majority of the TRR and accounted for 82.8% of the TRR (6.941 mg eq/kg). The second most abundant metabolite was fluopyram-7-OH/GA (isomer 1) and accounted for 4.3% of the TRR (0.363 mg eq/kg). Further components found were fluopyram-8-OH-GA (isomer 2), fluopyram bence GA, fluopyram-7-hydroxy, fluopyram-E-olefin and fluopyram-Z-otefin, each amounting to  $\leq 2.1\%$  of the TRR ( $\leq 0.174$  mg eq/kg). In total, 93.5% of the TRR was identified in goat liver (Table 6.2.3~13).

In goat kidney, the parent compound was identified in traces of < 1% of the TRR (<0.01 mg eq/kg). The main component was again floopyrame benzamide and anothed to 77.1% of the TRR (1.769 mg eq/kg). The second most abundant metabolite was fluopyram-7-OH-GA (isomer 1), accounting for 7.3% of the TRR (0.168 mg eq/kg), followed by fluopyram 8-OH-GA (isomer 2; 7.3% of the TRR or 0.168 mg eq/kg). Further components dentified were fluopyram-benzamide-SA, fluopyram-7-OH-GA (isomer 2), fluopyram-die H-GA, fluopyram-phenol-GA, fluopyram-7-OH-GA (isomer 2), fluopyram-die H-GA, fluopyram-phenol-GA, fluopyram-7-hydroxy and the parent compound, each amounting to  $\leq 2.5\%$  of the TRR ( $\leq 0.058$  mg eq/kg). In total, 95.4% of the TRR were identified in goat kidney (Table 6.2.3-16).

fluopyram-di OH-GA, fluopyram-phrenol-GA, fluopyram-7-hydroxy and the parent compound, each amounting to  $\leq 2.5\%$  of the TRR ( $\leq 0.05\%$  mg c/kg). In total, 95.4% of the TRR were identified in goat kidney (Table 6.2.3-16)



Table 6.2.3-11: Summary of identification and characterization of radioactive residues in the morning $\mathcal{D}_{\mu}^{\circ}$ milk of lactating goat after dosing of [phenyl-UL-14C] fluopyram at a daily dose rate of ŝ 1.91 mg eq/kg body weight for 5 consecutive days >

1.91 mg eq/kg body weight for 5 consecu	uve uays	g milk
	Mornią	g milk
TRR [mg eq/kg] =	0.2	276
Compound	َرَيْ of the TR	pg milk     v       mg ax, equiv//kg       0.002       0.002       0.002       0.002       0.002       0.002       0.001       0.001       0.001       0.001       0.001       0.001       0.001
AE C656948, a.s., fluopyram	S 0.7 D	č [*] 0.002 ~ č [*]
fluopyram-benzamide-SA (M31)	4.30%	<u></u>
fluopyram-benzamide (M25)	89.2	0° 6Q246 0° 4
fluopyram-7-OH-GA (isomer 1) (M09)	0.4	× × 0.001 ×
fluopyram-7-OH-GA (isomer 2) (M09)	· · · · · · · · · · · · · · · · · · ·	
fluopyram-benzamide-SA (M31) fluopyram-benzamide (M25) fluopyram-7-OH-GA (isomer 1) (M09) fluopyram-di-OH-GA (M21) fluopyram-phenol-GA (M07)		
fluopyram-phenol-GA (M07) fluopyram-8-OH-GA (M20), isomer 2 fluopyram-7-hydroxy (M08) fluopyram- <i>E</i> -olefin (M02) fluopyram- <i>Z</i> -olefin (M03)		0° 4 - 1
fluopyram-8-OH-GA (M20), isomer 2	Y A Y - A S	
fluopyram-7-hydroxy (M08)		
fluopyram- <i>E</i> -olefin (M02)		
fluopyram-7-OH-GA (isomer 2) (M09) fluopyram-di-OH-GA (M21) fluopyram-phenol-GA (M07) fluopyram-8-OH-GA (M20), isomer 2 fluopyram-7-hydroxy (M08) fluopyram- <i>E</i> -olefin (M02) fluopyram- <i>Z</i> -olefin (M03) Total identified		0.002
Total identified		<u>, 3° ,0,266</u>
Total identified	Mornin 	mg ax, equiv#kg 0.002 0.002 0.002 0.001 0.001 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.001 0.001 0.001 0.001 0.001 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002 0.002
Analysed extracts	[*] <i>©</i> 96.8 ©	vv 0.267
Analysed extracts		0.002 0.006
Volatiles **	\$99.5 E	<u>کَّ 0.006</u>
Volatiles ** Total extractable Unextractable residue (solids) Accountability * dichlorometrane/metranol eluates of SPE column during clean	, ^{O™} & 99.5, [™] ∂	0.275
Unextractable residues (solids)		0.001
Accountability N O N V N		0.276
<ul> <li>dichloromethane/methanol eluates of SPE column during clean</li> <li>distillates from contributation steps</li> </ul>	upSPE elugre	
	2	
	ð	
	S.	
Unextractable residues (solids) Accountability * dichlorometrane/metranol eluates of \$PE column during clean ** distillates from concentrationsteps		
Ŭ		



Table 6.2.3-12: Summary of identification and characterization of radioactive residues in the evening ______^ milk of lactating goat after dosing of [phenyl-UL-14C] fluopyram at a daily dose rate of 6 1.91 mg eq/kg body weight for 5 consecutive days >

1.91 mg eq/kg body weight for 5 consecu	luve days
	Evening milk
TRR [mg eq/kg] =	<b>0.276</b>
Compound	$\sim$ % of the TRR mg as equivake $\sim$
AE C656948, a.s., fluopyram	
fluopyram-benzamide-SA (M31)	4.30° 0.000 × ×
fluopyram-benzamide (M25)	
fluopyram-7-OH-GA (M09), isomer 1	
fluopyram-7-OH-GA (M09), isomer 2	
fluopyram-benzamide-SA (M31) fluopyram-benzamide (M25) fluopyram-7-OH-GA (M09), isomer 1 fluopyram-7-OH-GA (M09), isomer 2 fluopyram-di-OH-GA (M21) fluopyram-phenol-GA (M07)	
fluopyram-phenol-GA (M07)	
fluopyram-8-OH-GA (M20), isomer 2	
fluopyram-7-hydroxy (M08)	
fluopyram- <i>E</i> -olefin (M02)	
fluopyram-7-OH-GA (M09), isomer 1 fluopyram-7-OH-GA (M09), isomer 2 fluopyram-di-OH-GA (M21) fluopyram-8-OH-GA (M20), isomer 2 fluopyram-7-hydroxy (M08) fluopyram- <i>E</i> -olefin (M02) fluopyram- <i>Z</i> -olefin (M03) Total identified	
Total identified	
Total identified	Evening milk $0.276$ $0.276$ $0.276$ $0.276$ $0.004$ $1.7$ $0.004$ $4.3$ $0.004$ $884$ $6202$ $0.3$ $0.001$ $0.3$ $0.001$ $0.004$ $0.001$ $0.004$ $0.001$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.004$ $0.002$ $0.002$ $0.001$ $0.001$
Analysed extracts Losses * Volatiles ** Total extractable	[~] <u>@97.9</u> <u>~</u> <u>~</u> <u>0.223</u>
Losses *	0.002 0.002 0.001
Volatiles **	<u>605</u> <u>67</u> <u>67</u> <u>6001</u>
Volatiles ** Total extractable Unextractable residue (solids)	0.001
Unextractable residues (solids)	
Accountability N O N N N	
* dichlorometrane/metranol eluaites of SPE columny during clean	upSPE elugré
	3"
	Č,
	× ·
Analysed extracts Losses * Volatiles ** Total extractable Unextractable residues (solids) Accountability * dichlorometrane/methanol eluates of SPE colume during clean ** distillates from concentration steps	
õ	



Table 6.2.3-13: Summary of identification and characterization of radioactive residues in muscles of Summary of identification and characterization of radioacteric reaction of lactating goat after dosing of [phenyl-UL-¹⁴C] fluopyram at a daily dose rate of _6)[^] 1.91 mg eq/kg body weight for 5 consecutive days ð

		<u>o</u> r	
	Goat	muscle 🔊	
TRR [mg/kg] =	0.7	37 🔬	
Compound	% of TRR	🖉 mg a.s. equit	<u>Å Å</u> Å
AE C656948, a.s., fluopyram	- 💱		
fluopyram-benzamide-SA (M31)	0.7	<u>0</u> ,005	3 2 4
fluopyram-benzamide (M25)	29.6	0.719	°°, ô° ≰°
fluopyram-7-OH-GA (M09), isomer 1	00.3	\$ 0.00 <b>2</b>	C Q
fluopyram-7-OH-GA (M09), isomer 2			
fluopyram-di-OH-GA (M21)			× v
fluopyram-phenol-GA (M07)			4
fluopyram-8-OH-GA (M20), isomer 2		1 ₁ -0 ⁷	
fluopyram-7-hydroxy (M08)			
fluopyram- <i>E</i> -olefin (M02)		× 6 ⁴ - 6	
fluopyram-Z-olefin (M03)			
Total identified	6 6 9 <b>89</b> N 6	P	× V
Sum of unknowns		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	×
Analysed extracts	2 98.9 4 04 2 0 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4 0.20 4	© 0.729	
Losses *	~~ 0° 0.2° ~~	9 0.002 0.002	
Volatiles **			
Total extractable***	0° %99.40° «,	0.733	
Total extractable***		<u>ک</u> ک ^م 0.004	
Accountability		0.737	

dichlorometheme/methanol eluates of &PE column during clean up SPE eluge and teptane phase for fat

dichloromethalhe/methalhol eluales of SPE coulding during dean up SPE eluate and depitane phase for distillates form concentration steps of SPE could be and depitane phase (2.3% of TRR)
 total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an eluase (2.3% of TRR)
 total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an eluase (2.3% of TRR)
 total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an eluase (2.3% of TRR)
 total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an eluase (2.3% of TRR)
 total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an eluase (2.3% of TRR)
 total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an eluase (2.3% of TRR)
 total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an eluase (2.3% of TRR)
 total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an eluase (2.3% of TRR)
 total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an eluase (2.3% of TRR)
 total extracted for fat = sum of solvent extracted for fat = sum of solven



Table 6.2.3-14: Summary of identification and characterization of radioactive residues in fat of lactating goat after dosing of [phenyl-UL-14C] fluopyram at a daily dose rate of 1.91 mg eq/kg body Ś weight for 5 consecutive days S

weight for 5 consecutiv	c days	Č,	2.
	Goa	t fat 🔗 🔗	
TRR [mg/kg] =	0.3	199 <u>A</u> 🖉 🕷	
Compound	% of TRR	mg a.s. equix kg 🔍	
AE C656948, a.s., fluopyram	18.2		
fluopyram-benzamide-SA (M31)	~		* *
fluopyram-benzamide (M25)	49.1	Ø.196 Q	
fluopyram-7-OH-GA (M09), isomer 1	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		a O Ì
fluopyram-7-OH-GA (M09), isomer 2			, Ar
fluopyram-di-OH-GA (M21)			J ^v
fluopyram-phenol-GA (M07)			
fluopyram-8-OH-GA (M20), isomer 2			
fluopyram-7-hydroxy (M08)		4	¢
fluopyram- <i>E</i> -olefin (M02)	\$8.6 × v	× 60.034 5	»
fluopyram-Z-olefin (M03)		4 0 ⁵ 0.031 5 0.034 5 0.052	
Total identified	6 6 967 N	ີ <u>ເວັ 0</u> ີ 3886 ແັ	
Sum of unknowns		°°° - ∕ ~	
Analysed extracts	$\begin{array}{c} & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ \end{array}$	0.386	
Losses *	S 0 2.5 V	y* 0.010	
Volatiles **		~~~~~~	
Total extractable***	○ [~] ~99.2 ○ [*] &	0.396	
Unextractable residue (solids)		0.003	
Total extractable***	×	0.399	

dichloromethene/methanol eluaites of SPE column during dean up SPE elugie and testane phase for fat

dichloromethalhe/methalhol eluales of SPE coulding during dean up SPE eluate and deprivate phase for distillates form concentration steps of SPE could be and deprivate phase for distillates form concentration steps of SPE could be and deprivate phase (2.3% of TRR)
 *** Total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an ephase (2.3% of TRR)
 *** Total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an ephase (2.3% of TRR)
 *** Total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an ephase (2.3% of TRR)
 *** Total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an ephase (2.3% of TRR)
 *** Total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an ephase (2.3% of TRR)
 *** Total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an ephase (2.3% of TRR)
 *** Total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an ephase (2.3% of TRR)
 *** Total extracted for fat = sum of solvent extract (96.9% of TRR) and heat an ephase (2.3% of TRR)
 *** Total extracted for fat = sum of solvent extracted for fat = sum of s



	characterization of radioactive residues in liver of
lactating goat after dosing of [p 1.91 mg eq/kg body weight for	henyl-UL- ¹⁴ C] fluopyram at a daily dose rate of 5 consecutive days
	Goat liver of the second
TRR [mg/kg] =	8.379
Compound	% of TRR
AE C656948, a.s., fluopyram	0.6 7 0.047 7 0
fluopyram-benzamide-SA (M31)	
fluopyram-benzamide (M25)	8 ² /8
fluopyram-7-OH-GA (M09), isomer 1	$\begin{array}{c} 1.6 \\ 82.8 \\ 64.3 \end{array} \qquad \begin{array}{c} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 $
fluopyram-7-OH-GA (M09), isomer 2	
fluopyram-di-OH-GA (M21)	
fluopyram-phenol-GA (M07)	
fluopyram-8-OH-GA (M20), isomer 2	
fluopyram-7-hydroxy (M08)	
fluopyram- <i>E</i> -olefin (M02)	
fluopyram-Z-olefin (M03)	
Total identified	6 935 N C 23833 N
Sum of unknowns	
Analysed extracts	93.5 × 0× 0× 7.83¥
Losses *	
Volatiles **	$\sqrt[3]{0.4}$ $\sqrt[3]{0.4}$ $\sqrt[3]{0.031}$
Total extractable***	<u>→</u> 94.0 O [*] & → → 7.872
Unextractable residuce (solids)	5 6 Q O O O 0.507
Accountability N V ~	×60.0 © 8.379

dichlorometheme/methanol eluates of &PE column during clean up SPE eluge and teptane phase for fat

dichloromethal/methalol eluates of SPE column during clean up SPE eluzie and deplane phase fo distillates from concentration steps
 Total estracted fordat = sum of solvent extract (96.9% of TRR) and hereinane phase (2.3% of TRR)
 And the sum of solvent extract (96.9% of TRR) and hereinane phase (2.3% of TRR)
 And the sum of solvent extract (96.9% of TRR) and hereinane phase (2.3% of TRR)
 And the sum of solvent extract (96.9% of TRR) and hereinane phase (2.3% of TRR)
 And the sum of solvent extract (96.9% of TRR) and hereinane phase (2.3% of TRR)
 And the sum of solvent extract (96.9% of TRR) and hereinane phase (2.3% of TRR)
 And the sum of solvent extract (96.9% of TRR) and hereinane phase (2.3% of TRR)
 And the sum of solvent extract (96.9% of TRR) and hereinane phase (2.3% of TRR)
 And the sum of solvent extract (96.9% of TRR) and hereinane phase (2.3% of TRR)
 And the sum of solvent extract (96.9% of TRR) and hereinane phase (2.3% of TRR)
 And the sum of solvent extract (96.9% of TRR) and hereinane phase (2.3% of TRR)
 And the sum of solvent extract (96.9% of TRR) and hereinane phase (2.3% of TRR)
 And the sum of solvent extract (96.9% of TRR) and hereinane phase (2.3% of TRR)
 And the sum of solvent extract (96.9% of TRR) and hereinane phase (2.3% of TRR)
 And the sum of solvent extract (96.9% of TRR) and hereinane phase (2.3% of TRR)
 And the sum of solvent extract (96.9% of TRR) and hereinane phase (2.3% of TRR)
 And the sum of solvent extract (96.9% of TRR)
 And the sum of solvent extract (96.9% of TRR)
 And the sum of solvent extract (96.9% of TRR)
 And the sum of solvent extract (96.9% of TRR)
 And the sum of solvent extract (96.9% of TRR)
 And the sum of solvent extract (96.9% of TRR)
 And the sum of solvent extract



Summary of identification and characterization of radioactive residues in kidney@of Table 6.2.3-16: lactating goat after dosing of [phenyl-UL- 14 C] fluopyram at a daily dose rate of 1.91 mg eq/kg body weight for 5 consecutive days Ô

is i mg oq mg bouy we	ight for e consecutive days	O'	
	Goat	kidney 🔗 😽	
TRR [mg/kg] =	2.2	295 🔬 🔊	
	% of TRR	mg a.s. equix kg	9° 49
AE C656948, a.s., fluopyram	0.4 🐨	0.009	
fluopyram-benzamide-SA (M31)	2.5	° 0, <b>0</b> 58 ,5	× ×
fluopyram-benzamide (M25)	Z	<b>.</b> .769 <b>.</b>	Ô ^y 40
fluopyram-7-OH-GA (M09), isomer 1	07.3	¢° 0.168 ^C	ŗ "O"
fluopyram-7-OH-GA (M09), isomer 2	2.1.	0.048	
fluopyram-di-OH-GA (M21)		Q015 ~~	1 and a start of the start of t
fluopyram-phenol-GA (M07)		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
fluopyram-8-OH-GA (M20), isomer 2	3.6	_₹ _€ 0.092 _€	
fluopyram-7-hydroxy (M08)			
fluopyram- <i>E</i> -olefin (M02)			Ŝ.
fluopyram-Z-olefin (M03)			
Total identified	6 6 954 N		
Sum of unknowns	v 2.2 V A	0.082 0.014 0.014 0.051 0.051 0.051	
Analysed extracts	97.7 ⁴ 0 ⁵	© 2.24¥	
Losses *	N 07 -0 14	Y . Q	
Volution	9.7 N V	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
Total extractable***	0° ~98.4 0° «,	2.258	
Unextractable residu@(solids)	O S 1.6 O	0.037	
Total extractable***		2.295	
6 dichloromothor (mothor) all the of QDE.	a luten during Noon un ODE aluter on	d homiton a nhaga far fat	

dichloromethane/methanol eluates of &PE column during dean up SPE elugie and deptane phase for fat

- distillates the concentration steps  $\bigcirc^{\vee}$   $\swarrow^{\vee}$   $\overset{\vee}{\checkmark}$  Total extracted for that = sime of solvent extract (96.9% of TRFS **
- and heptane phase (2.3% of TRR)



One lactating goat was dosed orally for 5 consecutive days with [phenyl-UL-14C] fluopyram at a daily dose of 1.91 mg eq/kg of body weight and sachtriced 24 hours after the last dose.

The lactating goat extensively metabolised AF C565948, which represented 0.4%-18% of the TRR in all matrices except muscle. The label-specific metabolite fluopyram-benzamide was the main compound in milk and edible organs and assues accounting for 49.1–97.6% of the TRR. fluopyram-Z-olefin was found in significant amounts only in goat fat (43.1% of the TRR). Other minor metabolites accounted for < 5%of the TRR in milk and edible organs and tissues.

Based on the identified metabolites, the collowing metabolic routes were deduced: Ô

- hydroxylation of the ethylene bridge of the molecule resulting in fluopyram-7-hydroxy, fluopyram-8-hydroxy and a dihydroxylated compound
- by droxylation of the phenyl ring leading to fluopyram-phenol
- C conjugation of the hydroxylated metabolites with glucuronic acid



- Augyrapy

  - A comparison of the state of th



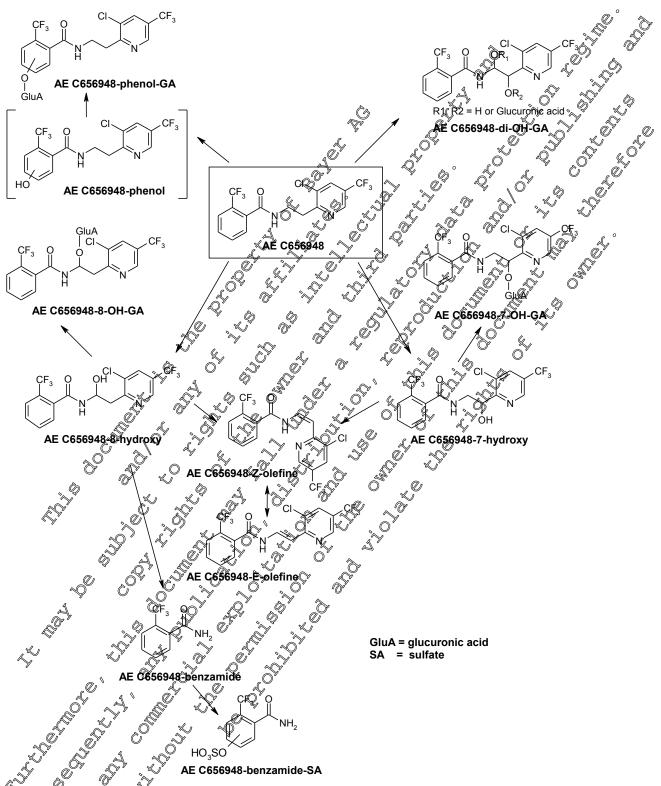


Figure 62.3-1: Proposed metabolic pathway of fluopyram in goat after treatment with [pheny]-UL-¹⁴C] fluopyram



TT1	$\sim$ $\delta'$ $\delta'$		
The study is valid and acce	ptable.		
Data Dainte			
Data Point:	KCA 6.2.3/02		
Report Author:			
Report Year:			
Report Title:	Metabolism of [pyridyl-2,6-14C]AE C65/048 in Seclaritying goa		
Report No:	MEF-06/32/ O' Q' L' X X X X X		
Document No:	$\frac{\mathbf{M}-29/849-01-1}{\mathbf{A}} \qquad $		
Guideline(s) followed in	US EPA OPPTS 869/1300 Health, anada PMIRA, Ref.: DOCO 6. DEU 9/0/14/EB/		
study:	amended by 96/8 v EC. Alpendov v		
Deviations from current test guideline:	n by applicant: ptable. KCA 6.2.3/02 2008 Metabolism of [pyridyl-2,6-14C]AE C65@48 in the lactating goal MEF-06/327 M-297849-01-1 US EPA OPPTS 8(9:1300, Health, Canada PMIRA, Ref.: DA CO 6. DEU 9(#14/FFC amended by 96/6/EC, Appendix * none yes, evalu@ed and accepted rev. 1 to Vol.3.07 DAR, b7 Auget 2010 references religion on b Yes, Sonductor under GLP/Oficially "ecogned testing facilities yes, evalu@ed and accepted rev. 1 to Vol.3.07 DAR, b7 Auget 2010 references religion on b Yes, Sonductor under GLP/Oficially "ecogned testing facilities yes, evalued and accepted rev. 1 to Vol.3.07 DAR, b7 Auget 2010 references religion on b Yes, Sonductor under GLP/Oficially "ecogned testing facilities"		
Previous evaluation:	yes, evalu@ed and accepted		
	rev. 1 to Vol.3 ODAR 37 Aug Qt 2010 references religid on)		
GLP/Officially recognised	Yes, Conductor under GLP/Opicially recognoed testing facilities		
testing facilities:			
Acceptability/Reliability:			
	A A A A A A A A A A A A A A A A A A A		
Q ^v			
Executive Summary S			
~ ( ) ( ) /			

The metabolism of [pyridyl, 26-14C] fluopyram was investigated in one lactating goat, which was orally dosed for 5 constructive ways at a rate of 20 mg a.s./kg of body weight per day (representing 44.62 mg a.s./kg Ged/day). The goat was sacrificed 24 h after the 5th administration. Radioactivity was measured in the excrete millo and plasma collected at timed sampling intervals, as well as in the liver, kidney, muscle and fat at sacrifice. The milk, edible organs and tissues and excreta (urine and faeces) were analysed for parent compound and metabolites by extraction, chromatographic separation techniques and spectroscopic methods

Until sacrifice, the excretion amounted to 80.35% of the totally administered radioactivity. An amount of 0.08% of the total dose was found in fulk. A sacrifice, the calculated total residue in the tissues and organs dissected from the body was approximately 0.85% of the total dose.

The FKR-varies in plasms followed a diurnal pattern. During the 8-hour period after each dosing, a significant increase was obtained followed by a decrease measured prior to the delivery of the next dose. It was shown that the radioactive residues reached a peak of about 0.19 mg/kg, corresponding to 9.5% of the equider to the dose at 4 hours after dosing. This indicated on the one hand a fast



absorption of the test item, a fast distribution of the systemically bioavailable compound-related radioactivity within and a quick elimination from the animal's body. The radioactive residues in plasma reached a plateau-level at about 50-60 hours after the first dosing. The equivalent concentration of radioactivity in the milk showed a constant low rate of 0.006–0.010 mg eq/kg from day 1 to the day of sacrifice. This showed that a plateau level was clearly reached. At sacrifice, highest mean equivalent concentrations occurred in liver (1.427 mg eq/kg). These values were followed in decreasing order by the  $\langle \rangle$ mean concentrations determined in the kidney (0.403 mg eq/kg), total body fat (0.372 mg eq/kg) and total body muscle (0.042 mg eq/kg). The radioactive residues were extracted with efficiencies of 30.8–97.4% from milk, edible organs or tissues and expreta with acetonitrile/water maxtures and O acetonitrile/water/aqueous ammonia mixtures, and identification was achieved by LC-MS/MS/CC-NMR, HPLC co-chromatography or comparison of PLC profiles.

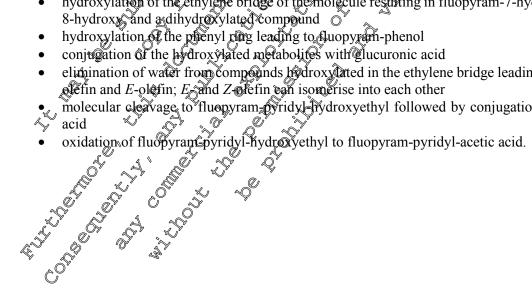
The lactating goat extensively metabolised fluopyram but parent compound was still the trajor compound in milk, muscle and fat (27.3%-46.4% of the TRR) and represented *ca*. 7-7% of the TRR in lives. The main metabolites in milk, muscle and fat were fluopyram-72 hydroxy (MOS) and fluopyram-Z-olefin (MOS), accounting each for more than 10% of the TRR, and represented up to 6.1% and \$1/1% of the TRR in the other matrices, respectively. The main compound in liver and Ridney was fluopyrane?7-OHGGA (M09, isomer 1), accounting for 24.2–35,1% of the TRR but only up to 6.6% of the TRR in the other matrices. Further important metabolites in fiver in kidney were Nuopyrum-8-01-GAQM20, Bomer 2; up to 17.7% of the TRR and up to 2.5% in other matrices) and fluopyram-7-OH-GA (M09, isomer 2; op to 16.3% of the TRR and up to 5.5% in other matrices). The Tabel-Specific metabolites fluopyram pyridyl-acetic acid (M40) and fluopyram-hydroxyethyl-GA (M37) were only found in kidney at \$5% and 4.3% of the TRR, respectively. 0

Further detected micor metabolites were fluopyram-E olefin (M02), Pluopyram-di-OH-GA (M21) and fluopyram-phenol $\mathfrak{GA}$  (M07) at  $\mathfrak{S}$ % of the TRR.

Ô Based on the identified metabolites, the following metabolic routes were deduced:

- hydroxylation of the ethylene bridge of the molecule resulting in fluopyram-7-hydroxy, fluopyram-• 8-hydroxy and adihydroxylated compound

- elimination of water from compounds hydroxy arted in the ethylene bridge leading to fluopyram-Z-
- molecular cleavage to fluopyram pyridyl hydroxyethyl followed by conjugation with glucuronic





## I. Materials and Methods A. Materials 1. Test Material: **IUPAC** Name N-{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]ethyl (trifluoromethyl)benzamide N-[2-[& hloro-5-(triftuoromethyl)-2 CAS Name Benzamide, pyridinyl]eth@-2-(trifluor@nethyl)- (9CI) AE C656948 Code name ×, Ľ Fluopyram Common name Empirical formula C16H11CIF6N2O CAS Number 58066 Molar mass g/nao Chemical structure positions of radiolabel Radiolabelled test material ÅE C**Ø**56948 1939 (radiotabelled) $\bigcirc$ Batch number BF 0 Original specific radioactivity uCi/mg 🖔 Ø3 MBaγmg ₅



### 2. Test Animals

. Test Animals		
Species		Goat (Capra hircus)
Breed		Goat ( <i>Capra hircus</i> )
Breeding facility		
Sex, number		One female lactating goat
Body weight		40 kg at test start
Age		ca. 27 months old at experiment start
Acclimatization		<i>ca.</i> 27 months old at experiment start 9 days Stafinless steel metabolism cage, approx, 20–25°C, 45562%
Housing		Stainless del metholisticage approx 20-25°C 455A2% &
	L.	rel. humidity, 12/12 hours light/dark O/cle, air changes: 10 15 changes/kt
Identification	á v	Skon markong w a start and a
Feed and water	C. 2 2 2 , 4	Ruminant feed, hay apples (ad libitum)
		Tap water ad libition 2 5
Health status		Acceptable
3. Study Design		Tapwater ad libition 2 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5
". Study Design		

### 1

Preparation of the dosing mixtures and administration?

In total, five gelatine capsules containing 84 mg each of the solid pooder were prepared one day before the first administration. In relation to a body weight of 40 kg, this anount of radioactivity corresponded to an actual dose of 2. Ong a sky by. Based on the experimentally determined food consumption this corresponds to 44%2 mg n.s./kg feed/day. . P  $\bigcirc$ 

The goat received daily one gelatine capsule administered orally using a capsule applicator. The administration was performed on five consecutive days in the morning after milking.

The identity of the test compound was confirmed by LC-MS/MS. The major remaining amount of the test item was stored in solid form in a freezer at \$18 °C and used in a respective laying metabolism study which was performed about 4 months later At that time the radiochemical purity was checked by HPLC analysis in order to demonstrate the stability of the test item during storage.

Sampling Collection and processing of blood



Micro-samples of blood were taken from the ear veins at 0.25, 0.5, 1, 2, 3, 4, 6, 8, 24, 32, 48, 56, 72, 80°, 96, and 104 hours after starting the experiment. The blood was collected in heparinized capillaries which were centrifuged afterwards using a haematocrit centrifuge for separation of blood cells and plasma. The plasma samples were weighed and prepared for radioactivity measurement by LSCS

### Collection and processing of milk

The goat was milked in the morning immediately prior to each administration, about Chours Pater in the afternoon, and directly before sacrifice (time schedule; 8, 24, 32, 48, 56, 72, 80, 9, 104, and 126 hours after the first administration). After weighing, one aliquot was taken from each simple for radioactivit measurement by LSC.

Collection and processing of urine Urine samples were collected in plastic vessels as quantitatively as possible under dry ice cooping in intervals of 24 hours after each administration. The vessels were changed immediately pefore the next administration. The collection funner was rinsed with deionised water into the same wine vessel of the respective collection period. After recording the total volumes, and alignot was taken from each sample for radioactivity measurement by LSC.

### Collection and processing of faeces

Faeces samples were collected as quantitatively as possible at room temperature in intervals of 24 hours after each administration, i.e. immediately before the next administration. The collecting grid was cleaned prior to each administration. No samples of the rinsing water were taken for radioactivity measurement. Each faeces fraction washomogenized after addition of water to get a wet paste before the total weight was recorded. One alique of each wet sample was weighed and prepared for radioactivity measurement by combustion/ESC.

### organs and tissues Sacrifice and collection of

For the collection of organs and tissues, the animal was acrificed ca. 24 hours after the fifth administration, a time distance that is consistent with normal slaughtering practices. The animal was anaesthetised by an intravenous tose of about 40 mg eykg by PentoParbital Na (Narcoren®), exsanguinated by cannulating the jugular veins and sacrificed by intracerdiac mjection with ca. 10 mL of the sacrificing agent "T 61®". The following organs and tissues were dissected: muscle (round and loin), fat (omental and perirenal), liver without gall bladder dridneys, and the gall bladder

The organs or tissue samples were then transferred into tarred plastic vessels and recording of the individual weights, liver, kidneys, fat and muscle samples were passed several times through a mincing machine in half-frozen state. One aliquet of each resulting tissue pulp was weighed and prepared for radioactivity measurement by combustion/LSC.

The gall@ladder was punctured for the collection of the bile fluid that was stored in a freezer for the (optional) metabolite analysis.



### **C. Analytical Procedures**

### **Extraction and fractionation:**

Samples of milk and edible tissues were extracted two or three times with acetonitrile/water nixtures/(ca. g/2), v/v).

The combined extracts were applied to C18 SPE cartridges to remove the lipid fraction of the patrix. The SPE percolate and the column wash with acetonitrile/water were combined and concentrated to the actions.

For liver two additional solvent extractions were performed with acetonitrile/water N/1; v/9 and with acetonitrile/water/aqueous ammonia (25%) (2/1/b v/v/v). These extracts were discarded due to low content of radioactivity.

For muscle and liver two further extraction steps were conducted with microwave assistance at elevated temperature. Solids from solvent extraction were extracted first with actonit ne/water (1/k v/v) and then with acetonit rile/water/aqueous ammonia (25%) (2/1/k, v/v/ ). Both microwave extracts from muscle were discarded due to very low residues. The acetonit rile/water extract from microwave assisted extraction of liver was purified by SPE for chromatographic analysis. For the acetonit rile/water/aqueous ammonia extract from liver several partition and SPE procedures were conducted by a chromatographic analysis was not possible due to low residues in the fractions obtained or interference of matrix.

### Analytical methods:

The radioactivity of all liquid samples was measured using adiquid scintillation counter. Solid samples were combusted using an oxidizer. The resulting  ${}^{14}\text{CO}_2$  was trapped in an alkaline scintillation cocktail. The TRR in the samples was calculated by summing up the radioactivity measured in different extracts and remaining solids after solvent extraction. The TRR was expressed in ang a.s. equivalents per kg sample weight.

Aliquots of all acetonitite/water extracts were analysed by HPLC. Ten metabolites as well as parent compound were identified by LC-MS/MS LC-16²NMR HPLC co-chromatography or comparison of HPLC profiles.

The MPLC was conducted using a reversed phase column and a gradient elution using a neutral water phase and an acetonitrile/methabol organic phase. The HPLC system was equipped with a radiodetector and a UV detector with variable wavelengths. The LOQ was derived from the average background level and the specific radioactivity of the adiolabelled test compound.

## Storage stability

Solvent extractions and first HPLC-analyses of the extracts from milk, muscle, fat, liver and kidney were performed within 1- 6 weeks after sacrifice of the lactating goat. Investigations on storage stability of radioactive residues in edible samples were therefore not required.



A second extraction of liver with a different methodology was performed after ca. 6 months of storage. These extracts showed mainly the same metabolites but differences in the proportions of compounds compared to the first extraction. The differences can be explained by partial degradation of metabolites caused by the procedures of the second extraction and are probably not related to storage of samples.

Storage stability of extracts was demonstrated for the extracts of milk, fat, the solvent extract of liver, and the extract of kidney for a storage time of ca. 3 to 5 months the extract of kidney for a storage time of ca. 3 to 5 months. 

### II. Results and Discussion

The metabolism in lactating goat of [pyridy 2,6-14] fluopy fam administrated at a vally dose 44.62 mg eq/kg in the feed corresponding to a daily intake of 2.0 mg/eq/kg/ody worght for 5 consecutive days was investigated. O

Until sacrifice 24 hours after administration of the tast dose, the mean excretion smounted on average to 80.95% of the radioactivity totally administered (Table 6.2.3-13) able 6.2.2- (). The time course of the excretion was characterised by a celatively constant rate starting at day 3 will test end (Table 6.2.3-18). Only 0.08% of the dose totally administered was measured in the milk secreted within the whole test period. At sacrifice, 24 h after the last administration, the total residue in the tissues and organs dissected from the body was calculated to about 0.85% of the total dose Based on the Values the recovery amounted to 91.89% (Table 6.2.3-17) Table 6.2.2-1)

The TRR-values in plasmo determined over the whole desting period in timed sampling intervals followed a diurnal pattern (Table 6.2.3-19). During the 8-hour period after each dosing, a significant increase was obtained followed by a decrease measured prior to the delivery of the next dose. For the 8hour period after the first dosing, blood samples were confected at shortor intervals in order to determine the exact course of the TRR-values in plasma. If was shown that the radioactive residues reached a peak of about 0.19 mg/kg, corresponding to 9.5% of the equidistribution concentration of the dose at 4 hours after dosing. This indicated an ongoing absorption of the test item, a rapid distribution of the systemically bioavailable compound-related ratioactivity within the body and a quick excretion. A plateau-level was reached at about 50-60 dours after the first dosing.

The total radioactive residues were determined in milk, faeces and urine produced from the first dose until sacrifice and in edible tissues and organs at sagaince. The highest mean active substance equivalent concentrations were measured in liver (1/27 mg/eq/kg) and kidney (0.403 mg eq/kg). These values were followed in decreasing order by total body fat (0.372 mg eq/kg) and total body muscle (0.042 mg eq/kg).

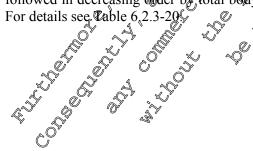




Table 6.2.3-17:	Recovery of radioactivity following oral administration of [pyridyl-2,6-14C]fluopyram	at å	~
	daily dose rate of 2.0 mg eq/kg body weight for 5 consecutive days	Ş	

ua	my use rate of 2.0 mg eq/kg body weight for 5 consecutive days	
Matrix	Recovery of radioactivity (% of the totally administrated radioactivity)	
Excreta ¹⁾	80.95	
Milk ²⁾		
Totally excreted	\$1.03 Q [¥]	
Tissues		<u>y</u>
Recovery	A 91.89 O 4	

Recovery in excreta obtained by adding recovery values of samples collected within the observation period of 5 days
 Recovery in milk calculated by adding recovery values of samples produced within the observation period of 5 days
 Values in *italics* were calculated from the values in the report

# Table 6.2.3-18: Time course of total radioactivity in excreta following oral administration of [poridy]-2.6 14C]fluopyram at a daily dose rate of 2.0 mg egg kg body weight for 5 consecutive days

	Time after the	Administration numb	
Matrix	first dosage 🗶	Administration numb	er and for the state of the second se
	(hours) 🖓		(s of weathy automistrated radioactivity)
	24		
			₩ 0×1.14 %
Urine	≥12 ÷¥		Excretion per day Construction of the second of the secon
	≫ ⁹⁶ 1		01.14 01.14 01.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.17 0.1
	2 120	Sacrifice . O	× × × × 2.53
Faeces of	$\begin{array}{c} & & & & \\ & & & & \\ & & & & \\ & & & & $	$\begin{array}{c} & & & & & & \\ & & & & & & \\ & & & & & $	× × × × × × × × × × × × × × × × × × ×
	<u></u> 0 [°] 48 [°] [°]	× 3, ~	5.67
Faeces SO	72 × 86	A A	5.67 5.67 7.21
O A	₹ 72 [°] « 96 296		5.67 7.21 6.06 6.21
	× 120 ×	Image: specific specif	6.31
~0		St in a	
~~ @ 1	Q S D		
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			
4			
×	× A ×		
\sim			
ø`.		, K	
es de			
	, S		
AN A A	, N		
× [×] O _×			
\bigcirc			



			lowing oral administration of [pyridyl-246- /kg body weight for 5 consecutive days
Matrix	Time after the first dosage (hours)	Administration number	[mg eq(kg plasma]
	0.25	Č.	
	1 2 3		0.164
	4 6		
Plasma	8 24		0 [°] 0.078
	32 48 56		O Y 0.627 X Y V V 0.695 V V V V 0.206 X V
			0.200 × 2 × 0.008 × 0.199 ×
	296 ° 104 1		× × 0.133
** no sample collected			

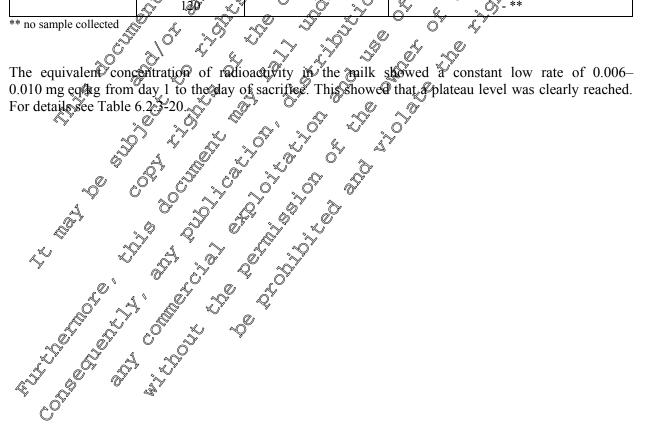




Table 6.2.3-20:	Time course of total radioactivity in milk following oral administration of [pyridyl-2,6-0° 14C]fluopyram at a daily dose rate of 2.0 mg eq/kg body weight for 5 consecutive days			
Matrix	Time after the first dosage (hours)	Administration number	Secretion period	
	8	1 .		
	24		<u> 0.006 y y y</u>	
	32	2		
Milk	48		0.067 Q G Q	
	56	and the second se		
	72	× . °		
	80			
	96			
	104		A 6 0.010 6 0'	
	120		0 ⁴ × 0,006 × 2 ⁴	
	A CONTRACTOR OF			

 Table 6.2.3-21:
 Distribution of cesidues in tissues and organs of lactating goats following or al administration of [pyridyl-2.6-14C] fluopyram at a daily dose rate of 2.0 mg eq/kg body weight for 5 consecutive days

weight for 5 consecutive days	
Matrix A htterval	TRA (mg 4, s. equiv./kg)
Liver of the Liver	× ,
Kidney and St St	0.403
Total body mus de by K 5 0	0.042
Total body fat 🔨 🌾 🏷 🕉	0.372
mg a.s. equiv./kg: @g parent equiva Onts per @g matrix O	

In evening milk pool 3.4% of the TRR (0050 mg eq/kg) was extracted with solvent extraction (acetonitrile/water). Following degreasing by SPE, most of the fadioactivity was contained in the percolate and wash (91,4% of the TRR or 0.048 mg eq/kg) and, after the concentration step, the aqueous remainder contained an of the fadioactivity. In total 93.4% of the TRR (0.050 mg eq/kg) was extracted, whereas 6.6% of the TRR (0.003 mg eq/kg) remained non-extractable in solids (Table 6.2.3-22).

In goat muscle, %7% of the TRR (0.036 mg eq/kg) was extracted with solvent extraction (acetonitrile/water). Following degreasing by SPE, all of the radioactivity was contained in the percolate and wash and, after the concentration step, the aqueous remainder again contained all of the radioactivity. After further extraction of the solids with acetonitrile/water (1/1; v/v) and acetonitrile/water/aqueous

After further extraction of the solids with acetonitrile/water (1/1; v/v) and acetonitrile/water/aqueous ammonia (25%) O/1/1; O/v, using a microwave at 120 °C, the alkaline microwave extract contained further 58% of the TRR (0.002 mg eq/kg) and the neutral microwave extract contained 1.7% of the TRR (0.004 mg eq/kg).

In total, 89,2.0% of the TRR (0.037 mg eq/kg) was extracted (Table 6.2.3-23).



In goat fat, 97.1% of the TRR (0.361 mg eq/kg) was extracted with acetonitrile/water. Following degreasing of the acetonitrile/water phase by SPE, most of the radioactivity was contained in the percolate and wash (96.1% or 0.357 mg eq/kg) and, after the concentration step, the aqueous remainder contained 95.1% of the TRR (0.354 mg eq/kg). In total, 97.1% of the TRR (0.361 mg eq/kg) was extracted, whereas 2.2% of the TRR (0.011 mg eq/kg) remained non-extractable in solids (Table 6.2.3-24).

In goat liver with conventional extraction, 54.7% of the TRR (0.780 mg eq/kg) was extracted with solvent extraction (acetonitrile/water). Following degreasing by SPE, most of the radioactivity was contained in \bigcirc the percolate and wash (53.7% or 0.766 mg eq/kg) and after the concentration step, the aqueous remainder contained 50.6% of the TRR (0.723 mg eq/kg).

After further solvent extraction of the solids with acetonitrile/water ([VV, v/v] with acetonitrile/water and acetonitrile/water/aqueous ammonia (25%) 2:1:1 (v/vv), the majority of the TRR remained in the solids (39.0% of the TRR or 0.556 mg eq/kg).

After further microwave extraction with acetomerile/water (14); v/v at 120 °C, the neutral microwave extract contained further 14.7% of the TRR (0.210 mg eq/kg). After the concentration step, the aqueous remainder contained 14.2% of the TRR (0.202 mg eq/kg). The majority of the TRR after microwave extraction was however still contained in solids (24.2% of the TRR (0.346 mg eq/kg). After a second microwave extraction with acetometrile/water/aqueous/ammodua (25%) (2/10; v/x^Q) at 120 °C all of the TRR was contained in the alkaline microwave extract. In total, 75% of the TRR (1.082 mg eq/kg) was extracted (Table 6.3-25).

In goat kidney, 9124% of the TRR (0.368 ng eq/kg) was extracted, with solvent extraction (acetonitrile/water). Following degreasing by SPE, most of the adioactivity was contained in the percolate and wash (90.9% of the TRR of 0.366 mg eq/kg) and, after the concentration step, the aqueous remainder contained 88.9% of the TRR (0.358 ng eq/kg). In total, 91,4% of the TRR (0.368 mg eq/kg) was extracted, whereas 8.6% of the TRR (0.035 mg eq/kg) remained nor-extractable (a solids (Table 6.2.3-26).

⊘ ^{*4} C]fláopyrattoat a daify dos©rate oC2.0 mg eq/kg body weight for 5 consecutive days		
V. 3. E. P. 9	Ev S Ev	ening milk pool
TRR, mg eq/kg		0.053
	% TRR	mg a.s. equiv./kg
Solvent Stract ¹)	93.4	0.050
Percolate and wash	93.4 91.1	0.048
Concentration Aqueous remainder	91.1	0.048
Eluate Solids	2.4	0.001
Solids	6.6	0.003
$\mathbf{DEC}^{(2)}$	6.6	0.003
Tota extraored	93.4	0.050
Total Strated Strategy Account about the first strategy of the	100.0	0.053
ČŐ.		

 Table 6.2.3-22:
 Extraction of radioactic residues from the evening milk pool after dosing of [pyridyl-2,6

 ^{4}C]floopyrant a daily doserate of 2.0 mg eq/kg body weight for 5 consecutive days



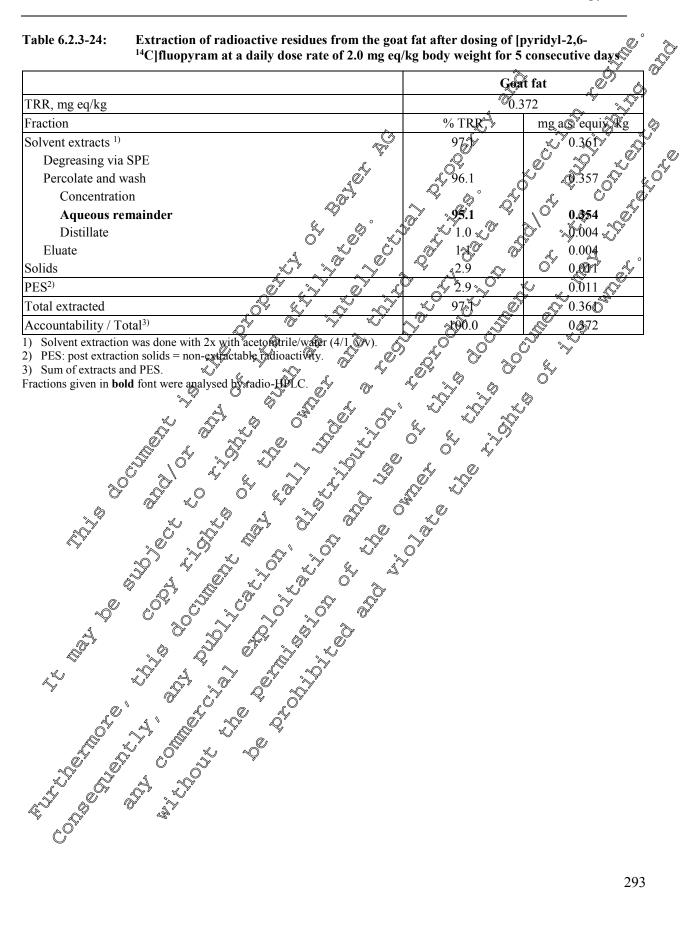
- 1) Solvent extraction was done with 3x with acetonitrile/water (4/1, v/v).
- 2) PES: post extraction solids = non-extractable radioactivity.
- 3) Sum of extracts and PES.

Table 6.2.3-23:

 Solvent extraction was done with 3x with aceton PES: post extraction solids = non-extractable rad 	litrile/water (4/1, v/v).
3) Sum of extracts and PES.	
Fractions given in bold font were analysed by radio-	HPLC.
	A. A A
Table 6.2.3-23:Extraction of radioactive	e residues from the goat muscle after dosing of [pysjdyl-2,6 🖉 🔬
¹⁴ C]fluopyram at a daily	dose rate of 2.0 mg/eq/kg body weight for 5 consecutive days
	HPLC. HPLC. e residues from the goat muscle after dosing of [pyridy]-2, of the second secon
TRR, mg eq/kg	
Fraction	% TRR mg als: equivals % TRR mg als: equivals % TRR mg als: equivals % 0.036 % % 0.001 % % 0.001 % % 0.001 % % 0.001 % 0.001 % 0.001 % 0.001 % 0.001
Solvent extract 1-2 ¹⁾	0 [°] 0 ⁸ 6.7 2 [°] 2 [°] 2 [°] 2 [°] 0.036 [°] 2 [°]
Degreasing via SPE	
Percolate and wash	× × × × × × × × × × × 0.036 × 1
Concentration	
Concentration Aqueous remainder Solvent extract 3 ⁻¹⁾	86.7 86.7 2.5 0.8 0.8 0.001 0.005 0.005 0.005 0.002
Solvent extract 3 ¹⁾	
Solids 1 Microwave solvent extraction	
Microwave solvent extraction	
Microwave extract (alkaline) 🖉 🌾	5.8 5.8 Q002
Microwave extract (neutral)	
Loss	
PES^{3}	
Total extracted	2 0.042
Accountability / Total ⁴	× × 100,0° × 0.042
1) Solvent extraction was done with 3x with sector	$\frac{1}{\sqrt{2}}$

- 2) Microwave extraction was performed with acetomtrile/water (1/10/v) and acetonitrile/water/aqueous ammonia (25%) 2:1:1 4) PES: pest-extraction solide = non-extractable adioactivity.
 4) Sum offectracts and PES
 Fractions given in **bold** (on were analysed by radio SPLC .
 A
 A
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 C
 <li (v/v/v) at 120 °C







	Goat liver
TRR, mg eq/kg	Sourt invertige I.427 % TRR mg a.s. equiv./kg % TRR 0.766 53.7 0.766 50.6 0.766 50.6 0.723 50.6 0.0044 100 0.0044 0.647 0.647 0.647 0.647 100 0.647 0.647 0.556 14.7 0.202 0.66 0.008 0.210 0.008
Fraction	% TRR mg a.s. eq@v./kg
Solvent extract ¹⁾	54 0 00780 ~ ~
Degreasing via SPE	50.6 50.0 50.0
Percolate and wash	\$ 53.7 \$ 0.760 \$ \$
Concentration	
Aqueous remainder	
Distillate	
Eluate	
Solids 1	\mathbb{O}^{*} \mathbb{O}^{*} \mathbb{O}^{*} \mathbb{O}^{*} \mathbb{O}^{*} \mathbb{O}^{*} \mathbb{O}^{*} \mathbb{O}^{*}
Further solvent extraction ²)	
Acetonitrile/water extract	\$ 29 × 20 × 0,071 0
Acetonitrile/water/ammonia extract	
Solids 2	
Microwave solvent extraction of the	
Microwave extract (neutral)	14.7 (° (° (° (° (° (° (° (° (° (° (° (° (°
Concentration	
Aqueous remainder 🚕 🕺	$\begin{array}{c} \begin{array}{c} & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & & \\ & & & & \\ & & & & & \\ & & & & & \\ & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & $
Aqueous remainder A Distillate A A	
Solius 5 As A A As	
Microwaye solvent extraction 4)	24.2 0.346
Microvave extract (alkaline)	0.346
PES ⁵)	
Total extracted	³ ³ 100.0 ³ 1.427
Accountability / Total ⁶⁾	1.427

 Solvent extraction was done with 3x with acetorful le/water (4/1, v/v).
 Further solvent extraction was performed with acetorful water 1:1 (v/v) followed by acetonitrile/water/aqueous ammonia (25%) 2:1:1 (v/v/Q).

(25%) 2:1:1 (v/v/Q.
3) Microwave extraction was performed with acetometrile/water/(1/1, v/2) at 120 °C
4) Microwave extraction was performed with acetometrile/water/aqueeds ammonia (25%) 2:1:1 (v/v/v) at 120 °C
5) PES: postextraction solids pron-extractable radioactivity.

6) Sum of suracts and PES Fractions serven in **bold** font were analysed by radio-HPEC.



Table 6.2.3-26:	Extraction of radioactive residues from the goat kidney after dosing of [pyridyl-2,6- 🔊	۵.
	¹⁴ C]fluopyram at a daily dose rate of 2.0 mg eq/kg body weight for 5 consecutive days	ð

	Goat kidney
TRR, mg eq/kg	0.403
Fraction	% TRR mg a.s. equiv./kg
Solvent extract ¹⁾	
Degreasing via SPE	
Percolate and wash	
Concentration	88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 88.9 8 8 8 8 8 8 8 8
Aqueous remainder	88.9 2.0 2.0 3.0 3.0 3.0 3.0 3.0 3.0 3.0 3
Distillate	88.9 88.9 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0
Eluate	
Solids	
PES ²⁾	
Total extracted	68 9 × 2 91 × × × × 0 0068 0
Accountability / Total ³⁾	acetofitrile/water (4/1 @v).
) Solvent extraction was done with 2x with	acetometrile/water (4/1 Ov).

2) PES: post extraction solids = non-extractable radioactivity 3) Sum of extracts and PES.

Fractions given in **bold** font were analysed by adio-HPL

For elucidation of metabolism all acetonitrile water extracts were analysed by HDLC. Ten metabolites as well as parent compound were identified by /MS, LC-H-NMR, HRLC co-chromatography or comparison of HPLC profides.

In evening make pool, the parent compound was the main compound and accounted for 42.5% of the TRR (0.023 mg cq/kg). The main metabolice was Muopyram-7-bydroxy amounting to 16.2% of the TRR (0.009 mg eq/kg), followed by fluopyram-Z-olefin accounting for 12.9% of the TRR (0.007 mg eq/kg). The metabolites fluopyram 7-OH GA (isomer 1 and 2), fluopyram-8-OH-GA (isomer 2) and fluopyram-*E*-olefin minor compounds and accounted each for < 5% of the TRR (< 0.005 mg eq/kg). In total, 79.4% of the TRR was identified in evening mile pool (Table 6.2.3-2%).

In goat muscle, the parent compound was the main component and accounted for 27.3% of the TRR (0.011 mg eq/kg). The main metabolites were flugpyram-7-hydroxy and fluopyram-Z-olefin (each 21.6% of the TRR or 0.009 mg co/kg). Fluopycam-7-OH-GA accounted for 6.6% (0.003 mg eq/kg) and 5.1% (0.002 mg eq/kg) of the DRR for some and respectively. Other metabolites found were fluopyram-8-OH-GA (isome 2°), and fluop ram- E° ole fing which accounted each for < 5% of the TRR (0.001 mg eq/kg). In total, 86.7% of the TRR was identified in goat muscle (Table 6.2.3-28).

In goat fat, the patent compound was the main component and accounted for 46.4% of the TRR (0.1/3 mg @/kg) The main metabolite was fluopyram-Z-olefin and accounted for 33.7% of the TRR (0125 mg/eq/kg). The second most abundant metabolite was fluopyram-7-hydroxy (12.8% of the TRR or



0.048 mg eq/kg). fluopyram-E-olefin was a minor metabolite (2.2% of the TRR, 0.008 mg eq/kg). In total, 95.1% of the TRR was identified in goat fat (Table 6.2.3-29).

In goat liver, the parent compound accounted for 7.7% of the TRR (0.110 mg eq/kg). The main component was fluopyram-7-OH-GA (isomer 1), accounting for 24.2% of the TRR (0.345 mg eq/kg). The second most @ abundant metabolite was fluopyram-8-OH-GA (isomer $\frac{1}{2}$) and accounted for 9.5% of the TRR (0.136 mg eq/kg), followed by fluopyram-7-hydroxy (6.1% of the TRR or 0.086 mg eq/kg) and fluopyram-Z-olefin (5.7% of the TRR and 0.081 mg eq/kg). Further components found were fluopyram-7-QD-GA (isomer 2), fluopyram-di-OH-GA, fluopyram-phenol-GA and fluopyram-E-olefin, each amounting to <5% of the TRR (<0.058mg eq/kg). In total, 62.4% of the RR was identified in goat liver (Table 6.2, 3-30)

indemon seithe FRE (09) indemon inde In goat kidney, the parent compound was not found. The main composent was fluor yram-AOH-GA (isomer 1) and amounted to 35.1% of the TRR (0.142 mg/eq/kg). The second most abundant metabolite was fluopyram-8-OH-GA (isomer 2), accounting for 10.7% of the TRR (0.971 mg eq/kg), followed by fluopyram-7-OH-GA (isomer 2; 16.3%) of the TRR or 0.066 mg/kg) The label-specific compound fluopyram-pyridyl-acetic acid accounted for 8.6% of the TRR (0.035 mg eq. (3)). Further components identified were fluopyram-hydroxyeth@-GA, fluopyram-oH-GA, fluopyram-phenol-GA and fluopyram-7-hydroxy, each amounting to < 5% of the βRR (≤ 0.017 βg eq/(g). In total, 87.9% of the TRR



Table 6.2.3-27: Summary of identification and characterization of radioactive residues in the milk of lactating goat after dosing of [pyridyl-2,6-14C] fluopyram at a daily dose rate of 2.0 mg eq/kg body weight for 5 consecutive days ~

TRR [mg/kg] =	Evening will need
	Evening milk pool
	_0.053
Compound	% of TRR / mg ass equiv rg
AE C656948, a.s., fluopyram	0.053 0.0053 0.023 0.023 0.023 0.001 0.001 0.002 0.001 0.002 0.000 0.002 0.0000 0.00000
fluopyram- pyridyl-acetic acid (M40)	
fluopyram-hydroxyethyl-GA (M37) fluopyram-7-OH-GA (M09), isomer 1	
fluopyram-7-OH-GA (M09), isomer 2	310^{10}
fluopyram-di-OH-GA (M21)	
fluopyram- pyridyl-acetic acid (M40) fluopyram-hydroxyethyl-GA (M37) fluopyram-7-OH-GA (M09), isomer 1 fluopyram-di-OH-GA (M21) fluopyram-phenol-GA (M20), isomer 2	
fluopyram-8-OH-GA (M20), isomer 2 fluopyram-7-hydroxy (M08) fluopyram- <i>E</i> -olefin (M02) fluopyram- <i>Z</i> -olefin (M03)	$3.1.0^{\circ}$ $3.1.0^{\circ}$ 0.002 $3.1.0^{\circ}$ 0.002 0.001° 0.002° 0.001° 0.002°
fluopyram-7-hydroxy (M08) fluopyram- <i>E</i> -olefin (M02)	
fluopyram-Z-olefin (M03)	329 329 329 320 320 320
fluopyram-7-OH-GA (M09), isomer 2 fluopyram-di-OH-GA (M21) fluopyram-phenol-GA (M27) fluopyram-8-OH-GA (M20), isomer 2 fluopyram-7-hydroxy (M08) fluopyram- <i>E</i> -olefin (M02) fluopyram- <i>Z</i> -olefin (M03) Total identified	\$79.4 s 079.4 s
Total identified	$\begin{array}{c c c c c c c c c c c c c c c c c c c $
Analyzed avtra at	
Analysed extract	⁵ 0.001
Not analysed	© 2.4 0.001 0.001 0.001 0.001 0.001 0.050
Losses * Volatiles ** Not analysed Total extractable	0.050
Unextractable residues & Dids	
Accountability	
Not analysed Total extractable Unextractable residues (solids) Accountability * dichlorometrane/metranol cluates of SPE common during clean ** distillates from concentration steps ** of the	



Summary of identification and characterization of radioactive residues in muscle of lactating goat after dosing of [pyridyl-2,6⁻¹⁴C] fluopyram at a daily dose rate of 2.0 mg eq/kg body weight for 5 consecutive days Table 6.2.3-28:

lactating goat after dosi	on and characterization of radi ng of [pyridyl-2,6- ¹⁴ C] fluopyra	
2.0 mg eq/kg body weigl	ht for 5 consecutive days	
	Goat 1	muscle 🖓 🖌
TRR [mg/kg] =	0.0	042
Compound	% of TRR	mg a.s. equity kg
AE C656948, a.s., fluopyram	27.3	0.01 ~ ~
fluopyram- pyridyl-acetic acid (M40)	-2	
fluopyram-hydroxyethyl-GA (M37)	Ser S	
fluopyram-7-OH-GA (M09), isomer 1	ذ6.6	
fluopyram-7-OH-GA (M09), isomer 2	5.1 .	$\begin{array}{c} & & & & & & & \\ & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & \\$
fluopyram-di-OH-GA (M21)	2.5	
fluopyram-phenol-GA (M07)		$\mathcal{O}^{\mathcal{O}}$ $\mathcal{O}^{\mathcal{O}}$ - \mathcal{L} \mathcal{A}
fluopyram-8-OH-GA (M20), isomer 2	× 2.5 × ×	
fluopyram-7-hydroxy (M08)		
fluopyram- <i>E</i> -olefin (M02)		J. 90.001 - 5
fluopyram-Z-olefin (M03)		
Total identified		
Sum of unknowns		
Analysed extract	<u>~~</u> <u>86.7</u> ~	© 0.036
Losses *	5 0 ⁷ - 0 ^{- 7}	
Volatiles **		
Not analysed *** 🖉 🖓		× 0.001
Total extractable ****	Q 5 89.2 0°	0.037
Unextractable residues (solids) *****	× ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	0.005
Accountability	<u>~</u> <u>*</u> * * 00.0 ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	0.042
* dichloro@ethaneApethano@luates @ SPE * dichloro@ethaneApethano@luates @ SPE distillates from @oncentration steps **** Muscle: solvent extraction ***** Muscle: PES after Solvent extraction (solid ***** Muscle: PES after Solvent extraction (solid ****** Muscle: PES after Solvent extraction (solid ************************************	V VO.0 V VO.0 V Qoffinn daring clean up V VO.0 V Qoffinn daring clean up V	₩¥ ,



Summary of identification and characterization of radioactive residues in fat of lactating ° Table 6.2.3-29: goat after dosing of [pyridyl-2,6-¹⁴C] fluopyram at a daily dose rate of 2.0 mg eq/kg body weight for 5 consecutive days

Table 6.2.5-29: Summary of identification and characterization of radioactive residues in to lactating goat after dosing of [prividy-2.6-10] [Integram at a daily dose rate of 2.0 mg crk. bdf weight for 5 consecutive days Image: Integration of radioactive residues in the lactating goat after dosing of [prividy-2.6-10] [Integram at a daily dose rate of 2.0 mg crk. bdf weight for 5 consecutive days Image: Integration of radioactive residues in the lactating goat after dosing of [prividy-2.6-10] [Integration of radioactive residues in the lactating goat after dosing of [prividy-2.6-10] [Integration of radioactive residues in the lactating goat after dosing of [prividy-2.6-10] [Integration of radioactive residues in the lactating goat after dosing of [prividy-2.6-10] [Integration of radioactive residues in the lactating goat after dosing of [prividy-2.6-10] [Integration of radioactive residues in the lactating goat after dosing of [prividy-2.6-10] [Integration of radioactive residues in the lactating goat after dosing of [prividy-2.6-10] [Integration of radioactive residues in the lactating goat after dosing of [prividy-2.6-10] [Integration of radioactive residues in the lactating dosing in the lactating goat after dosing of [prividy-2.6-10] [Integration of radioactive residues in the lactating dosing in the lactati
TRR $[mg/kg] =$ Compound% of TRRmg a.s. equiv. kg.AE C656948, a.s., fluopyram46.40.173fluopyram-pyridyl-acetic acid (M40)46.40.173fluopyram-hydroxyethyl-GA (M37)fluopyram-7-OH-GA (M09), isomer 1fluopyram-di-OH-GA (M21)fluopyram-8-OH-GA (M20), isomer 2fluopyram-7-hydroxy (M08)fluopyram-Z-olefin (M02)fluopyram-Z-olefin (M03)Total identified95.10.354Sum of unknownsAnalysed extractLosses *
Compound % of TRR mg a.s. equiv./kg AE C656948, a.s., fluopyram 46.4 0.173 fluopyram-pyridyl-acetic acid (M40) - - fluopyram-hydroxyethyl-GA (M37) - - fluopyram-7-OH-GA (M09), isomer 1 - - fluopyram-7-OH-GA (M09), isomer 2 - - fluopyram-Benol-GA (M21) - - fluopyram-8-OH-GA (M20), isomer 2 - - fluopyram-7-hydroxy (M08) - - fluopyram-Z-olefin (M02) - - fluopyram-Z-olefin (M03) - - Total identified - - Sum of unknowns - - 0.354 Losses * - - 0.004
fluopyram-di-OH-GA (M21) fluopyram-benol-GA (M07) fluopyram-8-OH-GA (M20), isomer 2 fluopyram-7-hydroxy (M08) fluopyram- <i>E</i> -olefin (M02) fluopyram- <i>Z</i> -olefin (M03) Total identified Sum of unknowns Analysed extract Losses *
fluopyram-di-OH-GA (M21) fluopyram-benol-GA (M07) fluopyram-8-OH-GA (M20), isomer 2 fluopyram-7-hydroxy (M08) fluopyram- <i>E</i> -olefin (M02) fluopyram- <i>Z</i> -olefin (M03) Total identified Sum of unknowns Analysed extract Losses *
fluopyram-di-OH-GA (M21) fluopyram-benol-GA (M07) fluopyram-8-OH-GA (M20), isomer 2 fluopyram-7-hydroxy (M08) fluopyram- <i>E</i> -olefin (M02) fluopyram- <i>Z</i> -olefin (M03) Total identified Sum of unknowns Analysed extract Losses *
fluopyram-di-OH-GA (M21) fluopyram-benol-GA (M07) fluopyram-8-OH-GA (M20), isomer 2 fluopyram-7-hydroxy (M08) fluopyram- <i>E</i> -olefin (M02) fluopyram- <i>Z</i> -olefin (M03) Total identified Sum of unknowns Analysed extract Losses *
fluopyram-di-OH-GA (M21) fluopyram-benol-GA (M07) fluopyram-8-OH-GA (M20), isomer 2 fluopyram-7-hydroxy (M08) fluopyram- <i>E</i> -olefin (M02) fluopyram- <i>Z</i> -olefin (M03) Total identified Sum of unknowns Analysed extract Losses *
fluopyram-di-OH-GA (M21) fluopyram-Benol-GA (M07) fluopyram-8-OH-GA (M20), isomer 2 fluopyram-7-hydroxy (M08) fluopyram-Z-olefin (M02) fluopyram-Z-olefin (M03) Total identified Sum of unknowns Analysed extract Losses *
fluopyram-di-OH-GA (M21) fluopyram-Benol-GA (M07) fluopyram-8-OH-GA (M20), isomer 2 fluopyram-7-hydroxy (M08) fluopyram-Z-olefin (M02) fluopyram-Z-olefin (M03) Total identified Sum of unknowns Analysed extract Losses *
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
Analysed extract
$\frac{\text{Sum of unknowns}}{\text{Analysed extract}} \xrightarrow{\circ} 95.1 \xrightarrow{\circ} 0.3 \xrightarrow{\circ} 0.3 \xrightarrow{\circ} 1 \xrightarrow{\circ} 0.004$
$\frac{\text{Sum of unknowns}}{\text{Analysed extract}} \xrightarrow{\circ} 95.1 \xrightarrow{\circ} 0.3 \xrightarrow{\circ} 0.3 \xrightarrow{\circ} 1 \xrightarrow{\circ} 0.004$
Analysed extract
Losses * $\beta = \beta^{\gamma} + \beta^{\gamma} +$
Losses * $\beta = \beta^{\gamma} + \beta^{\gamma} +$
Volatiles ** Not analysed Total extractable Unextractable residues (solids) Accountability * dichloro@ethane@ethano@luates @ SPE column during clean up ** dichloro@ethane@ethano@luates @ SPE column during clean up ** dichloro@ethane@ethano@luates @ SPE column during clean up ** dichloro@ethane@ethano@luates @ SPE column during clean up
Not analysed Not analysed Total extractable Unextractable residues (solids) Accountability * dichloro@ethane@luates @ SPE column draing clean up ** dichloro@ethane@luates @ SPE column draing clean up ** distillates from @ncentration steps
Total extractable 974 0.361 Unextractable residues (solids) 3.9 0.011 Accountability 100.05 0.372 * dichloromethano@luates 0 SPE coffumn during clean up ** distillates from concentration steps
Unextractable residues (solids) Accountability * dichloromethane/methano@luates of SPE column during clean up ** distillates from concentration steps
Accountability * dichloromethane-fuethanoQuluates of SPE column daring clean up ** distillates from concentration steps
* dichloro@ethano@luates@SPE coffirm draing clean up ** distillates from concentration steps
** distillates from concentration steps
The second se



lactating goat after dosi	on and characterization of radi ng of [pyridyl-2,6- ¹⁴ C] fluopyra	
2.0 mg eq/kg body weig	ht for 5 consecutive days	
	Goat	liver a start
TRR [mg/kg] =	1.4	
Compound	% of TRR	$\begin{array}{c} & & & & \\ & & & & \\ & & & & \\ &$
AE C656948, a.s., fluopyram	7.7 💎	
fluopyram-pyridyl-acetic acid (M40)	-	
fluopyram-hydroxyethyl-GA (M37)	A O	
fluopyram-7-OH-GA (M09), isomer 1	©24.2	
fluopyram-7-OH-GA (M09), isomer 2		0.090 0.0914
fluopyram-di-OH-GA (M21)		
fluopyram-phenol-GA (M07)	2.0 2.0 3.5 4.1 5.7 5.7 5.7 5.7 5.7 5.7 5.7 5.7	
fluopyram-8-OH-GA (M20), isomer 2 fluopyram-7-hydroxy (M08)	$\begin{array}{c} \begin{array}{c} \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} $	
fluopyram- <i>E</i> -olefin (M02)		2 4 058 4 AF
fluopyram-Z-olefin (M02)	3	
Total identified	24.2 2.1 2.0 2.0 9.5 61 61 624 2.0 61 624 624 2.0 2.0 2.	
Sum of unknowns		\sim 0.000
Analysed extract	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.035 · · · · · · · · · · · · · · · · · · ·
Losses *	N 04.8 7	$\sqrt[3]{0}$ 0.014
Volatiles **	A BT A	×0.052
Not analysed ***	6.4 6	₩ 20091
Total extractable ****	Q 5758 0	× × 1.082
Unextractable residues (solids)*****	<u>~</u> ~~222 @	0.346
Accountability	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~
 dichlorofiethane/frethano@luates @ SPE distillates from concentration steps Liver, solvent extracts 4 and 5 Siver: by solvent extracts 4 and 5 Siver: by solvent extracts 4 and 5 Siver: Diver: PES after first microwave extraction Control of the solution of the		×V*



 Table 6.2.3-31:
 Summary of identification and characterization of radioactive residues in kidney of lactating goat after dosing of [pyridyl-2,6-14C] fluopyram at a daily dose rate of 2.0 mg eq/kg body weight for 5 consecutive days

2.0 mg eq/kg bouy weig	git for 5 consecutive days	Č,	
	Goat	kidney 🔊	
TRR [mg/kg] =	0.4		
Compound	% of TRR	🦉 mg a.s. equix	Kg , ? .
AE C656948, a.s.,	- 💎	<u> </u>	
fluopyram-pyridyl-acetic acid (M40)	8.6	<i>€</i> 0. Ø 35	
fluopyram-hydroxyethyl-GA (M37)	A	. 017 ≉	
fluopyram-7-OH-GA (M09), isomer 1	35.1	\$0.14 2	Ŭ JOŬ
fluopyram-7-OH-GA (M09), isomer 2	16.3	0.066	
fluopyram-di-OH-GA (M21)	× 19 ×	y 🖉 🖉 🕺	× v
fluopyram-phenol-GA (M07)	199 5 5.2 5 17.7 9 17.7 9	0.066 0.066 0.007 % 0.013 0.07%	.1
fluopyram-8-OH-GA (M20), isomer 2	17.2° °		
fluopyram-7-hydroxy (M08)		, O [™] Q.004	
fluopyram- <i>E</i> -olefin (M02)			
fluopyram-Z-olefin (M03)	87.9 87.9		
Total identified	87.9 87.9 87.9 87.9 87.9 87.9 87.9 87.9 87.9 9 87.9 9 9 9 9 9 9 9 9 9 9 9 9 9	0.001 0.004 0.	K ²
Sum of unknowns		0 ⁰ .004 [*]	Y
Analysed extract	88.9 4 64 5 64 0.50 4	0.358	
Losses *	N 0.50 N 2	y & 0.002	
Volatiles **	\$ <u>\$</u> .0 <u>\$</u>	0008 · · · · · · · · · · · · · · · · · ·	
Not analysed 🔬 🖧		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
Total extractable	8 91 A O	<u> </u>	
Unextractable residues (solids)	Q [×] QX a. (
Accountability & A	<u></u>	0.403	
* dichloromethane/methano/pluates of SPI	E column during clean up	×Ų	
 dichloromethane/methano@luates @ SPI distillates from @ncentration steps 	E column during clean up	,	
** distillates from Concentration steps	ATTIL Conclusion		
	AllI. Conclusion		
	©III. Conclusion		

One lactating geat was dosed orally for 5 consecutive days with [pyridyl-2,6-14C] fluopyram at a daily dose of 2.0 mg eq/kg of body weight and sacrificed 24 hours after the last dose.

The lactaing goat extensively metabolised AE C565948, but it was still the major compound in milk, muscle and fat (27.3, 46.4% of the TRR) and represented ca. 7.7% of the TRR in liver. The main metabolite in milk, muscle and fat were fluonyram-Thydroxy and fluopyram-Z-olefin, accounting each for up to 21.6 of the TRR, respectively, and represented op to 6.1% and 5.7% of the TRR in the other matrices, respectively. The main compound in fiver and kidney was fluopyram-7-OH-GA (isomer 1), accounting for 24.2–35.1% of the TRR, but only up to 6.6% of the TRR in the other matrices. Further important metabolites in liver in Ridney were thropyram-8-QH-GA (isomer 2; up to 17.7% of the TRR and up to 2.5% in other matrices). The label-specific metabolites fluopyram-pyridyl-acetic acid and fluopyram-hydroxyethyl-GA were only found in kidney at 8.6% and 4.3% of the TRR, respectively.

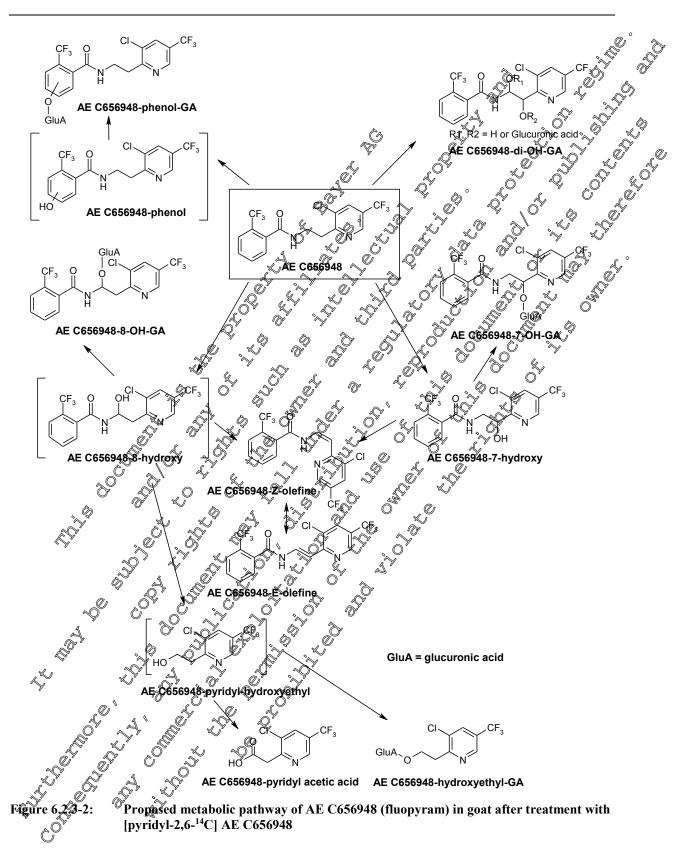
Further detected minor metabolites were fluopyram-*E*-olefin, fluopyram-di-OH-GA and fluopyram-phenol/GA at <5% of the TRR.



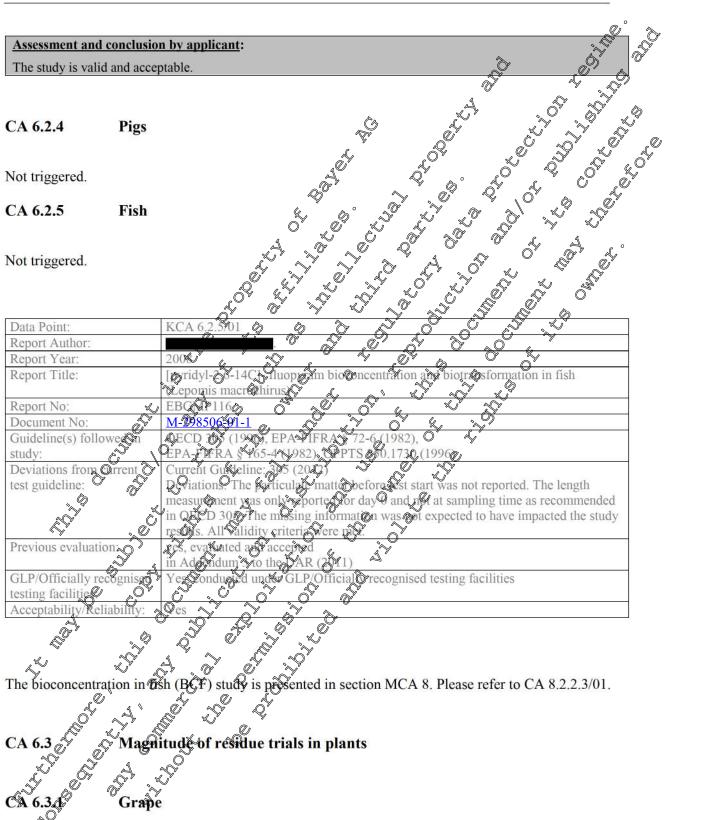
Based on the identified metabolites, the following metabolic routes were deduced:

- hydroxylation of the ethylene bridge of the molecule resulting in fluopyram-7-hydroxy fluo 8-hydroxy, and a dihydroxylated compound •
- hydroxylation of the phenyl ring leading to fluopyram phenol •
- •
- hydroxylation of the phenyl ring leading to huopyrand phenol conjugation of the hydroxylated metabolites with glucuronic acid elimination of water from compounds hydroxylated in the ethylene bridge leading to huopyrand the into each other the state of •
- conjugation of the hydroxylated metabolites with glucuronic acid.
 elimination of water from compounds hydroxylated in the ethylene bridge leading to fluopyram. 2, olefin and E-olefin; E- and Z-olefin can isometise into each other of a conjugation with glucuronic acid.
 oxidation of fluopyram-pyridyl-hydroxyethyl followed fly conjugation with glucuronic acid.
 oxidation of fluopyram-pyridyl-hydroxyethyl followed fly conjugation with glucuronic acid.
 oxidation of fluopyram-pyridyl-hydroxyethyl followed fly conjugation with glucuronic acid.
 oxidation of fluopyram-pyridyl-hydroxyethyl followed fly conjugation with glucuronic acid.
 oxidation of fluopyram-pyridyl-hydroxyethyl followed fly conjugation.









Information on the intended use pattern (GAP) is summarised in Table 6.3.1-1.



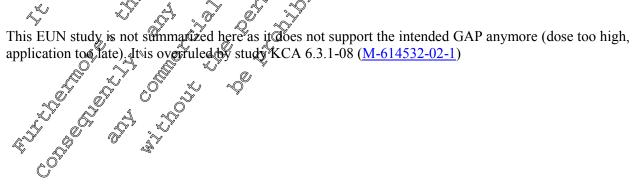
Table 6.3.1-1: Use patterns (critical GAP) for the spray application of Fluopyram in/on grape **European fields (northern and southern residue regions)**

Formulation	F/ GH	No. of appl.	Growth stage at application (BBCH Code)	Application rate per treatment (g as ha)	Water volume (L/Ha)	Interval (days)	
FLU+TFS SC500	F*	2	53-73	50	\$500-750	014	
F field			L.	\sim		Q° ô	

Baseline dossier

fluopyram are part of the baseline dossies Residue trials submitted during the first indusion fulfil the intended GAP anymore.

	KCAG5.1/05 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
Data Point:	KCAG3.1/0
Report Author:	
Report Year:	
Report Title:	Determination of the residues of AE C656948an on prove after spraying of AE
×.	C654748 (500 SC) in the field in Nonhern France and Germany
Report No:	$RA^{2}61 RF$ q r q r $O' ~ q$ r
Document No:	<u>49-296805-01-</u>
Guideline(s) folloved in	EU-Ref. Council Directive 9, A14/EIG of July 15, 1991, Annex II, part A, section 6 and Anney W, parts section 8
Guideline(s) folloved in study:	and Annex 41, part 2, section 8 Residues in or on Freater Froduce, Food and Feed EC Guidance Working Document
	Residues in or on Vreater Froduce, Food and Feed EC Guidance Working Document
	7029/V095 rev 5 (1995-07-225 US-EIA OPD 3 Guideline No. 860.1500
	Support mental V
Deviations from current test guideline:	
Provious evoluation	
Previous evaluation	yes, exclusived and accepted of the second s
GLP/Officially recognized	Yes, conducted under GIO/Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes 2 4 5 6 6
	Yes 2 AF B B
× ×	





Data Point:	KCA 6.3.1/02
Report Author:	
Report Year:	2008
Report Title:	2008 Determination of the residues of AE C656948 in/on grape after low-volume of raying of AE C656948 (500 SC) in the field in Southern France
	of AE C656948 (500 SC) in the field in Southern France
Report No:	RA-2647/06
Document No:	<u>M-296564-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/414/EC of July 15 991, Annex II oart A Section and Annex III, part A, section 8 Residues in or on Treated Products, Food and Bed EC Guidano Work g Dooment 7029/VI/95 rev. 5 (1997-07-7), Equivalent to US EPA OPP S Guideline Str. 860, 600 (SUPP)
study:	and Annex III, part A, section 8 4
	Residues in or on Treated Products, Food and Ec Guidano Work g Dooment
	7029/VI/95 rev. 5 (1997-07-20),
	Equivalent to US EPA OPPS Guideline Nr. 860, 600 (SUPP)
Deviations from current	7029/VI/95 rev. 5 (1997-07-25), Equivalent to US EPA OPT S Guideline NY. 860, 900 (SUPP)
test guideline:	
Previous evaluation:	yes, evaluated and recepted @ @ Q rev. 1 to Vol.3 of OAR BC August 2012 seferences relief on)
	rev. 1 to Vol.3 of DAR BC August 2012 seferences relief on)
GLP/Officially recognised	
testing facilities:	Yes, conducted ender (http://officially.revognisgotestingstacilities
Acceptability/Reliability:	Yes y y y y y y y y y
	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
	Yes y y y y y y y y y y y y y y y y y y y
	when the first of the second s

This EUS study is not summarized for as to does not support the intended GAB anymore (dose too high,
This EUS study is not summarized here as 10° does not support the intended GAB anymore (dose too high, application too late). It is overruled by studies (SCA 6.3.1-10 (<u>M-65) 354-024</u>) and KCA 6.3.1-11 (<u>M-65) 354-024</u>)
643609-02-1).
$\underbrace{643609-02-1}_{67}$

Data Point:	
	KCA 6.3.1 (0)
Report Author:	
Report Year ??	
Report Title.	Determination of the Residues of AE @65694@in/on table grape after spraying of AE
	Determination of the residues of AE @65694@in/on table grape after spraying of AE C65948 (50 SC) in the End in Spain, Portugal, Italy and Greece
Report No:	RA-2613406 3 3 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4
Document No:	$\underline{M}-296714-0124$
Report No: Document No: Guideline(s) followed ino study:	EUSef: Concil Directive 91/414/OCC of July 15, 1991, Annex II, part A, section 6 act Anney III, pro A, section 8
study:	a Anne VIII, pro A, section 8 S
× •	Residues in or an incace into dets, i bod and i eeu Le Ouidance working Document
	702 C $1/95$ A 2 3 $(1057-07-07)$;
	Ecovalent US KVA OPATS Guideline No. 860.1500 (SUPP)
Deviations from current	$a_{\rm one} \sim \sqrt{2} \sqrt{2}$
test guideline:	
Previous evaluation:	yes waluated and wepted
	reveal to Val.3 of VAR B7 August 2012 (references relied on)
GLP/Officia Orrecognised	es, conducted under GLP/Officially recognised testing facilities
testing facilities.	
Accepta Mity/Ronability	Yes
testing factories: A ccepta dity/Restability	
Ô	



This EUS study is not summarized here as it does not support the intended GAP anymore (dose too high, application too late). It is overruled by studies KCA 6.3.1-10 (M-653354-02-1) and KCA 6.3.1-11 (M-643609-02-1).

Data Point:	KCA 6.3.1/04
Report Author:	
Report Year:	
Report Title:	Determination of the residues of AE C656948 fron grape after ow-volume spoying and spraying of AE C65694 (0500 SC) in the field in Northest France and Germany
Report No:	RA-2500/07
Document No:	<u>M-298193-01-1</u>
Guideline(s) followed in	<u>M-298193-01-1</u> EU-Ref: Council Directive 9% 14/EIC, of July 15, 1901, AngeX II, part A, section 6
study:	and Annex III, part A section 8; Readues infor on Treated Products 1 ood and Feed.
	Equivalent to USEPA CRYTS Chydeline Io. 86(7), 500 (SUPP)
Deviations from current test guideline:	Equivalent to USEPA ORFTS Gradeline to . 860 500 (SOPP)
Previous evaluation:	yes, evaluated and accepted
	rev. 1 to Vol.3 @DAR @ Aug at 2012 Pefere @es relief on)
GLP/Officially recognised	Yes, anducted under CLP/Operially@cognied testing facilities
testing facilities:	
Acceptability/Reliability:	

This EUN study is not summarized here as it does not support the interfaed GAP anymore (dose too high, application too late). It is overruled by study KSA 6.3 P 08 (M_2 614582-02-10)



This EUS study is not summarized here as it does not support the intended GAP anymore (dose too high, application too late). It is overruled by studies KCA 6.3.1-10 (M-653354-02-1) and KCA 6.3.1-11 (M-643609-02-1).

Data Point:	KCA 6.3.1/06
Report Author:	
Report Year:	
Report Title:	Determination of the residues of AE C656948 from table grap Oifter sprying O AE C656948 (500 SC) in the fig/O in Spain, Portugal and taly
Report No:	RA-2502/07
Document No:	<u>M-298633-01-1</u>
Guideline(s) followed in	M-298633-01-1 EU-Ref: Council Directive 9% 14/ERG of July 15, 1901, Ang X II, part A, section 6
study:	and Annex III, part A section 8: Readues in on Treated Products Food and Feed.
	Equivalent to USEPA ORY TS Guideline No. 8667, 500 (SUPP)
Deviations from current test guideline:	Equivalent to USCPA ORPTS Gradeline to . 860-500 (SOPP)
Previous evaluation:	yes, evaluated and accepted 2012 reverse relieven and accepted 2012 reverse relieven and accepted and accepte
	rev. 1 to Vol.3 ODAR to Aug 2012 Vefere Des relief on)
GLP/Officially recognised	Yes, anducted under CLP/Opticially @cognised testing facilities
testing facilities:	
Acceptability/Reliability:	

This EUS study is not summarized here as it does not support the interfeed GAP anymore (dose too high, application too late). It is overrailed by studies KCA (0.3.1-10) (M-653354-02-1) and KCA (0.3.1-11) (M-643609-02-1).

Data Point: KO\$ 6.3.1/07
Report Author: $\sqrt{2}$
Report Year: 2008 2 0 0
Report Title:Q AF \$6569 \$500 \$\$ - Magnitude, the residue on small fruit vine climbing
sügrour 3F, except fuzőv kiwiðrit
Report No:
Document To: <u>M-299437-0171</u> &
Guideline (s) followed in EPR Reference: QPTS 200.1500, Crop Field Trials
study MRA Beference DACO 7.4.1 Supervised Residue Trial Study
PMR& Reference: 12, 20 7.4.2, Residue Decline Study
Deviations from current non v v
test guideline A Q A Q
Previous evolution Ses, evaluated and accepted
C rev to Vold of DAR B7 August 2012 (references relied on)
GLP/Orocially@cognised Yo, conducted under GLP/Officially recognised testing facilities
testing facilities: A. Co
Acceptabil@/Relignity: Yes
$\mathcal{O}^{\mathcal{O}^*}$



This US study is not summarized here as EU data are required for this renewal dossier. It is overruled by studies KCA 6.3.1-08 (M-614532-02-1), KCA 6.3.1-10 (M-653354-02-1) and KCA 6.3.1-11 (M-643609-02-1).

Supplementary dossier

Residue trials were conducted in Europe (north and south) at the intended of at a similar GAI

In the <u>Northern zone</u>, eight residue trials were conducted in the 2016 growing season with a higher dose of rate compared to the supported GAP. As all other GAP parameter respect the GAP can downscaling factor is applied to the residue results. According to EFSA technical Report (EFSA supporting oublication 2018-EN-1503), the proportionality concept can be applied to residue data from field trials conducted within a dose rate range of between 0.3x and 4x the GAP dose rate.

As the northern zone trials were applied at a BBCH growth stage of 69 (instead of 73 in the representative GAP), it is demonstrated below that the residues obtained from trials treated a BBCH 69 are comparable with residues from trials treated at BBCH 73. The comparability is shown below with the help of SEU data. In the <u>Southern zone</u>, eight residue trials were conditized in the 2019 growing season

- Study 17-2112 : 2x37.5g @j/ha, last application BBCD 73, interval @12 days
- Study 17-2128 : 2x50g av ha, last application at BBCH 73, interval H-12 days 炎

 Table 6.3.1- 2:
 Overview of European residue relats conducted in grape per geographical

 "residue region" and vegetation period
 Image: Second Seco

Crop	No. of independent trials Report No Document number Begion Vegetation period Σ Communication Document number 2016 2017 Σ Communication Communication Communication	Reference
Wine	NEU 8 8 8 8 6 (FLO SC500) <u>M-614532-02-1</u>	KCA 6.3.1/08
Wine grape	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	KCA 6.3.1/10 KCA 6.3.1/11

Northeen zone

For the comparison of data sets obtained after applications of fluopyram on vines at BBCH 73 Vs BBCH 69, two sets are taken from Southern European trials.

- Study 16-2197 (M-61 678-01, KCA 6.3.1/09): 2x100 g ai/ha, last application at BBCH 69, interval 12 days
- Study 17-2112 (<u>42-653354-02-1</u> KCA 6.3.1/10) : 2x37.5 g ai/ha, last application at BBCH 73, interval 12 days
- Study 97-2128 (<u>M-643609-02-1</u>, KCA 6.3.1/11): 2x50 g ai/ha, last application at BBCH 73, interval



As the dose rate is the only GAP parameter which differentiate the studies, the study results from 17-21/2and 17-2128 are upscaled to make the residue data comparable with study 16-2197 which is applied at twice 100 g ai/ha.

Table 6.3.1- 3:	Upscaled residues of SE	U trials conducted at BBC	H 73 to simu	late 2 application	
	at 100 g ai/ha	۵.	×7	, Ô [°] ô [°] , Q	

		0		(CA	,	
Study number	Trial number	Dose rate (g ai/ha)	Interval (days)	BBCH at application	Residue at harves (mg/kg) reponed unround	residues x
	17-2112-01	2 x 37.5	7	∞73	\$0.01 0.006	
17 2112	17-2112-02	2 x 37.5	12	× 7,¢° ړ	\$ 0.03 6 x 9.030	0.078 × V
17-2112	17-2112-03	2 x 37.5	12	× 790° ×73° ×73° ×73°	0.014 0.012	0.036
	17-2112-04	2 x 37.5	ð,	73	~<0.01 <u>1</u> 0000	9 0,002
Study number	Trial number	Dose rate (g ai/ha)	Paterval (days)	BBCH at application	reported unround	led 2
	17-2128-01	2 x 50	<u>,</u> ≪12 0	A3 .0	0.04 80.01	© [∞] ≫0.02
17-2128	17-2128-02	2 ¥ 50 🔬	125	73	Ø.01 & 0.91	0.02
1/-2128	17-2128-03	× 2 x 50 °	2°2	¢ 73°	0.038	0.076
	17-2128-04	2 x 50	َنْهُ 11 مَ [ْ]	<u></u>	0.033	0.066
				57 57 59 57		100 10

		Ś			y _N y	<i>a</i>	O	N I	
Table 6.3.1- 4:			Ň.				~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.	100 10
Table 6.3.1- 4:	Resta	ues of	SEU (ria	als condu	icted at B	RCH (by with 2	jäppl. at	100 g ai/ha

Study number S	Trial® number	Døse rate (g ai/ha)	Interval ©	BBCH at application	Residues at harvest
A S	16-2197-01		12	\$ 6 \$	0.030
	16-219502	x2 x 100	. Ô [™] 2 , >	<u>د</u> 69 م	0.030
	16-2097-03	2 x 90	× 120°	0 [°] 69	0.015
16-2197	1@2197-00	2×100 C	d ² ô		< 0.01
10-2197	16-2197-05	$2 \times 100^{\circ}$	Q ¹²	<u>م</u> و	0.035
l d	້ 16-2197-06ວ	2 2 200	F 12	s 69	0.015
	16-2197-07	2 x 100	\$ ¹²	69	< 0.01
S.	16-2197-08	2 x 100	Q 12	69	< 0.01

The two data sets are submitted to clatistical tests to show if it can be considered that they belong to the same population. The comparability test Whitney Mann Willcoxon show that the two data sets are comparable. The Krusk Walks test (appropriate test according to FAO report 2009) concludes that the data samples are likely to come from the same population.

As a conclusion, residues in grapes at harvest are similar after two applications of fluopyram when the last application is done either at BBCH 69 or BBCH 73 in southern Europe.



By extrapolation, we can consider that residue data at harvest are similar also in Northern Europe after two applications of fluopyram when the last application is done either at BBCH 69 or BBCH 73. Thus, the sight residue trials from the study 16-2157 (M-614532-02-1, KCA 6.3.1/08) and conducted with the last application at BBCH 69 are considered acceptable.

Nevertheless, the northern study 16-2157 was conducted at a higher application rate of 2x100 g/ha compared to the representative GAP. As all other GAP parameter respect the GAP, a downscaling factor is applied to the residue results. According to EFSA Technical Report (EFSA supporting publication 2078-EN-1503), the proportionality concept can be applied to residue data from field trials conducted within a dose rate range of between 0.3x and 4x the GAP dose rate.

	KCA 6.3.1/08
Data Point:	KCA 6.3.1/08 A R A A
Report Author:	
Report Year:	
Report Title:	Amendment for 1 to that report - Determination of the residers of floopyranon/on
_	grape after spray application of fluopyram SC 500 for Germany, the United Kingdom,
	Hungary and Northern Exance S. St O G St K
Report No:	
Document No:	$M - 60/7532 - 02^{-1}$ $M = 0^{-1}$
Guideline(s) followed in	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21
study:	October 2009 concerning the placing of plant protection products on the market
*	OEC Guideline for the Testing of Chemicals on Gran Field Trial (TG 509
-\$*	published in September 2009
Deviations from current test guideline: Previous evaluation:	US EPA OCSPP 860.1500, Crop Field Trial
Deviations from curtont	
test guideline:	
Previous evaluation:	No not proviously submitted Study was not found in DAR/RAR and the Addenda
$\langle \mathcal{A} \rangle$	Study was not found in DAR/RAR and the Addenda
GLP/Officially recognised	Yes, conducted under OBLP/OTHCIally recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes in the second secon

Materials and Methods 🔏

Eight residue trials on grapes were conducted in northern Europe (in Germany, the United Kingdom, Hungary, and northern France) during the 2016 Gason. Two spray applications (each) for treated plot 1 (T1) and treated plot 2 (T2) were carried out with Fluopyram SC 500 (SC 500). These applications were conducted with the interval between applications of 12 days and at the application rates of 0.2 L/ha corresponding to the application rates of 0.4 kg a.s./ha and water rates between 500 – 1000 L/ha.

As the dose rate is higher than the intended GAP (2x100g as/ha Vs 2x50g as/ha), the residues are downscated by applying the scaling factor of 0.5.

Each tual contained two plots representing applications in different BBCH stages: Plot 1 (T1) includes last (2nd) application at BBCH 69 and plot 2 (T2) includes last (2nd) application at BBCH 79. The aim was to verify the impact of the BBCH stage of the latest application in the final residues at harvest.

For both plots, samples were collected at BBCH 79, BBCH 85, and BBCH 89.



All field samples were shipped deep-frozen under monitored conditions during shipment. The field samples were stored in a freezer at \leq -18 °C until preparation of the examination samples.

For the preparation of examination samples, the deep-frozen field samples were shreaded and homogenised with dry ice in a cutter and transferred into polystyrene boxes and stored at ≤ -18 for until analysis.

Samples were analysed according to the analytical method 00984/M003 (2015, <u>M467323-03-</u> <u>1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EV regulatory regulatory builting within SANCO/3029/99 rev 4.

However, slight adaptions were made to the extraction procedure described within the analytical method modification 00984/M003 which are as follows: residues were extracted from 5.0 of sample material by extraction using a shaker (15 min) with a mixture of acetonitrile water (4-1, v:x). The filtering procedure under low vacuum was replaced by a centrifugation step. Then, 0.5 mL of internal standard solution (1 mg/L) were added to the extract followed by 5 min centrifugation at 050 rpm at 10.°C and further proceeded to the HPLC-MS/MS analysis

The linearity was demonstrated in each analytical batch with a 4/x weighted calibration curve established with at least 5 concentration levels.

The quantification was done by interval standardization using isotopically stable table tabelled internal standards. All final extracts were analysed within two days after the preparation. Fuopycan and fuopycan benzamide were found to be stable in extracts of matrices of plant origin for at teast four weeks at 4 ± 3 °C which was tested within the validation of method 00984/M003

The Limit of Quantification (LOQ), expressed as fluoryram, defined as the dewest validated fortification level, was 0.01 mg/kg.

Finding

In order to check the performance of the method, concurrent recovery determinations were included in each set of analyses (at least one recovery for ten audy samples). Control samples from the study were fortified to be used as the recovery samples. The apparent residues in the control samples used for the performance of recoveries were below 30 % of the LOQ. The recoveries were not corrected for apparent residues in the control samples.

The mean recoveries per fortification level were within the range of 70 % – 110 % except for the LOQ level for fluopyram (116 %) and for the LOQ level for fluopyram-benzamide (111 %). However, these recoveries were within the criteria of the DECD guidance document ENV/JM/MONO(2007)17. Thus, these results were considered acceptable. The RSD values were below 20 %. The overall mean concurrent recoveries were in the acceptable range of 70% and 110% with the RSD < 20%.

The storage period of deep-frozen samples intended for the analysis of fluopyram and its metabolite fluopyram-benzamide ranged between 82 and 172 days. The detailed results obtained for bunch of grapes samples in northern Europe are summarized in the Table 6.3.1- 6, where the scaling factor and the total residue downscaled are also presented.

Genclusions 2 . S

Eight supervised residue trials on grapes were conducted in northern Europe with the application of Fluopyram SC 000 (SC 500) at a higher rate than required in the supported GAP (2x100g as/ha Vs 2x50g as/ha), and according to GPP. Samples of bunch of grapes were analyzed for the residues of fluopyram and its metabolite fluopyram benzamide. The results of the trials presented above show residues at harvest for the plots with last application at BBCH 69 :

•C Fluopyram residues range between <0.01 and 0.04 mg/kg.



Fluopyram-benzamide residues were <0.01 mg/kg when the last application was done at BBCA 69.

B

The total residue of fluopyram (sum of FLU + FLU-benzamide, expression as fluopyram) after downscaling to the right dose (2x50g Vs 2x100g ai/ha)), range between $\sqrt{501}$ and 0.049 mg/kg

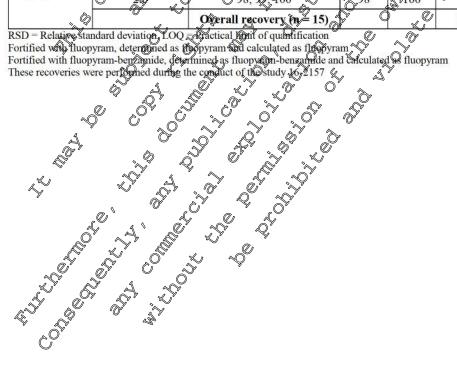
Assessment and conclusion by applicant:

The study is acceptable.

The residue level in these GLP trials was corrected with a poportionality actor according to Report (EFSA supporting publication 2018-EN-1503). Ø

Recovery Ő Portion Fortification RSD analysed level (mg/kg) Individual Mean Max Min recoveries Fluopyram (AE C656948) Ô 112 115: 0.01 109; 109; 110; 111 110 0.9% grape / bunch 0.10 100 1.5 of grapes \$99: 10 102 099 2.0 \$102 1010 Ô \cap Overall recovery (4+13) tie \sim 3.8 2 **K** Fluopyram-benzamide 10, M10; 10, 111; 4 114 113 C 1.3 112; 113; 113 10 107 \$106 grape / bunch L, 104; 105; 106; 107 1.2 0.16 of grapes 98: 99: 900 98 **\$100** 99 1.0 \bigcirc Obserall recovery (n = 15)107 4.8

Table 6.3.1- 5: Concurrent recovery data for Fluopy am (study



BAYER ER

Page 314 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Арј	olication rate treatment	per	Dates of treatment / Application interval	Growth stage at Ost treatment	Portion analyzed	Growth stage at sampling	K) [©] *	s (mg/kg) [×]				PHI (days
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	P ^{TO(c)}	(d)		(d)	C656948	AEO C 656948 - benzamide	Total residue calc.	Scaling factor	Scaled residue	(e)
6-2157-01 16-2157-01- 11 Germany 77704 Dberkirch Europe, North 7 2016	Grape Muscat bleu; table grapes	1) 2003 2) 12.06.2016 - 22.06.2016 3) 25.08.2016 - 02.09.2016	100 100		1250 NS	10.06.2016/0 22.00.2016/12 50.000		r ré			A Y	calc. *	0.5 \$\$	0.025 0.017 <u>0.012</u>	0 51 65
16-2157-01 16-2157-01- T2 Germany 77704 Oberkirch Europe, North F 2016	Grape Muscat bleu; table grapes	1) 2003 2) 4 00:2016 - 22.06.2016 3) 25.08.2016 - 02.09.2016		800 F 800 F 102 F	12.5 × 125 0		Putito Datase Da 73-13-10 Da 73-13-10 Da 73-10 Da 73-10 D	R ^E E	79 79 85 89 20 20	0.12 0.38 0.085	<0.01 <0.01 <0.01 <0.01	0.13 0.31 0.14 0.095	0.5	0.065 0.16 0.070 0.048	0 0 22 36
6-2157-02 6-2157-02- 11 Germany 9356 Eichstetten Europe, North	Grape Acolon) 2009 2) 13.06.2016 - 23.06.2016 3) 05.09.2016 - 15.09.2016 - 15.09.2006 - 15.0				2006.20160 22.06.2008/12	69	bunch of grapes	79 85 89	0.028 0.021 <0.01	<0.01 <0.01 <0.01	0.038 0.031 <0.02	0.5	0.019 0.016 ≤0.01	0 51 78



Page 315 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

												<u> </u>		<u>e</u>	2
									Â		Ô	<u>D</u>	_	2 Julie	- CLO-
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Арг	olication rate treatment	per	Dates of treatment / Application interval	Growth stage at last « treatment	Portion malyzed	Growth stage at sampling	Beinu P	es (mg/kg)	ection	197 197		PHI (days)
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	(c)@\$ ⁵			(d) (d) (d)	C050948	SE €656948 benzamde	çal	al."	Scaled Residue	(e)
16-2157-02 16-2157-02- T2 Germany 79356 Eichstetten Europe, North F 2016	Grape Acolon	1) 2009 2) 13.06.2016 - 23.06.2016 3) 05.09.2016 - 15.09.2016	100	800 800	12.5 12.5 * 12.5	47.07.2016/02 97.07.2016/02 12 97.07.2016/02	27200 27200 5	Sunch of S	279 \$ 79 85 0 \$ 85 0 \$ 80 0 \$ 0 \$		0.044 0.046 0.026 2 ⁶ 0.026	0.37	e f	0.19 0.34 0.17 0.075	0* 0 16 43
2016 16-2157-03 16-2157-03- T1 United Kingdom GL181LS Newent Europe, North F 2016	Grape Sauvignon Blanc; White grape	1) 1997 2) 11.07.2010 - 25.07.2016 3) 42 07.2016 10.2016	oject		Carl Or) et		0,15 0.087 0.087 0.087	<0.01	0.16 0.062 0.097	0.5	0.080 0.031 <u>0.049</u>	18 44 74
16-2157-03 16-2157-03- T2 United Kingdom GL181LS Newent Europe, North F 2016	Grape Sauvignon Blanc; White grape	1) 1007 2) 11.07.2016 2 25.07.2016 3) 12.10.2016 - 17.10.2016 - 17.10.2016			h6.999	06.08.2016/0 × 08.2016/12 016.12 016.12 016.12 016.12 016.12 016.12 016.08 000 016.08 00000000000000000000000000000000000	Jun 1	Brunch of	79 79 85 89	0.16 0.38 0.070 0.062	<0.01 <0.01 <0.01 <0.01	0.17 0.39 0.080 0.072	0.5	0.086 0.20 0.04 0.036	0* 0 26 56
E JI	ther the	and witch		De Ei	Ohr					<u>.</u>					315



Page 316 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

												a)
									Ċ.		T			J'Ille	- CLO-
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Арј	plication rate treatment	per	Dates of treatment / Application interval	tractfront	Portion malyzed	Growth stage at sampling	Residu	ی بر ^{سری} es (mg/kg)	20til	190 190		PHI (days)
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	(c) (c)		~~ ^{e°}	(d)	AE C656948	©C656948- C benzamide	Total residue çalç	Solating factor	Scaleat residue	(e)
16-2157-04 16-2157-04- T1 Hungary H-4461 Nyirtelek - Ferenctanya Europe, North F	Grape Cserszegi fuszeres; White grape	1) 2001 2) 16.05.2016 - 30.05.2016 3) 10.09.2016 - 25.09.2016	100	700 700	14.285 14.285	G ^Y CID 6		r E		OCUIT	ent ent	0.062	EF °	0.12 0.04 <u>0.031</u>	0 85 94
2016 16-2157-04 16-2157-04- T2 Hungary H-4461 Nyirtelek - Ferenctanya Europe, North F	Grape Cserszegi fuszeres; White grape	1) 2001 2) 16.05 2006 30 05.2016 10.09.2016 - 25.09.2016		100 5 200 5 2015 9 2015 9	OF RBY				89 79 89 89	0.20 0.46 0.12 0.12	(0.01) (0.01) (0.01) (0.01)	0.21 0.47 0.14 0.12	0.5	0.11 0.24 0.07 0.06	0* 0 53 62
2016 16-2157-05 16-2157-05- T1 Hungary H-3905 Monok Europe, North F 2016	Grape Furmint; White grape	1) 1986 2) 12.05.2016 - 25.05.2016 3) 01.09.2016 - 15.09.2016			14.285	203 .06.201 6 0	\$ O *	bunch of	79 85 89	0.10 0.054 0.041	<0.01 <0.01 <0.01	0.11 0.064 0.051	0.5	0.055 0.032 <u>0.026</u>	0 84 93
Č.	thertune	any witch	N ^L	10 ⁶ 21	Olive Depe										316



Page 317 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

												A		R	>
									Ĉ		9IC			J I The	-O-O-
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Арј	plication rate treatment	per	Dates of treatment / Application interval	Growth stage at last « treatment	Portion Smalyzed	Growth stage at sampling	Residu	es (mg/kg)	ect ^{itor}			PHI (days)
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	(c)e ² ⁺		19 1700	(d) 7 (d) 7	AE C656948	SE C656948 benzamde	Total residue cal©	0	Scaled Residue	(e)
16-2157-05 16-2157-05- T2 Hungary H-3905 Monok Europe, North F 2016	Grape Furmint; White grape	1) 1986 2) 12.05.2016 - 25.05.2016 3) 01.09.2016 - 15.09.2016	100	700 700	14.285 14.285	^{gu} ch		Legu:					Cont of the second seco	0.085 0.19 0.075 0.075	0* 0 53 62
16-2157-06 16-2157-06- T1 France, north 51220 BRIMONT Europe, North F 2016	Grape pinot noir	1) 1999 2) 21.06.2016 - 03.07.2016 3) 20.99 2016 - 2009 2016	je ^{c*}		02		0° 69 N ⁶⁶			0.0730 @335 0.049 0.049	<0.01 <0:01	0.083 0.045 0.059	0.5	0.042 0.023 <u>0.030</u>	0 57 79
16-2157-06 16-2157-06- T2 France, north 51220 BRIMONT Europe, North F 2016	Grape pinot noir	1) 1999 2) 21.00.2016 1 - 03.07.2016 3) 20.09.2016 - 20.09.2016	100 00 00 00 00 00	720 720 120 110 10 11 10 11 10 11 10 11 10 11 10 11 10 11 10 11 10 11 10 11 10 11 10 11 10 11 10 11 10 11 10 11 10 11 10 11 10 10		02 27.07.2016/0 08.08.0016/12 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10 1 1 79	bursh of Stapes	ř 79 79 85 89	0.15 0.30 0.18 0.12	<0.01 <0.01 <0.01 <0.01	0.16 0.31 0.19 0.13	0.5	0.08 0.16 0.095 0.065	0* 0 21 43
EUI	thermo	ant on com		De Pi	Older	y									317

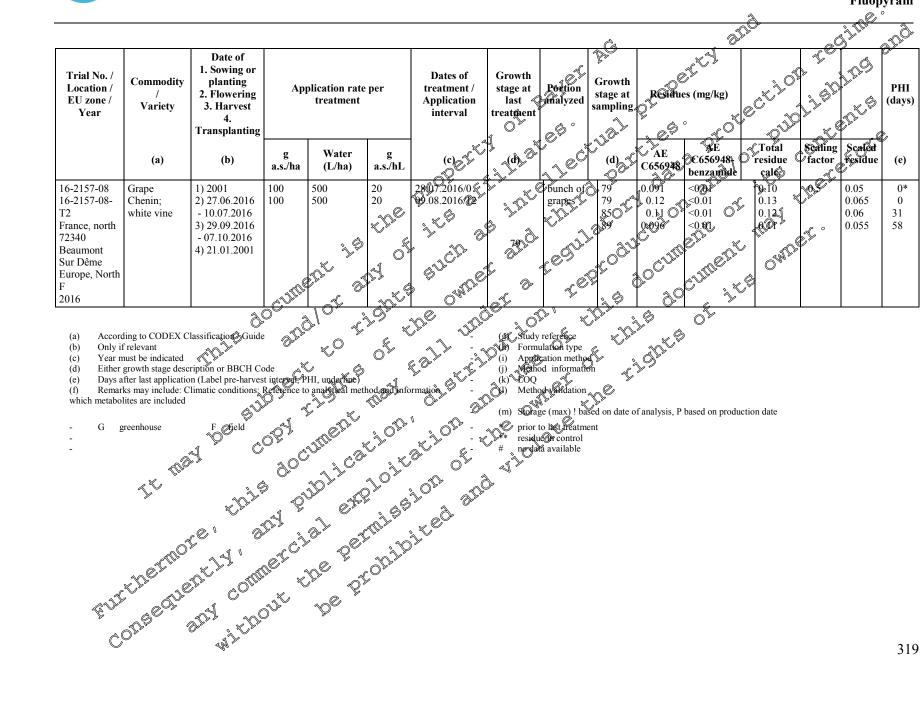


Page 318 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

												a .		<u>e</u>)
									Â		9.j		_	J I The	- CLO-
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Арј	plication rate treatment	per	Dates of treatment / Application interval	Growth stage at last « treatment	Portion Inalyzed	Growth stage at sampling	Residu	ی (mg/kg) • • • • • • • • • • • • • • • • • • •	sctio?			PHI (days)
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL		i jan	~~ ^{e°°}	d Q	AE C656948	C656948+ C benzamide		al (Scaled residue	(e)
16-2157-07 16-2157-07- T1 France, north 41150 Mesland Europe, North F 2016	Grape Chardonnay; white vine	1) 1956 2) 22.06.2016 - 06.07.2016 3) 05.10.2016 - 07.10.2016	100	500 500	20 20 5 0 5 0 5 0 7	^{guçîn} e		regui)		C656948 0.91 0.085 0.056 C ¹ 0.0 ¹ 0.056 0 ¹ 0.0 ¹	ent and a start	9:12 0.095 0.066		0.06 0.048 <u>0.033</u>	0 68 82
16-2157-07 16-2157-07- T2 France, north 41150 Mesland Europe, North F 2016	Grape chardonnay; white vine	1) 1956 2) 22.06.2016 - 06.072016 3.02 10.2016 - 07.10.2016		500 49.222223 50 50 50 50 50 50 50 50 50 50 50 50 50	Carl .					0.080 9.21 0.13 0.098		0.099 0.22 0.14 0.11	0.5	0.050 0.11 0.07 0.055	0* 0 39 53
16-2157-08 16-2157-08- T1 France, north 72340 Beaumont Sur Dême Europe, North F 2016	Grape Chenin; white vine	1) 2001 2) 27.06.2010 2 10.07.2016 3) 29.09.2016 - 07.10.2016 4) 21.01.2001 0 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1				28.06.2016/0 × 30-07.2016/12	69	Brunch of	79 85 89	0.11 0.065 0.030	<0.01 <0.01 <0.01	0.12 0.075 0.040	0.5	0.06 0.038 <u>0.02</u>	0 61 88
E JII	there are	ant la com any com		De Bi	0 7 p =										318



Page 319 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram





Southern zone

	\sim
Data Point:	KCA 6.3.1/10
Report Author:	
Report Year:	
Report Title:	Amendment no. 01: Determination of the residues of trifloxystrobic and AB C656948 in/on grape after spray application (high Volume and low-volume) of AC
-	C656948 in/on grape after spray application (high Volume and low-volume) of A
	Amendment no. 01: Determination of the residues of trifloxystrobic and AF C656948 in/on grape after spray application (high Volume and low-volume) of AE C656948 & CGA279202 SC 500 in Italy, southern France and Spain
Report No:	17-2112
Document No:	<u>M-653354-02-1</u>
Guideline(s) followed in	Regulation (EC) No 116 2009 of the European Parliament and of the Council of 21
study:	October 2009 concerning the placing of plant protection products on the market
	OECD Guideline for the Testing of Chemicals on Crop Field Trial OG 509
	OECD Guideline for the Testing of Chemicats on Crop Field Trial (°G 509) published in September 2009) V O V O V O V O V O V O V O V O V O V
	US EPA OCSP 860.4500, Crop Field Prial OV
Deviations from current	
test guideline:	
Previous evaluation:	No. not previously submitted of A of A
	Study was not found in DAR A AR apd the Addenda O $\sim O$
GLP/Officially recognised	Yes, conducted under GLP/Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
ž.	

Materials and Methods

Four residue trials of grapes were conducted in southern Europe (in Italy, in southern France, in Spain) during the 2017 season. Two spray applications were carried out with PLU+TFS SC 500, a SC (suspension concentrate) formulation contracting 250 g/L of fluoryram and 250 g/L of trifloxystrobin.

For the purpose of the result for floopyram and its metabolite fluopyram-benzamide will be presented discussed

The applications were conducted with the interval between applications of 12 days (except for the trial 17-2112-01 and 97-2112-04 for which the application interval was 7 and 9 days, respectively) and at the application rates of 0.15 0/ha corresponding to the application rate of 0.038 kg a.s./ha and water rates between 200 - 1000 L/ba.

The last application was performed at BBCH 73 (and application).

Samples of grapes were collected at the BBCH stage of 73, 79, 85, and 89.

All field samples were shipped deep-trozen under monitored conditions during shipment. The field samples were stored in a freezer at ≤ 18 °C until preparation of the examination samples.

For the preparation of examination samples, the deep-frozen field samples were shredded and homogenized with dry see in a cutter and transferred into polystyrene boxes and stored at \leq -18 °C until analysis.

Samples were analysed according to the analytical method 00984/M003 ($\underline{1}, 2015, \underline{M-467323-03-1}$, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented



within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues were extracted from 5 g of sample material by extraction with a mixture of acetonitrile water (4:1, v:v). The final determination was performed with HPLC-MS/MS.

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established with at least 5 concentration levels.

The quantification was done by internal standardization using sotopically stable labelled overnal standards The Limit of Quantification (LOQ), expressed as fluopyram, defined as the lowest validated fortification

level, was 0.01 mg/kg.

The time between the beginning of the specimen preparation (extraction) and the specimen analysis did not exceed 16 days while stored at 1-9 °C in the datk. Flugpyram and flugpyram benzamide were found to be stable in extracts of matrices of plant origin for at least four weeks at 4 ± 3° C which was tested within the validation of method 00984/M003.

Findings

The apparent residues in the control sample used for the determination of tecovenes were below 30 % of the LOQ. Recoveries were not conjected for apparent residues in the control samples used for these determinations.

In order to check the performance of the method, recovery determinations were oncluded in each set of analyses (at least one recovery for ten study samples). Control samples from the study were fortified to be used as the recovery samples. All the recovery determinations were performed concurrently to the analyses of control and treated samples from the study. Ø

The mean recoveries per fortification level-were within the range of 70% – 14%% and the RSD values were below 20 %. The overall mean concurrent recoveres were also in the acceptable range of 70 % and De Co 110 %, with the RSD < 20 %.

The storage period of deep Grozen samples introded for the malysis of fluopyram and fluopyrambenzamide ranged between 263 and 382 days. The detailed results obtained for bunch of grapes samples in southern Europe are summarized in the Table 03.1-8.

Conclusions

Ő Four supervised stidue trials of grapes were conducted in southern Europe with the application of FLU+TFS SC 500 at the required rates (within ± 25% of the supported GAP) and according to GLP. After a last application at BBCH 76, the samples of bun of grapes were analyzed for the residues of fluopyram and its metabolite fluopyrm-benzamide The results of the trials presented above show residues at harvest.

- Fuopyram residues range between <0.01 and 0.03 mg/kg.
- Fluopyram-benzamide residues were <0.01 mg/kg.
- The total residue of flug fram frum of FLU + FLU-benzamide, expressed as fluopyram) range between 0.02 and 0.04 mg/kg

Assessment and conclusion by applicante,

The study is acceptable.C

 Table 63.1-7: Concurrent recovery data for Fluopyram (study 17-2112)



analysed	1	F	Recovery (%)			
	level (mg/kg)	Individual recoveries	Min	Max	Mean	RSD	
Fluopyram (A	AE C656948)		1		·	0°	
	0.01	79; 80; 89; 90; 90; 109	79	109	80	12.0 、	Ô ^y ô ^g ,
grane / hunch	0.10	82; 83; 87; 87; 88; 89	827	89	Ø.86	3.3	
of grapes	0.30	85	×	- (85		
		Overall recovery (n=13) 🚁	<u>s</u> e	<u>Á</u>	8,8	<i>.</i> 08.5	\$ <u>\$</u>
Fluopvram-	benzamide		ȴ	~~		Q. A	
1.7	0.01	80; 84; 90; 90; 104	ری 80 م	©104 √	90%	240.2	
grape / bunch	0.10	77; 82; 82; 86; 91	9 77×	14	≈ 788	\$15.4	°∕y v
of grapes		Overall recovery (n ≠10)		Ŷ,	. 89 a	12.5	à l'
		Individual recoveries 79; 80; 89; 90; 90; 109 82; 83; 87; 87; 88; 89 85 Overall recovery (n=13) 80; 84; 90; 90; 104 77; 82; 82; 86; 11 Overall recovery (n=14) = Practical limit or quantification uopyram and effculated as fluopyr mined as fluopyram benzamides h a b c c a c a a b c a b b c b c b c <th></th> <th></th> <th></th> <th></th> <th></th>					
Å							



Page 323 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting		cation ra reatmen	it	Dates of treatment / Application interval	Growth stage at last treatment	Portion analyzed	Growth Stage at exampling	Besidues Participation	* O~ `	5050 50 ⁵⁰	PHI (dags)	69 60.
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	Le QLO	(da)	1 D	C LANCO	as AL	as AE	residue	(e)	
17-2112-01 Italy 95045 C. da Incarrozza; Misterbianco (CT) Europe, South F 2017	Grape Alicante; Red berries	1) 2007 2) 10.05.2017 - 25.05.2017 3) 01.09.2017 - 30.09.2017	37.5 37.5		6.25 625	19.05.2017/0 26.05 2017/7		25 Joës		0.07 0.028 0.028 0.04 0.04 0.04 0.04 0.04 0.04 0.05		0.088 0.24 0.038 <0.02 <u><0.02</u>	0 1 80 104	(c) 47-2112 (d) SC (fluopyram 250 g/L) (t) Spraying (j) Analytical method: 00984/M003 (k) LOQ: 0.01 mg/kg (l) Method Validation Data : 00984/M003, 17-2112 (m) Storage: bunch of grapes: 382 days
17-2112-02 (taly 76123 Andria Europe, South F 2017	Grape Sangiovese; Red variety	- 30.09.2017 - 30.09.2017 - 1) 15.02.1994 2) 20.05.2017 - 06.06.2017 - 06.06.2017 - 15.09.2017 - 15.09.2017					ALD OF UT	bayen of	85 89	0.19 0.19 0.11 0.043 0.030	<0.01 <0.01 <0.01 <0.01 <0.01	0.085 0.20 0.12 0.153 <u>0.040</u>	0* 0 15 44 72	(g) 17-2112 (h) SC (fluopyram 250 g/L) ,trifloxystrobin 250 g/L) (i) Spraying (j) Analytical method: 00984/M003 (k) LOQ: 0.01 mg/kg (l) Method Validation Data : 00984/M003, 17-2112 (m) Storage: bunch of grapes: 349 days
E VI	olgeon		out out	, 10 ¹ th ^e	-2 ^{-2²}	il ^g te ^c	>							3:



Page 324 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

												1	A.	n ^e
										Ĉa		O.D.	Ju	and the state
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application rate per treatment			treatment / s Application	Growth stage at last treatment	unity 200	Growth stage at sampling			Pt (da)		$\begin{array}{c} & & & \\ & & & & \\ & & & &$
	(a)	(b)	0	Water (L/ha)	g a.s./hL	(c)		L'IAU L'IAU		fluorvram As AE C656948	as AE C656948	Scalc.	e e	
17-2112-03 France, south 30290 Saint Victor la Coste Europe,	Grape Viognier; Grape White	1) 01.04.1990 2) 20.05.2017 - 31.05.2017 3) 10.09.2017 - 20.09.2017		200 200	18.8 18.8	31.05.2017/0 0.06.2017/0 5		burch of grapes	73 79 6 8 9 8 9	0.024 0.024 0.024 0.024 0.006 0.014	0.00 0.00	0.026	0* 0 3. 45 67 93 4	(g) 17-2112 (h) SC (fluopyram 250 g/L) (h) SC (fluopyram 250 g/L) (h) Spraying (i) Analytical method: 00984/M003 (k) LOQ: 0.01 mg/kg
South F 2017	Grape	1) 01 04 2007	0CU	ي کا ⁰ 100&	3.75	500	73 . 20	ب کی Bunch of	1		SC S	0.030	0*	(1) Method Validation Data : 00984/M003, 17-2112 (m) Storage: bunch of grapes: 357 days (g) 17-2112
Spain 46842 Rugat Europe, South F 2017	Macabeo; white variety	- 29.05.2017 3) 20.08.2017	37.3 20	1000		105.20170 09.06.20170 09.06.20170 09.06.20170			73 O ² 79	0.078 0.014 0.014 0.01 0.01	<0.01 <0.01 <0.01 <0.01	0.088 0.028 <0.02 <u><0.02</u>	0 12 62 76	 (h) SC (fluopyram 250 g/L ,trifloxystrobin 250 g/L) (i) Spraying (j) Analytical method: 00984/M003 (k) LOQ: 0.01 mg/kg (l) Method Validation Data : 00984/M003, 17-2112
	T. C.				CO'	OT COL	of and	J ¹⁰ "						(m) Storage: bunch of grapes: 360 days
(a) Accor (b) Only	rding to CODEX if relevant	Classification / Gui	de (e)	Ren	vs after last	upplication (Libe	l pre-harvest ir conditions; Re	nterval, PHI, ference to ana	underline) alytical metho	(h) d (i)	Formulation ty Application me		(l) (m)	Method validation Storage (max)
(c) Year (d) Eithe G green	must be indicate r growth stage de house	Classification / Gui Scription of BBCH Control of Frield	Con Con Con (g	info Stud prio	dy reference or to be ure	atten métabolites au atment	re included			(j) (k) **	Method inform LOQ residue in cont		#	! based on date of analysis P based on production date no data available
Ŷ Ĉ	, OD DE	OID'I LI	<u></u>	F										324



Data Point:	KCA 6.3.1/11
Report Author:	
Report Year:	2019
Report Title:	Amendment no. 1 to final report - Determination of the residues of triflowstrobia and AE C656948 in/on grape after spray application of AE C656948 & CGA279202 SC 500 in southern France, Italy, Spein and Bulgaria
Report No:	17-2128
Document No:	<u>M-643609-02-1</u>
Guideline(s) followed in	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21
study:	October 2009 concerning the placing of plant protection products on the market OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009).
Deviations from current test guideline:	
Previous evaluation:	No, not previously submitted Study was not found in DAR RAR and the Addenda
GLP/Officially recognised	Yes, conducted under GLP/Officially recognised @sting meilities
testing facilities:	
Acceptability/Reliability:	Yes Y A Q A Q A

Materials and method

Four residue trials on grapes were conducted in southorn Europe (in Italy southern France, Spain, and Bulgaria) during the 2013 season. Two spray applications on plot T 2/2nd application at BBCH 73, interval 21 days) and two spray applications on plot T2 2nd application at BBCH 73, interval 12 days) with FLU+TFS. So 500, a suspension concentrate formulation containing 250 g/L fluopyram and 250 g/L trifloxystrobin.

For the purpose of this renewal, only results for flug yrans and its metabolite fluopyram benzamide will be presented discussed

The applications were conducted at the application rates of 0.2 L/ha corresponding to the application rate of 0.05 kg a.s. Ba and water rates between 500 - 1000 L/ha

The last application was performed at BBCH 73 (2nd application). Samples of grapes were collected at the BBCH stage of 73, 79, 85, and 89.

All field samples weld shipped deep-frozen under monitored conditions during shipment and arrived at PVTL in good condition. For the trials 12-2128-01 and 17-2128-03 the 24 h mean temperature was above -18 °C (T=-17°C, no impact on the residues). The field samples were stored in a freezer at \leq -18 °C until preparation of the examination samples.

For the preparation of examination samples, the deep-frozen field samples were shredded and homogenized with dry ise in a cutter and transferred into polystyrene boxes and stored at \leq -18 °C until analysis.

Samples were analysed according to the analytical method 00984/M003 (**Mathematical**, 2015, <u>M-467323-03-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CAV 4, which comply with the EU regulatory requirements outlined within SANCO 3029/99 rev 4.



Residues were extracted from 5 g of sample material by extraction using a shaker (15 min) with a mixtare of acetonitrile/water (4:1, v:v). After filtration the extracts of the solutions were diluted by adding the internal standard and made up to volume. An aliquot of the extracts was injected into a HPLC-(MSOIS).

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established with at least 5 concentration levels.

The Limit of Quantification (LOQ), expressed as fluopyram defined as the lowest validated fortification level, was 0.01 mg/kg.

The quantification was done by internal standardization using isotopical stable labelled internal standards. The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established

with at least 5 concentration levels.

The time between the beginning of the specimen preparation (extraction) and the specimen analysis and not exceed 7 days while stored at 1-9 °C in the dark. Fluopyram and fluopyram benzamide were found to be stable in extracts of matrices of plant origin for at least four weeks at 4 ± 3 °C which was tested within the validation of method 00984/M003.

Findings

The apparent residues in the control ample used for the determination of recoveries were below 30 % of the LOQ. Recoveries were not corrected for apparent residues in the control samples used for these determinations.

In order to check the performance of the method, recovery determinations were included in each set of analyses (at least one recovery for ten study samples). Control samples from the study were fortified to be used as the recovery samples. All the recovery determinations were performed concurrently to the analyses of control and treated simples from the study.

The mean recoveries per fortification level were within the range of 70% - 110% and the RSD values (when applicable 23) were below 20\%. The overall mean concurrent recoveries were also in the acceptable range of 70% and 10% with the RSD 20%.

The storage period of deep-frozen samples intended for the analysis of fluopyram and fluopyrambenzamide anged between 258 and 356 days. The detailed results obtained for bunch of grapes samples in southern Europe are summarized in the Table 6.3.1 $\sqrt{20}$

Conclusions & S

Four supervised resiductrials on grapes were conducted in southern Europe with the application of AE FLU+TFS SC 500 at the required rates and according to GLP. After a last application at BBCH 73, the samples of bunch of grapes were analyzed for the residues of fluopyram and its metabolite fluopyrambenzamide. The results of the trails presented above show residues at harvest.

- Fluopyram residues range between 0.01 and 0.04 mg/kg.
- Fluopyrant benzamide regidues fere <001 mg/kg.
- The total residue of fluopyram (sum of FLU + FLU-benzamide, expressed as fluopyram) range between 0.02 and 0.648 mg/kg.

Assessment and conclusion by applicant:

The study is acceptable



	Fortification		Recovery ((%)		~	J. J
analysed	level (mg/kg)	Individual recoveries	Min	Max	Mean	RSD	
Fluopyram (Al	E C656948)			•	×,		Ô ^y X ^o
	0.01	93; 100; 100; 100	2	100	<i>6</i> ,98	3.6 🗶	
grape / bunch	0.10	87; 90; 91; 94	<i>*</i> 87	94	S 91	3Q	\$° ×
of grapes	0.70	90	3 ^{0°} -	- 69	90	<u> </u>	Ŷ, ĵ
		Overall recovery (n=9)) V	~	<i>2</i> 94 <i>(</i>	5.3	
Fluopyram-b	enzamide	×,	ð° á	° L	× .~		
<i>(</i> 1 1	0.01	86; 90; 100 [°]	⁽¹⁾ 86	100	s de la companya de l	\$7.8	
grape / bunch of grapes	0.10	97; 102; 198 , 🖉	, M	~ Q 8	⁰ 102	5.4	à l
0 4		Overall recovery (n ≠6)	~ -	ð -	> 970 [×]	8,3	
ET T		ecovery data for Fluop					

BAYER

Page 328 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting		cation ra reatmen		Dates of treatment / Application <u>interval</u>	Growth stage at last treatment	Portion analyzed	Growth Ostage at Sampling	Residue	08 es (@gg/kg) 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	o ^{tec}	PHÝ (Cays)	Deads on trial Deads on trial Def C C C C C C C C C C C C C C C C C C C
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL			1.10 ² .6.	L'inf	fluopyram as AP C656948	FLU benzamide Oris AE C656948	Total residue Ocalc.	(e) [×]	f) (f)
17-2128-01 17-2128-01- T1 France, south 66200 Elne Europe, South F, 2017	Grape Cabernet Sauvignon	1) 2000 2) 21.05.2017 - 30.05.2017 3) 03.09.2017 - 09.09.2017	50 50	500 500 ED		07.06.2017/0 2806.2017/ 21 5	WRET	grapes		9.008 0.017 0.020		0.045 0.027 0.099	0 57 68	(g) 17-2128 (h) SC (fluopyram 250 g/L) (i) Spraying (j) Analytical method: 00984/M003, 17-2118
7-2128-01 7-2128-01- 72 France, south 56200 Elne Europe, South 7, 2017	Grape Cabernet Sauvignon	1) 2000 2) 21 05 2017 	2 ^{3ec}		K.B M	38.06.2012 <u>13</u> E. O. J.	t T ID	vgrapes		×0.994	0.01 <0.01 <0.01 <0.01	0.10 0.033 <0.02 <u>0.020</u>	0 26 57 68	 (k) LOQ: 0.01 mg/kg (l) Method Validation Data : 00984/M003, 17- 2128 (m) Storage: bunch of grapes: 356 days
17-2128-02 17-2128-02- F1 (taly 40053 Bazzano Europe, South F, 2017	Grape Pignoletto	1) 2011 2) 3005.2017 15.06.2017 3) 06.09.2017 - 06.09.2017				2406.2017/0 91.07.2017/29 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0	93 🔨	O grapes &	73 79 85 89	0.031 0.018 0.011 <0.01	<0.01 <0.01 <0.01 <0.01	0.041 0.028 0.021 <0.02	0 21 43 57	(g) 17-2128 (h) SC (fluopyram 250 g/L, trifloxystrobin 250 g/L) (i) Spraying (j) Analytical method: 00984/M003, 17-2118 (k) LOQ: 0.01 mg/kg
EUI	thermo pheeduc	2) 3605-2017 -115.06.2017 -06.09.2017 -07.00 -	DU ^E	Ja ^l J ^{al}	PETTO PTO	pi ^j	¥							32



Page 329 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram

												- 8		<u> </u>
										Ĉa		OTT .		difter allo
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting		cation ra reatmer		Dates of treatment / Application <u>interval</u>	Growth stage at last treatment	Portion analyzed	Growth stage at sampling		e ^{fr} of	otec	PULL	Details operrial
	(a)	(b)	g a.s./ha	Water (L/ha)		(c) 5				C656948	as AF C656948	a a	*	
17-2128-02 17-2128-02- T2 Italy 40053 Bazzano Europe, South F, 2017	Grape Pignoletto	1) 2011 2) 30.05.2017 - 15.06.2017 3) 06.09.2017 - 06.09.2017	50 50	600 600		0 1 1.07.20 1 0 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	Where the second	6 9-72 9-72		¥ , 6	20°CUINE	0.046 0.026 0.021 0.020	21 43 0	(1) Method Validation Data : 00984/M003, 17- 228 (m) Storage: bunch of grapes: 343 days
17-2128-03 17-2128-03- T1 Spain 50549 Malejan Europe, South F, 2017	Grape Garnacha	3) 25.09.2017 - 17.10.2017					ET ID	builden of grapes	85 89 89	0,130,010 9.063 0.038 0,922	\$0.01	0.12 0.073 0.048 0.038	0 14 56 98	 (g) 17-2128 (h) SC (fluopyram 250 g/L, trifloxystrobin 250 g/L) (i) Spraying (j) Analytical method:
17-2128-03 17-2128-03- T2 Spain 50549 Malejan Europe, South F 2017	Grape Garnacha	1) 199 2) 15:05:2017 10:06:2017 3) 25:09:2017 - 17:10:2017				9.06.20170 28.06.20170 28.06.201712 0 2 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	73 50 05 010	bunch of grapes	93 79 85 89	0.21/0.010 0.11 0.074 0.038	<0.01 <0.01 <0.01 <0.01	0.22 0.12 0.084 <u>0.048</u>	0 14 56 98	00984/M003, 17-2118 (k) LOQ: 0.01 mg/kg (l) Method Validation Data : 00984/M003, 17- 2128 (m) Storage: bunch of grapes: 356 days
EVI	therno	21 15:05:2017 - 10:06:2017 - 17:10:2017 - 17:10:10:2017 - 17:10:2017 - 17:10:2017	DOLC *	* 1 ⁹⁰ 2 ⁹⁰	Pr.									329



Page 330 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

												3		<u> </u>
										Ĉa		9. Bor		ditte apo
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting		ation ra eatmen	1	Dates of treatment / Application <u>interval</u>	Growth stage at last treatment	Portion analyzed	Growth stage at sampling		€ ^{EE}	otec) PHI (days) C	Details operrial
	(a)	(b)	0	Water (L/ha)	g a.s./hL	(c) 5					as AF C656948	calc	K (PC) 2	
17-2128-04 17-2128-04- T1 Bulgaria 4400 Pazardjik Europe, South F 2017	Grape Merlo	1) 2005 2) 09.06.2017 - 20.06.2017 3) 15.09.2017 - 30.09.2017		1000 1000	5.0 × 5.0 ×	0006.2017.0 30.06.2017.0 50.000000000000000000000000000000000	NALET.	e Spr Spr	~ ^e ?			0.33 0.067 0.34 0.037	53 805 805	g/L ,trifloxystrobin 250 g/L) (i) Spraying (j) Analytical method:
17-2128-04 17-2128-04- T2 Bulgaria 4400 Pazardiik	Grape Merlo	3) 15.09.2017 - 30.09.2017	50 Out		K [®]	\$0.00.2017/ <u>11</u> & 0	A ALA	with the second se	85 89 0 ⁷ 2 ⁷	0.67 0.074 0.030 0.033	<0.01	0.68 0.084 0.040 <u>0.043</u>	0 32 53 80	00984/M003, 17-2118 (k) LOQ: 0.01 mg/kg (l) Method Validation Data : 00984/M003, 17- 2128 (m) Storage: bunch of grapes: 354 days
(a) Accord (b) Only if (c) Year m (d) Either G greenh	The content of the co	Classification / Gue		Definition	after say in ark Day in mation wh y reference to the form	The second secon	pre-harver in motions; Ref includeet	E cerval. PNL f Pregcolo ana	inderline) lytical method	(h) 1 (i) (j) (k) **	Formulation type Application metho Method informat LOQ residue in control		(m)	Method validation Storage (max) ! based on date of analysis P based on production date no data available
Ċ	⊃».	W. L.												330



Based on the residue definition for risk assessment, the sum of fluopyram and fluopyram -benzamide expressed as fluopyram, the total residues for grapes are summarized in the Table 6.3.1-11.

Table 6.3.1-11: Summary of fluopyram total residue data for grape trials (after results scaling for NEU)

			A	
Crop	Region/Indoor (a)	Trial results relevant to the Optical GAP (mg/kg)	STMR (b)	HR [*] 7 (C) (C) (C) (C) (C) (C) (C) (C) (C) (C)
	NEU	<0.01 ; 0.012 ; 0.020 ; 0.026 ; 0.030 ; 0.027 ; 0.033 ; 0.049	0.028	
Grape	SEU	2x <0.02 ; 2x 0.020 ; 0.024 ; 0.040 ; 0.043 ; 0.043 ; 0.048 ;	*	0048 0 5 °
	NEU/SEU	$ \begin{array}{c} <0.01 ; 2x < 0.02 ; 0.012 ; 3x 0.020 ; 0.024 ; \\ 0.026 ; 0.030 ; 0.043 ; 0.043 ; 0.040 ; \\ 0.043 ; 0.048 ; 0.049 \end{array} $	0.025	

(a) NEU or SEU for northern or southern outdoor triats in EU on the state
(b) STMR: Supervised Trials Median Residue
(c) HR: Highest residue

Ô

CA 6.3.2 Strawberry

Data on residues in strawberry were submitted for the first inclusion of fluopyram under Regulation (EC) N°. 1107/2009.

For strawberry, a total of 26 European supervised residue trials (9 from Northern Europe, 9 from Southern Europe and 8 in greenhouse) and 40 North American trials performed from 2006 to 2007 were available to support these representative uses.

As strawberry is not représentative uses for the current active substance renewal dossier, these below lister trials will not be summarized for a sake of clarity

	Residue tria	s	
	*ear > > > ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	References Report No. Authors, year	Total number of trials
NEU S 5 5 5		<u>M-295412-01-1</u> 2007	9
4 A - 2 A	\$ Q 4	M-298093-01-1 2008	9
	~ -	<u>M-295419-01-1</u> 2007	0
	4	<u>M-298098-01-1</u> 2008	9

Table 6.3.2-1: First inclusion Duopy am residue trials conducted on strawberry



		Residue tria	ıls	
	Y	ear	References	Tota@number of
Zone	2006	2007	References Report No.	triak
GH	8	-	M-295155701-1 2007	
US	-	10	M-200045-01-1 2008	

CA 6.3.3 Tomato

Data on residues in tomato were submitted for the first inclusion of fluopyram upder Regulation (EC) N° . 1107/2009.

For tomato, a total of 22 European supervised residue thats (10 field trials from Southern Europe and 12 in greenhouse) performed from 2006 to 2007 were available to support these representative uses.

As tomato is not representative uses for the current active substance renewal dosoer, these below listed trials will not be supmarized for a sake of clarify.

Table 6.3.3-1:	First inclusion	fluopyram	residue ti	ials conducto	ed on tomaro
----------------	-----------------	-----------	------------	---------------	--------------

Residucitrial	Se 2, 9,	102V
Zone	References Beport No. Authors, year	Total number of trials
$SEU = \frac{\sqrt{3}}{\sqrt{3}} \frac{\sqrt{3}}{$	2007	10
$MGH \xrightarrow{Q} \xrightarrow{Q} \xrightarrow{Q} \xrightarrow{Q} \xrightarrow{Q} \xrightarrow{Q} \xrightarrow{Q} \xrightarrow{Q}$	<u>M-290788-01-1</u> 2007	12
MGH 8 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<u>M-297499-01-1</u> 2008	
	<u>M-299989-01-1</u> 2008	11
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		



Ĩ

Ø i

CA 6.3.5 Apple

Information on the intended use pattern (GAP) is summarised in Table 6.3.4-1.

Use patterns (critical GAP) for the spray application of Pluopyram in on apple in Ø Table 6.3.4-1: European fields (northern and southern residue regions)

GAP number	Formulation	F/ GH	No. of appl.	Growth stage at application (BBCH Code)	Sg a.s./ha)	Water xolume (L/ha)	Interival (days) (days)
1	FLU SC500	F*	1	A 7,1889 0	Q75 0	500-100g	
F field			Å	, , ~, ~, ~, ~, ~, ~, ~, ~, ~, ~, ~, ~,		O ^v	

F field

n apple and pear at a similar Residue trials supporting GAP 1 were conducted in Europe Worth and GAP during the 2019 growing season. Ø Ô

Ø Overview of European residue trials conducted in apple & pear per geographical Table 6.3.4- 2: "residue region" and regetation period to support GAP & Ò

		· * _				
	A.C.	No. of independe	nt trials	Report No (Formulation)	Docement number	
Crop	Region	Harvest 2019		(Formulation)	Docament	Reference
	Region	apple pear				
	è «			E19RP062	≪ <u>№-757113-01-1</u>	KCA 6.3.4/01
Ô	NEU				<u>M-755638-01-1</u>	KCA 6.3.4/02
Pome friets	,		<u>} 8.</u>	🐠 🖉 🖉 🖉 🎸		
Pome fronts	. (€LU SC250) « EL90€P105 ET9RP 100	<u>M-757080-01-1</u>	KCA 6.3.4/03
	SEU	4% ~.4		ETARPLOO	<u>M-755520-01-1</u>	KCA 6.3.4/04
NEU = northern El	, St		y <u>y</u> i	ET9RP 106 AGLU SC250)		
NEU = northern E	U field	SHEU = southern EU file	eld	. <u></u>		
~	°s %		0^{γ}			
Norther	ne 💊	Stu = second rem EUV FR		Č,		
stor S	× ľ	AN				
A CONTRACTOR		Steu = section Elyster				



Data Point:	KCA 6.3.4/01
Report Author:	
Report Year:	
Report Title:	Determination of the residues of AE C656948 in/on apple after a spray application of
	fluopyram SC 250 in Germany, United Kingdom, The Netherlands and Belgium
Report No:	E19RP062
Document No:	<u>M-757113-01-1</u> ©
Guideline(s) followed in	Regulation (EC) No 1107/2009 of the European Parsament and of the Council of 2
study:	Regulation (EC) No 1107/2009 of the European Parsament and of the Council of 26 October 2009 concerning the placing of plant projection products on the market OECD Guideline for the Testing of Chemicals on Crop Field Total
	OLED Guidenne for the result of chemicals a crop ried intal
	(TG 509 published in September 2009)
	US EPA OCSPP 860.1500, Crop Field Trial O
Deviations from current	none & a so w so so
test guideline:	
Previous evaluation:	No not providually all mitted and a second
	No, not previously submitted a star of the
GLP/Officially recognised	Yes, conducted under Step/Officially, recognized testing facilities
testing facilities:	
Acceptability/Reliability:	Yes of or of the second

Materials and methods

Four residue trials on apples were conducted in northern Europe (in Germany United Kingdom, the Netherlands and Belgium) during the 2019 season

One spray application was conducted with Fluopyram SC 250 a SC formulation containing 250 g/L of fluopyram.

The target application rate was 0.03 kg as/ba x m height with a pre-harvest interval of 14 days.

As the canoples height ranges between 2.5 and 3.5 m these applications rates corresponds to a range of 0.070 - 0.092 kg as/ha.

At harvest, each field sample was placed in doubled labelled bags and stored deep-frozen within 24 hours after sampling and until dispatch will field samples were shipped deep-frozen under monitored conditions during shipment and arrived in good condition. The field samples were stored in a freezer at \leq -18 °C until preparation of the examination samples.

For the preparation of examination samples, the deep-frozen field samples were shredded and homogenized with dry ice in a cutter. Representative parts of the chredded samples were transferred into polystyrene boxes and stored at ≤ 4.8 °C.

Samples were analysed according to the analytical method 00984 (**Mathematical**, 05/02/2007, <u>M-283301-01-1</u>, see MCA section 4.1.2) Full details and accordable validation data to support this method are presented within document M-CA 4 which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev A.

Briefly, residues were extracted from \Im g of sample material by two successive extractions using a high speed bunder with a mixture of acetonitrile:water (80:20; *v*:*v*). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

didution performed under acidic conditions and measured in negative electrospray ionization for the determination of FLU-PCA and positive ion mode for FLU-methyl-sulfoxide.



 dilution performed under basic conditions and measured in positive electrospray ionization for the determination of fluopyram, FLU-benzamide, FLU-PAA and FLU-7-hydroxy.

*Due to its instability, the analytical standard of fluopyram-pyridyl-acetic acid (BCSAA10139) was made available under its sodium salt form (BCS-AA10189) which was used as reference item.

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established with at least 5 concentration levels. For each calibration curve the correlation coefficient R was above 0.92.

The quantification was done by internal standardization using isotopically stable labelled internal standards. The Limit of Quantification (LOQ), expressed as fluopyram, defined as the lowest validated fortification level, was 0.01 mg/kg.

The examination samples were kept deep-frozen unful their analysis. The quantity necessary for analysis was weighed while the sample was still deep-frozen, and the remaining sample was immediately returned to the freezer. All final extracts were analysed within 24 hours

Findings

In order to check the performance of the method, recovery determinations, were included in each set of analyses. Control samples from the study were fortified to be used as the recovery samples. All the recovery determinations were performed concorrently to the analyses of control and treated samples from the study. The apparent residues in the control sample used for the determination of recoveries were below 30 % of the LOQ. Recoveries were not corrected for apparent residues in the control sample used for the determination of recoveries were below 30 % of the LOQ. Recoveries were not corrected for apparent residues in the control samples used for these determinations.

The mean recoveries per fortification level were within the range of 70 % 10 % and the RSD values were below 20 %. The everall dean concurrent recoveries were also in the acceptable range of 70 % and 110 %, with the RSD 20 %.

The storage period of deep frozen samples intended for the analysis of fluopyram and its metabolites ranged between 199 and 257 days.

The detailed results obtained for apple samples in northern Europe are summarized in the Table 6.3.4-4.

Conclusion 🔬 🕺

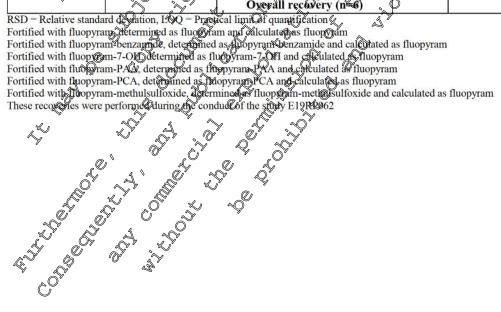
Four supervised residue trials on apples were conducted in northern Europe with the application of Fluopyram SC 250 actine required rate correspondions to the supported GAP (1x75 g as/ha, PHI=14 days), and according to GLP. Samples of apples were analyed for the residues of fluopyram and its metabolite fluopyram-benzamide (AEE) 48815 alias, FLU-benzamide), fluopyram-pyridyl-acetic-acid (BCS-AA10139, at as FLU-PAA), fluopyram pyridyl-carboxylic acid (AE C657188, alias FLU-PCA), fluopyram-fluopyram-fluopyram-methyl-sulfoxide (AE1344122, alias FLU-methyl-sulfoxide). The resides of the trials presented above show the following residues 14 days after last application.

- Fluopyram residues rangebetween 0.02 and 0.04 mg/kg.
- Fluopyram-benzamide@esidues were 0.01 mg/kg
- FLU-Z-OH residues were 601 mg kg
- FLLPAA residue were ≤0.01 mg/kg
- FILU-PCA residues were <0.010mg/kg
- FLU-methyl-sulfoxide residues were <0.01 mg/kg

The fotal residue of fluopyram (sum of FLU + FLU-benzamide, expressed as fluopyram) range between 0.03 and 0.05 mg/kg.



				and the second se	F	Y .~~		
able 6.3.4-3:	Concurrent recove	ery data for Fluopyram (stu	dv E19RP	062	Å.			
Portion	Fortification		Recovery (~~ A		
analysed	level (mg/kg)	Individual 🏾 🌋		P062) Max Max				
		recoveries 🖧	Min	Max	Alean	RSD		
Fluopyram (AE	C656948)		Ô ^V	(o Q	Ň ×		
	0.01	95, 102, 108	95	\$ 103	100	0 4.4		
apple / fruit	0.10	94, 95, 96	94 %	96 *	V95 Q	1.0		
		Overall recovery (n=6)		~	O 98 ~~	280		
Fluopyram-ber			R C			4		
	0.01	, 100, 102	Q.96	102	099	3.1 C°		
apple / fruit	0.10	\$ 93, 94, 98	93	. 8	95 🚭	0.6		
		Overall recovery (n=6)		XX A	97	3.6		
Fluopyram-7-OF	I (BCS-AA10065)					0		
	0.01	96, 100, 108	♦ 96 8	108	§101 Ø	6.0		
apple / fruit	0.10	2 95 95, 96 C	30	a 0%	§ 95	0.6		
	~~~~	Overall recovery (n76)		õ _s c	28	5.2		
Fluopyram-PA	A (BCS-AA10139)	& ES al	SUY O	Ū,				
	0.01	5 95, 1 <b>0</b> , 103 °	95 ×	.168	99	4.1		
apple / fruit		92, 96, 106	127	~ 106 ×	98	7.4		
	~ ~ ~	Overal recovery (n=60	& . Ì		99	5.4		
Fluopyram-PCA	(AE C677188)		0 &	<u>کې</u>				
		80, 82, 95 ~		95	86	9.5		
apple / fruit		82,97, 100 S?	@ ^{\$2} ~	@ 100	93	10.4		
2		Sverall recovery (n=0)	K K	1 Alexandress of the second se	89	10.0		
Fluopyram-me	thylstofoxide(AE134	14122) 🗸 🖉 🖉						
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.01	A 95, 97, 1060	126	106	100	5.5		
apple / frank		87,94,84	087	94	92	4.4		
«\y		Overall recovery (n 6)	0×		69	6.4		



BAYER

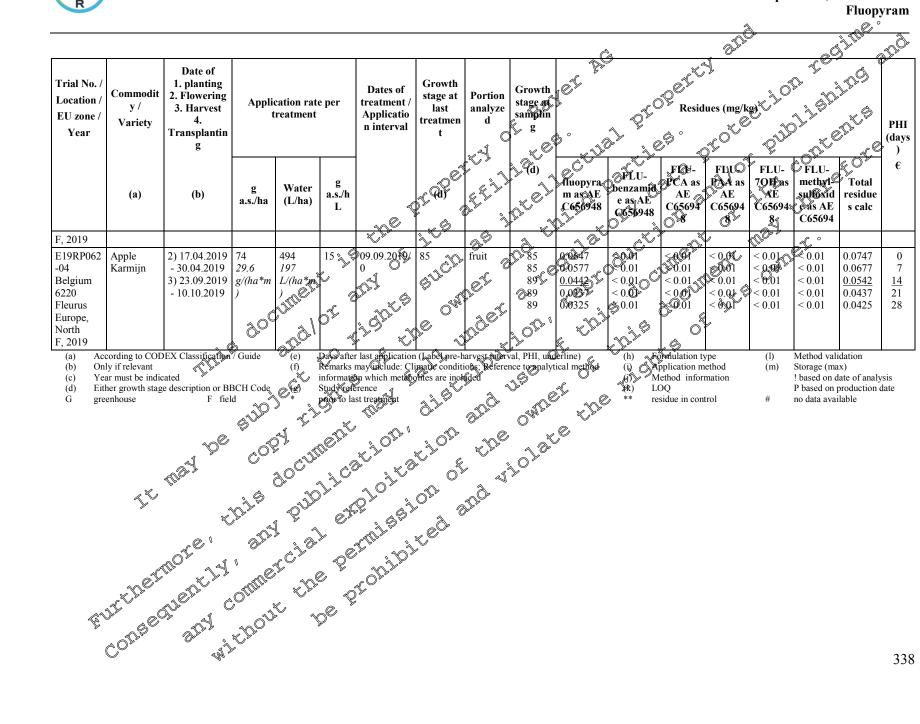
Page 337 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No. / Location / EU zone / Year	Commodit y / Variety	Date of Date of 1. planting 2. Flowering 3. Harvest 4. Transplantin g	Appli	cation rate reatment	e per	Dates of treatment / Applicatio n interval			sampling contractions (mg/kg) of contractions						pore pore	PH (day)	
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./h L	K DE		8 ⁹		Studopyra m as AE C656948	benzámid e as AE C656948	C65694	C65694	/UT as	FEU- methyl- sulfoxid e as AE 65694	Total residue s calc	€
E19RP062 -01 Germany 51399 Burscheid Europe, North F, 2019	Apple Jonagold	1) 2012 2) 19.04.2019 - 29.04.2019 3) 25.09.2019 - 18.10.2019	72.8 29.1 g/(ha*m)	849 340 L/0.0m	8.57×				79 81 085 87 89 1 0	0.04275 0.04275 0.00284 0.02284 0.02284	<pre>0.01 < 0.01 < 0.01 < 0.0 < 0.0 < 0.01 </pre>	Q.01	 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	0.0678 0.0527 0.0325 <u>0.0384</u> 0.0323	$\begin{array}{c} 0\\7\\ \underline{14}\\21\\28\end{array}$
E19RP062 -02 United kingdom SG8 8SS Great Chishill, near Royston Europe,	Jonothan	1) 2005 2) 18.04.2019 - 10.05.2019 3) 23.09.2019 - 07.10.2019	69.6 27.8 g/(ha*m) G	580 236 (ha*m) 5 1			, 1, 6 ⁵	9.D.D.	089 089 089 089 089	0.045 0.045 0.0341 0.0218 0.0218 0.0144 0.0144	<0.01 <0.01 <0.01 <0.01 <0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	0.0535 0.0441 <u>0.0379</u> 0.0315 0.0241	$ \begin{array}{c} 0 \\ 7 \\ \frac{13}{20} \\ 27 \end{array} $
North F, 2019 E19RP062 -03 Netherland s 1608 HG Wijdenes Europe, North	Apple Elstar	1) 2008 2) 15.04.2019 - 01.05.2019 30.6.08.2019 - 15.09.2019	91.9 30.6 5 g//ha*m			2 14.08 (19) 9 (10) 14.08 (19) 9 (10) 14.08 (19) 14.08		fruit	81 85 85 87 87	0.0681 0.0347 <u>0.0258</u> 0.0232 0.0252	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	0.0781 0.0447 <u>0.0358</u> 0.0332 0.0352	$\begin{array}{c} 0\\ 7\\ \underline{14}\\ 21\\ 28 \end{array}$

337



Page 338 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram





Data Point:	KCA 6.3.4/02
Report Author:	
Report Year:	2020
Report Title:	Determination of the residues of AE C656948 in/on pear after spray application of fluopyram SC 250 in Germany and Hungary
Report No:	E19RP083
Document No:	<u>M-755638-01-1</u>
Guideline(s) followed in	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of
study:	21 October 2009 concerning fre placing of plant protection products on the market
	21 October 2009 concerning the placing of plant protection products on the market US EPA OCSPP 860.1500, crop Field Trial
	OECD Guideline for the Testing of Chenoreals on Crop Field Trail
	OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2005)
Deviations from current test guideline:	none A to Q A to A to A
Previous evaluation:	No, not previously submitted of the transformed of
GLP/Officially recognised	Yes, conducted under GLP/Øfficially recognised testing facilities
testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes v v v v v v v v v v v v v v v v v v v

Materials and methods

Four residue trials on apples were conducted in northern Europe (in Germany and Hungary) during the 2019 season.

One spray apprication was conducted with Duopyram SC 250, a SC formulation containing 250 g/L of fluopyram.

The target application rate was 0.03 kg as ha x or height with a pre harvest interval of 14 days.

As the canopies height tange between 2.5 and 3.5 m, these applications rates corresponds to a range of 0.075 - 0.096 kg as 6a.

At harvest, each field sample was placed in doubled labelled bags and stored deep-frozen within 24 hours after sampling and until dispatch. All field samples were supped deep-frozen under monitored conditions during shipment and arrive din good condition. The field samples were stored in a freezer at \leq - 18 °C until preparation of the examination samples \sim

For the preparation of examination samples, the deep frozen field samples were shredded and homogenized with dry ice in a conter. Representative parts of the shredded samples were transferred into polystyrene boxes and stored at ≤ -18 C.

Samples were analysed according to the analytical method 00984 (**Mathematical**, 05/02/2007, <u>M-283301-01-1</u>, see MCA section 4.4.2). Full details and acceptable validation data to support this method are presented within document, M-CA-4, which comply with the EU regulatory requirements outlined within SANCO(2029/99) rev 40

Brieffy residues were extracted from 5 g of sample material by two successive extractions using a high speed blender with a mixture of acetonitrile:water (80:20; v:v). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

Ô



- dilution performed under acidic conditions and measured in positive electrospray ionization for the determination of FLU-PCA.
- dilution performed under basic conditions and measured in positive electros pray ionization for the determination of fluopyram, FLU-benzamide and FLU-PAA.

*Due to its instability, the analytical standard of fluopyram-pyridyl-acetic acid (BCS-AA10130) was made available under its sodium salt form (BCS-AA10189) which was used as reference item.

The linearity was demonstrated in each analytical batch with a 1/x weight a calibration our established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 999 The quantification was done by internal standardization using isotopic of y stable labeled internal standards The Limit of Quantification (LOQ), expressed as floopyram, defined as the lowest validated fortification level, was 0.01 mg/kg.

The examination samples were kept deep-frozen until their malysis The quantity pecessary for analysis was weighed while the sample was still deep-frozen, and the remaining sample was immediately returned to the freezer. All final extracts were analysed within 24 hours

Findings

In order to check the performance of the method, recovery determinations were included in each set of analyses. Control samples from the study were for field to be used as the ecovery samples. All the recovery determinations were performed concurrently to the analyses of control and treated samples from the study.

The apparent residues in the control sample used for the determination of recoveries were below 30 % of the LOQ. Recoveries were not corrected for apparent residues in the control samples used for these determinations.

The mean recoveries per fortification level were within the range of 70% -% and the RSD values 110 were below 20 %. The overall mean concurrent recoveres were also in the acceptable range of 70 % and 110 %, with the RSD < 20 %.

The storage period of deep-frozen samples infended for the analysis of fluopyram and its metabolites ranged S between 315 and 353 days.

The detailed results obtained for apple samples in northern Europe are summarized in the Table 6.3.4-6.

C

Conclusion

Four supervised residues trials on apples were conducted in northern Europe with the application of Fluopyram SC 250 at the required rate corresponding to the supported GAP (1x75 g as/ha, PHI=14 days), and according to GLD. Samples of apples were analysed for the residues of fluopyram and its metabolite fluopyram-benzamide (DEF148915, Jias CLU-borzamide), fluopyram-pyridyl-acetic-acid (BCS-AA1013 alias FLU-PAA) and fluop ram-pyridyl carboxylic acid (AE C657188, alias FLU-PCA). The results of the trials presented above show the following residues 14 days after last application.

- Fluopyrant résidues range between 0.05 and 0.09 mg/kg.
- Fluopyram-benzamidecresidues were 0.01 mg/kg
- FLU-RAA residues were <0.01 mg/kg
- FLIGPCA residues were < 0.01 mg/kg
- be total residue of floopyrand (sum of FLU + FLU-benzamide, expressed as fluopyram) range between 0.06 and 0.10 mg/kg.



Assessment on d	Lanualusian bu anal	·				
The study is acco	<u>l conclusion by appl</u> eptable.	<u>icant</u> :			7	
Table 6.3.4- 5:	Concurrent recov	ery data for Fluopyram 🕼	dy E19RF	2(§\$3)		
Portion analysed	Fortification level (mg/kg)	Individual	Recovery () Mean	N ON
Fluopyram (AE G	C656948)	A CONTRACTOR OF THE OWNER OWNER OF THE OWNER OWNE OWNER OWNE			\sim	
	0.01	96, 100, 101	96 %	101	N99 0	
pear / fruit	0.10	93 97, 98	93	× 98	O 96%	2.8
		Overall recovery (n≠6) ℃	1 Contraction of the second se		98	3.0
Fluopyram-ben	zamide		Q.	.~~	ŐY "a	r L°
And the	0.01	\$106, 108, 113	106	Û.	1 109 🛇	204
pear / fruit	0.10	10 94, 94, 95, °	Ø	\$ 95	× 94	20.6
		Overall/recovery (n=6)			£972	0 8.2
Fluopyram-PA	A (BCS-AA10139)		N N		206)
	0.01	99, 90, 111	20	a OII	103	6.4
pear / fruit	0.10	\$ 94, 97, 98	.04	0 98	(96	2.2
n	×.	& Overall recovery (n=6)	LOY . Q		Q100	5.9
Fluopyram-PCA	(AE C657188)			~~~	Ô	
	0.01	23, 96, 92, 7 , 9, 101, 391 , 0	34	×\$99 ×	96	2.6
apple / fruit	9.10	8, 101, 01 . O	\$ 96	101	99	2.9
		Overall@ecover@(n=6)	p' 👋	, Y	98	3.0

apple / fruit 910 9 96, 101, 01 9 96, 96 RSD = Relative standard deviation, HOQ = Proveral Recovery (n=6) Fortified with fluopyram determined as fluopyram and calculated as fluopyram. Fortified with fluopyram benzamele, determined as fluopyram. Denzamele and calculated as fluopyram. Fortified with fluopyram PCA determined as fluopyram. Fortified with fluopyram fluopyra



Page 342 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

												3			,
Table 6.3.4- 6: Total residue calcula				<u>-755638</u>	- <u>01-1</u>) s	tudy on pea	ır		t PC		NET O		at a co	i 109 I I II I	9.Ug
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting		cation rate treatment	e per	Dates of treatment / Application interval	Growth stage at last fratment	Portion analysed	Growth stage at sampling	PIOP PICP	BGid DEU- benzamid CC56948	ues (mgtig		PHI (days)	
	(a)	(b)	g a.s./ha	Water (L/ha)	a s BL	QIOF JES	(Q) (Q)			Ĉ,	BEU- benzamide as AlO C656948	1940- PCA as AE-1 C656948	100- PAA as AE C656948	Total residues calc	(e)
E19RP083-01 Germany 79346 Endingen- Königschaffhausen Europe, North F, 2019	Pear Williams christ; table pears	1) 14.12.2013 2) 01.04.2019 - 15.04.2019 3) 13.08.2019 - 27.08.2019	UIRC	769 256 L/(ha*m) D		31.07.2019/0		fruit	81 85 85 87 89 89	0.0913 0.0937 0.0462 0.0298 0.0298		<0.01	<pre><0.01 <0.01 <0.01 <0.01 <0.01 <0.01</pre>	0.1013 0.1037 <u>0.0562</u> 0.0502 0.0398	$ \begin{array}{c} 0\\ 6\\ \underline{14}\\ 22\\ 28 \end{array} $
E19RP083-02 Germany77704 Oberkirchnussbach Europe, North F, 2019	Pear Williams Christ	1) 1995 2) 01094.2019 19:04.2019 3) 14.08.2019 - 30.08.2019	96.13 3000 g/(ha*m)x	, Ġ	^ع ر م	\$¥.07.2019.00	10 ^{01tr}	Oruit C	0 ⁸⁷ 89	0.104 0.100 0.0738 0.009 0.0311	 0.01 <0.01 <0.01 <0.01 <0.01 <0.01 	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	0.114 0.11 <u>0.0838</u> 0.0719 0.0411	$\begin{array}{c} 0\\ 6\\ \underline{14}\\ 22\\ 28 \end{array}$
E19RP083-03 Hungary H-3360 Heves Europe, North F, 2019	Pear Vilmos	1) 05.05.2015 2) 17.06.26 - 24.062019 3) 05.08.2019 019.08.2019 4) 14.03.2016	75.3 30.1 g/(ha ² m)	201 201 []/(hat*m)	1020	22,07,5919/0	* De	fruite S ^{REE}	810 87 87 89	0.173 0.0932 <u>0.0875</u> 0.0515 0.0593	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	0.183 0.1032 <u>0.0975</u> 0.0615 0.0693	$0 \\ 7 \\ 14 \\ 21 \\ 28$
E19RP083-04 Hungary H-3985 Alsoberecki Europe, North F, 2019	Pear V	1) 20.04.2001 2) 14.06.2019 - 21.06.2019 3) 05 08 2019 - 19.08.2019 4) 25.03.2008	994 30.1 g/(ha*)m	603 201 L/(ha*@ C		23.07.2000/0	81 4	fruit	81 85 87 87 89	0.200 0.121 <u>0.0822</u> 0.0490 0.0546	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	$\begin{array}{c} 0.21 \\ 0.131 \\ \underline{0.0922} \\ 0.059 \\ 0.0646 \end{array}$	$ \begin{array}{c} 0 \\ 6 \\ 13 \\ 20 \\ 27 \end{array} $
(a) According to (b) Only if relev (c) Year must b) (d) Either grave G greenhets Ether grave	CODEX Classi ant e influenced listage descripti			Remarks may	v include. (which meta	Of (Label pre-har Climatic condition bolites are includ	ns; Reference			(i) Applic(j) Method(k) LOQ	ation type ation method 1 information in control	(l) (m) #		hax) date of anal production	date
ě		19~													34



Southern zone

Data Point:	KCA 6.3.4/03
Report Author:	
Report Year:	2020
Report Title:	Determination of the residues of AE C656948 in/on apple after a spiral application of fluopyram SC 250 in Italy, southern France and Portugal
	fluopyram SC 250 in Italy, southern France and Fortugal
Report No:	
Document No:	<u>M-757080-01-1</u>
Guideline(s) followed in	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 2
study:	October 2009 concerning the placing of plant protection products on the marker
	OECD Guideline for the Testing of Chemicals on Crop Field Field
	(TG 509 published in September 2009)
	US EPA OCSPP & Crop Field Total A O
Deviations from current	none
test guideline:	
Previous evaluation:	No, not proviously submitted
GLP/Officially recognised	Yes, conducted under CLP/Officially & cognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yages of 2 and a the second se

Materials and method

Four residue tricks on apples were conducted in southern Europe (in Italy, France and Portugal) during the 2019 season. One spray application was conducted with Flippyram SC 250, a St formulation containing 250 g/L of

One spray application was conducted with Flippyram/SC 250, a SC formulation containing 250 g/L of fluopyram?

The target application rate was 0.03 kg as that x m height with a pre harvest interval of 14 days.

As the canopies height ranges between 2.8 and 3.2 no these applications rates corresponds to a range of 0.087 - 0.096 kg as/ha

At harvest, each field sample was placed in doubled labelled bags and stored deep-frozen within 24 hours after sampling and until dispatch All field samples were shipped deep-frozen under monitored conditions during support and arrived in good condition. The field samples were stored in a freezer at \leq - 18 °C until preparation of the examination samples.

For the preparation of examination samples, the deep-frozen field samples were shredded and homogenized with dry ice in a cutter. Representative parts of the shredded samples were transferred into polystyrene boxes and stored at ≤ 18 °C

Samples were analysed according to the analytical method 00984 (**Markov**, 05/02/2007, <u>M-283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA A which comply with the EU regulatory requirements outlined within SAMCO/3029/99 rev 4.



Briefly, residues were extracted from 5 g of sample material by two successive extractions using a high speed blender with a mixture of acetonitrile:water (80:20; v:v). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

- dilution performed under acidic conditions and measured in positive electrospray ionization for the determination of FLU-PCA and negative ion mode for FLU-methyl-sulfoxide.
- dilution performed under basic conditions and measured in positive electrospray ion Pation or the determination of fluopyram, FLU-benzamide, FLU-BAA and FLU-hydroxy.

*Due to its instability, the analytical standard of fluopyram-pyridyl-acetic acid (BCS-A&10132) was made available under its sodium salt form (BCS-AA10189) which was used as reference item.

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above (299. The quantification was done by internal standardization using isotopically stable labelted internal standards. The Limit of Quantification (LOQ), expressed as fluopyrane defined as the lowest validated for fiftcation

level, was 0.01 mg/kg.

The examination samples were kept deep-frozen until their analysis. The quantity becessary for malysis was weighed while the sample was still deep trozen, and the remaining sample was immediately returned to the freezer. All final extracts were analysed within 24 hours.

Findings

In order to check the performance of the method, tecovery determinations were included in each set of analyses. Control samples from the study were forthfied to be used as the recovery samples. All the recovery determinations were performed concurrently to the analyses of control and treated samples from the study. The apparent residues in the control sample used for the determination of recoveries were below 30 % of the LOQ. Recoveries were not corrected for apparent residues in the control samples used for the determinations.

The mean recoveries per fortification level were within the range of 70% - 110% and the RSD values were below 20%. The overall mean concurrent recoveries were also in the acceptable range of 70% and 110%, with the RSD < 20%.

The detailed results obtained for apple samples in northern Europe are summarized in the Table 6.3.4-8

Conclusion

Four supervised residue trials on apples were conducted in southern Europe with the application of Fluopyrath SC 250 at the required rate correspondion to the supported GAP (1x75 g as/ha, PHI=14 days), and according to GLP. Samples of apples were analysed for the residues of fluopyram and its metabolite fluopyram-benzamide (ATF148815, trias FLU-benzamide), fluopyram-pyridyl-acetic-acid (BCS-AA10139, alias FLU-DAA), fluopyram-pyridyl-carboxylic acid (AE C657188, alias FLU-PCA), fluopyram-7-hydroxy (BCS-7A10065, alias FLU-7-OH) and fluopyram-methyl-sulfoxide (AE1344122, alias FLU-nothyl-sulfoxide). The results of the trials presented above show the following residues 14 days after last application.

- Vuopycam residues range between 0.03 and 0.10 mg/kg.
- Fluopyram benzamide residues were <0.01 mg/kg
- FLU-7-OD residues were <0.01 mg/kg
- JLU-PAA residues were <0.01 mg/kg
- FLU-PCA residues were <0.01 mg/kg



- FLU-methyl-sulfoxide residues were <0.01 mg/kg •
- The total residue of fluopyram (sum of FLU + FLU-benzamide, expressed as fluopyram) range between 0.04 and 0.11 mg/kg.

Assessment and conclusion by applicant: The study is acceptable.

apple / fruit Fluopyram-benzai	0.01 0.10 0.40	Individual recoveries	Keeøvery (* Min 999 93(*	Max 2 1107	Meân 906 297	R SD
Fluopyram (AE C65 apple / fruit Fluopyram-benzai	6948) 0.01 0.10 0.40	re@veries@ 20 90,106,107,110 93,98,99 2,101,493,104,409	999 930		Meany Que	RSD
Fluopyram-benza	0.01 0.10 0.40	93,98,99 Q 101, 193, 104, 109	999 4 93		906	44
Fluopyram-benza	0.10 0.40	93,98,99 Q 101, 193, 104, 109	93	s P		44
apple / fruit Fluopyram-benzan apple / fruit	0.40	Q 101, 193, 104 109	01		x 97 V	
Fluopyram-benza						
	mide	Or mall mark (mark)	1 ×111	×109 Å	103	453.3
	mide	weran recovery (n=11)	1 Chan		203	5.1
apple / fruit			X X	- A		
apple / fruit	0.01	× 99, 99, 104, 109	29	Q09	C 103 ×	4.7
apple / fruit	0.10	× ,29, 100, 102 L	Q99	0102	\$00	1.5
	0.40	S, 99, 101, 105	C 98. 9	105	Q01	3.1
	~~~~ (	Operall recovery (n=11)			ش 101	3.3
Fluopyram-7-OH (B	<u> </u>		- <del>V</del> ř		<u> </u>	-
	0.01	× 3 98, 101, 100, 106 ×	S 98 6	1060	103	3.6
	0.10	96.98.99 ×	960	ØŶ	98	1.6
apple / fruit	5 0.40 ×	\$ 99.102.103.106	99	106	103	2.8
LC LC	× ×	Qverall resovery (n=11)	an a	<b>V</b>	101	3.4
Fluopyram-PAA (	BC& AA10039)	O LO LY &	C V	8		
	0.01	85, 92, 98, 10,	867	101	94	7.5
×* [	0K10 K	80, 84, 910		91	85	6.6
apple / from	0.40	\$ 90,93,90,95	×80 ∼ 90	95	93	2.3
		Overall recovery (n=11)	p –		91	6.8
Fluopyram-PCA (Al	C657188	Overall recovery (n=11)	1			
1. Q	2001	91, 101, 104, 107	91	107	101	6.9
	0 0.10	C \$98, 100 101 5	98	101	100	1.5
apple / fruit	040	95, 97, 99, 100	95	100	98	2.3
A.	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Overall recovery (n=11)			99	4.3
Fluopy am-methy	sulfexide (AE134					2
	~~ 0.0k	102, 102, 107, 107	102	107	105	2.5
1 N N	V OAD . O	99.99, 101	99	101	100	1.2
apple / fruit	Q.40 C	92, 97, 100, 108	92	108	99	6.8
e Contraction of the second		Over all recovery (n=11)			101	4.7
SD = Relative midard	eviation, LOO = Pract	cal limit of quantification				

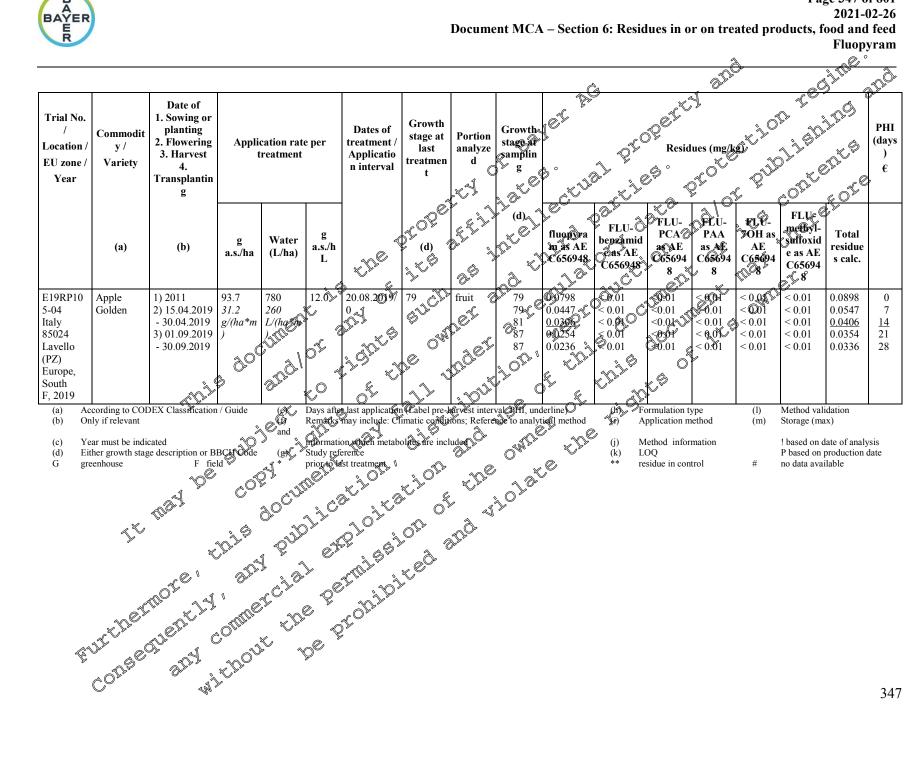


Page 346 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No. / Location / EU zone / Year	Commodit y / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplantin g	11	cation rate reatment	e per	Dates of treatment / Applicatio n interval	Growth stage at last treatmen t	analyze	Growth stage at samplar		à pr	Se Resid		() () () () () () () () () () () () () (	))))))))))))))))))))))))))))))))))))))	z. pr ^{ze}	PHI (day ? ) €
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./h Is	the of		ſ		6656948	OFLU- benzamid e aş QAE Ge 56948	as AE	FLO PAA as AE C65694	FLU- 701 as AE C65694	FLU- methyl- sulfoxid e as AE C65694 8	Total residue s calc.	
E19RP10 5-01 Italy 44124 San Martino FE Europe, South F, 2019	Apple Fuji	- 30.04.2019 3) 09.09.2019 - 30.09.2019	) <u>3</u> 0	and ,					1. ⁵⁰	0,100 0,9635 0.0392 0.0264 0.0264 0.0492		<0.01 (0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<pre>&gt;&lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01</pre>	<0.01 <0.01 <0.01 <0.01 <0.01	0.114 0.0735 0.0492 0.0364 <u>0.0592</u>	$\begin{array}{c} 0\\7\\ \underline{14}\\21\\28\end{array}$
E19RP10 5-02 France, south 31340 Vacquiers Europe, South F, 2019	Apple Golden delicious	1) 2000 2) 05.04.2019 - 20.04.2019 3) 20.09.2019 - 01.10.2019 - 01.10.2019 - 01.10.2019 - 01.00.2019 - 01.00.2019 - 15.00.2019 - 15.00.2019 - 23.08.2019 - 23.08.2019 - 23.08.2019 - 23.08.2019	95.8 28 g(ha*m ) CO	1120 349 % Ly(ha*m			OP OP		87 87 89 89 89 89 89 89 89 89 89 89 89 89 89	0.0624 0.0258 ©0258 <u>0.0264</u> 0.0230	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	0.0724 0.0358 0.0358 <u>0.0364</u> 0.033	0 7 <u>14</u> 21 28
E19RP10 5-03 Portugal 2540-558 Braçais Europe, South F, 2019	Apple Brock Field	1) 06.04.200% 2) 07.05 2019 - 15,092019 302 08.2019 23.08.2019	90.4 30.1 g/(ha*m x	1060 352 L/(ha m L/	8.590 °	30.07 2019/ 2 10 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2	77	fruit	77 78 81 81 81	0.173 0.110 <u>0.0988</u> 0.0804 0.0870	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	<0.01 <0.01 <0.01 <0.01 <0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	0.183 0.12 <u>0.1088</u> 0.0904 0.097	$\begin{array}{c} 0\\7\\ \underline{14}\\21\\28\end{array}$



Page 347 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram





Data Point:	KCA 6.3.4/04
Report Author:	
Report Year:	2020
Report Title:	Determination of the residues of AE C656948 in/on pear after spray application of fluopyram SC 250 in France (South), Spain and Portugal
Report No:	E19RP106
Document No:	<u>M-755520-01-1</u>
Guideline(s) followed in	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21
study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guideline for the Festing of Chemicals on Crop Field Trait (TG 509 published in September 2009) US EPA OCSPP 860.1500 Crop Field Trait
Deviations from current test guideline:	
Previous evaluation:	No, not previously submitted with a start of the start of
GLP/Officially recognised	Yes, conducted under @LP/Officially occognized testing facilities
testing facilities:	
Acceptability/Reliability:	Yes y y y y y y

#### Materials and method

Four residue triats on pear were conducted in southern Europe (in France, Spain and Portugal) during the 2019 season. 250, a Sc formulation containing 250 g/L of One spray application was conducted with Floopyram SC fluopyram

The target application rate was 0.03 kg as/ba x m height with a pre harvest interval of 14 days.

As the canopies height ranges between 2.5 and 2.7 mothese applications rates corresponds to a range of 0.075 – 0.080 kg ås/ha Q

At harvest, each field sample was placed in doubled labelled bags and stored deep-frozen within 24 hours after sampling and until dispatch All field samples were shipped deep-frozen under monitored conditions during shipment and argived in good condition. The field samples were stored in a freezer at ≤- 18 °C until preparation of the examination samples.

For the preparation of examination samples, the deep-frozen field samples were shredded and homogenized with dry ice in a cutter."Representative part of the shredded samples were transferred into polystyrene boxes and stored at ≤ 18 °C

Samples were analysed according to the analytical method 00984 (Martin 05/02/2007, M-283301-01-1, see MCA section 4.1.2), Full details and acceptable validation data to support this method are presented within document M-CA 40 which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

348



Briefly, residues were extracted from 5 g of sample material by two successive extractions using a high speed blender with a mixture of acetonitrile:water (80:20; v:v). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

- dilution performed under acidic conditions and measured in positive electrospray ionization for the determination of FLU-PCA.
- dilution performed under basic conditions and measured in positive electrospray ion ation for the determination of fluopyram, FLU-benzamide and FLP-PAA.

*Due to its instability, the analytical standard of fluopyram-pyridyl-acetic scid (BCS-A&10132) was made available under its sodium salt form (BCS-AA10189) which was used as reference item.

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above (299. The quantification was done by internal standardization using isotopically stable labeled internal standards. The Limit of Quantification (LOQ), expressed as fluopyrang defined as the lowest validated for fiftation

#### level, was 0.01 mg/kg.

The examination samples were kept deep-frozen untik their analysis. The quantity becessary for analysis was weighed while the sample was still deep brozen, and the remaining sample was immediately returned to the freezer. All final extracts were analysed within 24 hours.

#### Findings

In order to check the performance of the method, tecovery determinations were included in each set of analyses. Control samples from the study were forthied to be used as the recovery samples. All the recovery determinations were performed concurrently to the analyses of control and treated samples from the study. The apparent residues in the control sample used for the determination of recoveries were below 30 % of the LOQ. Recoveries were not corrected for apparent residues in the control samples used for these determinations.

The mean recoveries per fortification level were within the range of 70% - 110% and the RSD values were below 20%. The overall mean concurrent recoveries were also in the acceptable range of 70% and 110%, with the RSD < 20%.

The detailed results obtained for apple samples in northern Europe are summarized in the Table 6.3.4-10.

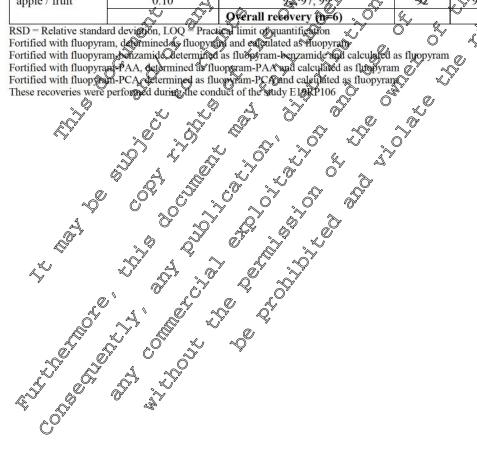
## Conclusion

Four supervised residue trials on apples were conducted in southern Europe with the application of Fluopyrath SC 250 at the required rate correspondion to the supported GAP (1x75 g as/ha, PHI=14 days), and according to GLP. Samples of apples were analysed for the residues of fluopyram and its metabolite fluopyram-benzamide (AEF148815, anas FLU-benzamide), fluopyram-pyridyl-acetic-acid (BCS-AA10139, alias FLU-PAA) and fluopyram-pyridyl-carboxylic acid (AE C657188, alias FLU-PCA). The results of the trials presented above show the following residues 14 days after last application.

- Fluepyram cesidues range between 0.08 and 0.21 mg/kg.
- Etwopyram-benz@mide tesidue@were <0.01 mg/kg
- TLU-RAA residues range between <0.01 and 0.03 mg/kg.
- FLUPCA residues were <0.01 mg/kg
- The total residue of fluopyram (sum of FLU + FLU-benzamide, expressed as fluopyram) range between 0.09 and 0.22 mg/kg.



The study is acc	eptable.			Ĩ	<b>&gt;</b>	
				- A	, 	
Table 6.3.4- 9:	Concurrent recove	ery data for Fluopyram (stud				
Portion	Fortification		Recovery (%		N N	Ň.
analysed	level (mg/kg)	Individual	Min	Max	Mean S	
Fluopyram (AE	C656948)		A A		o Q	RSD
	0.01	91, 93, 20	91	2 96	<b>\$</b> 3	2.0 2.0 2.0
pear / fruit	0.10	93, 94, 98	93 %	98	N 95 Q	2.
		Overall recovery (n=6)		98 98 0 105	O 94	2.6
Fluopyram-ber	nzamide		× ×	Ô		4
	0.01	tol, 104, 405	Q101	10	ð Ø3	2.0¢°
pear / fruit	0.10	S 90, 93, 93 S	90,->	, Or	92 🛇	
		Overall recovery (n=6)			> 98	6.6
Fluopyram-PA	A (BCS-AA10139)				<u> </u>	0
	0.01	91, 95, 102	91	100	\$96 9	5.8
pear / fruit	0.10	Q [*] 91, 95, 102 2 92, 95, 96 Q [*] 6	920	096	0 94 y	2.2
	0.10	voverall recover⊗ (n=6)	Q	o _s c	<b>2</b> 5	4.1
Fluopyram-PCA	(AE C05/188)				0.	
	0.01	0 3 92,10, 105 0 3 92,10 105	2	\$105	in 199 (199 (199 (199 (199 (199 (199 (199	6.7
apple / fruit	0.10	\$ 93.97.92 ~ ·	*2	\$99	J [°] 96	3.8
		Overall redvery (0=6)		y sy	98	5.2





Page 351 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting		ication rate treatment	per	Dates of treatment / Application interval	Growth stage at last treatment	Portion	Growth Stage at sampling	31 ²	€°Re €°Re	Ques (mg			PH ) (day
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./ht			D ^{ECD.}		fluonyram Ass AE C656948		FLŮ PCA as AE C656948	C656948	Total residues calc	(e)
E19RP106-01 France, south 13570 Barbentane Europe, South F, 2019	Pear Williams	1) 1959 2) 20.05.2019 - 01.06.2019 3) 01.08.2019 - 30.08.2019	75.4 30.2 g/(ha*m)	L(Du*m)		\$3.07.2019 \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	79° 8 DEF ZEF	Druit	5 87 87 87 87 87 87	0.131 0.0771 0.000 9.0672		©01 <0.01 <0.01 0.00 0.01	<0.01 <0.01 <0.01 <0.01	0.168 0.141 <u>0.0871</u> 0.0717 0.0772	$ \begin{array}{c} 0\\ 8\\ \underline{14}\\ 22\\ 28 \end{array} $
E19RP106-02 Spain 46370 Chiva Europe, South F, 2019	Pear Castell	1) 2001 2) 15.05 2019 - 3) 65 2019 3) 5 06.2019 - 30.06.2019	75 30.0 g/(ha*m)	250 L/(tra, m)		¥ .*	rijoji		89 89 89 89 89 89	0.347 0.252 0.205 0.177 0.05	<0.01 •0.01 •0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 0.0123 0.0192 0.0262	0.357 0.262 <u>0.215</u> 0.187 0.115	$0\\6\\\frac{14}{21}\\27$
E19RP106-03 Spain 80520 Jumilla Europe, South F, 2019	Pear Ercolini	1) 1991 2) 10.05.2019 - 31.05.2019 3) 15.07 2019 - 25.0 2019	78:0 90.2 g/(ha*m)	6555 10 232 L/(ha*m) 10	12.05 100 100 100 12.05	20.06.28150	77 J.D.J. & D.C.	fruit C	77 C 81 L 87 89 89 89	0.150 0.0984 <u>0.0752</u> 0.0519 0.0412	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 0.0100 0.0239 0.0288 0.0303	0.16 0.1084 <u>0.0852</u> 0.0619 0.0512	$     \begin{array}{r}       0 \\       7 \\       \underline{14} \\       21 \\       27     \end{array} $
2500 Caldas la Rainha Europe, South F, 2019	Rocha 🔊	3) 15.08.2019 - 09.09.2019	79.5 29.6 g/(ha*m)	671 248 1,400 m)		0708.2019/09	85 4 8700 4	feelit	85 85 89 89 89	0.104 0.120 <u>0.0751</u> 0.0133 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	0.114 0.13 <u>0.0851</u> 0.0233 <0.02	$ \begin{array}{c} 0 \\ 7 \\ \underline{14} \\ 21 \\ 27 \end{array} $
(b) Only if	relevant	Classification / Guine cription or BBCH F field Charlen W h	(f)	Days afte Remark of ormatic Study refe prior to a	Transformer	ation (Jabel pre Canatic cond netabolites are ind	-harvest interv itions; Referen	al, PHI, unde	erline) cal method	(i) Aj (j) M (k) L0	ormulation type oplication metho ethod informati OQ sidue in control	od (	(m) Storage ! based P based	validation (max) on date of anal on production available	



Based on the residue definition for risk assessment, the sum of fluopyram and fluopyram-benzapade expressed as fluopyram, the total residues for pome fruits are summarized in the Table 6.3.4-11

Сгор	Region/Indoor (a)	Trial results relevant to the critical GAP (mg/gg)	
	NEU	0.036, 0.038, 0.038, <b>0</b> , 054, 0.056, 0.684, 0.092	
Apple/Pear	Apple/Pear SEU	0.036, 0.041, 0.059, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085, 0.085,	0.22
	NEU/SEU	2x0.036, 2x0.038, 0.041, 0.054, 0.056, 0.059, 0.084, 2x0.085, 0.087, 0.092, 0.098, 0.19, 0.22	
	d Trials Median Residue	or trials in SU member states	

Summary of fluopyram total residue data for pome fruits totals to be supported Table 6.3.4-11:

Summary of Huopyram metabolites data for pome fruits trials to be supported Table 6.3.4-12:

Сгор	Region/Indoor	O Trial results relevant to the critical GA	P (mg/kg)
	(a) (a)		
		FLU-PAG SFLU-PCA FEW-70A	FLU- methylsulfoxide
	C'NEU .	3 - 3 - 3 - 3 - 3 - 3 - 3 - 3 - 3 - 3 -	4x<0.01
Apple/Pear	O SER V	7x 0.01, 0, 03 × 8x<0.01 4x<0.01	4x<0.01
	NEU/SEU	5x<0.01 & 8x<0.01	8x<0.01

in the second se (a) NEU of SEU for northern of southerprot (b) STMR: Supervised Trials Median Residue (c) HR: Highest residue CA 6.3.6

. Ø Information on the intended use pattern (GAP) is Summarised in Table 6.3.5-1.

Ś Table 6.3.5- 1: 2 Use patterns (critical GAP) for the spray application of Fluopyram in/on barley in European fields (northern and southern residue regions)

GAP number Formulation	F/ GH	No. of appl.	Growth stage at application (BBCH Code)	Application rate per treatment (g a.s./ha)	Water volume (L/ha)	Interval (days)	PHI (days)	
------------------------------	----------	--------------------	-----------------------------------------------------	-----------------------------------------------------	---------------------------	--------------------	---------------	--



1	BIX+ EC260	FLU+F )	PTΖ	F	1	30-61	78	200-400	-	
2	BIX+1 EC260	FLU+F )	ΥZ	F	1	30-61	39	200-3000	- +	
F field	·			·			Č V	<u><u></u></u>		
Residue t	rials to su					40	north and so	C	AP GARS	St 40 ^s
Table 6.3	8.5-2:	Over	view o	f Euroj	pean res	sidue trais c	onducted in b	anley per g	geographical	
		"resi	due re	gion'' a	and vege	etation period	u vớ vý			~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
		N						N N	s ís	$\sim$
		NO.	of ind	epender	nt trials _"		C C	Nº N		
Crop	Region			epender on perio		Report	førmul:	ation 🚕	Bocument,	Skeference
Сгор	Region			on perio		Report No.	Førmul:	ation	Bocument number	<b>Reference</b>
Сгор		Vo 2012	egetatio	on perio	od 2018 2	<b>No.</b> 12,2130	Formula BIX+FLU+P	, 0' TŽÉC26@	number <u>M-4759081-00</u>	KCA 6.3.5/01
Сгор	<b>Region</b> NEU	Ve	egetatio	on perio	od 2018	<b>No.</b> <b>No.</b> <b>12</b> <b>12</b> <b>13</b> <b>12</b> <b>13</b> <b>12</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b> <b>13</b>	Førmul BIX+FLU+P FLU+PTZ	, 0° TŽ ÉC2602 8E2505	number	Keterence KCA 6.3.5/01 KCA 6.3.5/02
Crop Barley		Vo 2012	egetatio	on perio 2017 4	od 2018	<b>No.</b> 12,2130	Formula BIX+FLU+P	TÉ ÉC26@ 8E250 TZ E©234	number M-47081-00 M-72556-02- Q-655243-01-	Keterence           I         KCA 6.3.5/01           -1         KCA 6.3.5/02           -1         KCA 6.3.5/03
		Vo 2012	<b>2013</b>	on perio 2017 4	od 2018 2	<b>No.</b> 12,2130 5 12,2163 217-2055 12,2035 12,2035 12,2035 12,2035 12,2035 12,2035 12,2004	Formul BIX+FLU+P FLU+PTZ FLU+ISY BIX+FLU+P BIX+CUU+P2	TZ EC260 8E250 TZ EC234 TZ EC260 5Z EC260	number M-4420081-00 M-472556-02- M-655225-01- M-474260-04- M-479739-01-	Keterence           I         KCA 6.3.5/01           -1         KCA 6.3.5/02           -1         KCA 6.3.5/03           -1         KCA 6.3.5/04           -1         KCA 6.3.5/05
	NEU	<b>V</b> ( 2012 11	egetatio	on perio 2017 4	od 2018	<b>No.</b> 122130 5 122163 017-2085 122932 13-2004 07-2018	Førmul BIX+FLU+P FLU+PTZ FLU+ISY BIX+CLU+P BIX+CLU+P FLU*ISY*P	TZ EC260 8E250 TZ EC234 TZ EC234 TZ EC260 TZ EC260 TZ EC260	number M-47,081-00 M-47,2556,02 M-655,22 M-655,22 M-474260-04 M-479739-01 M-656993-01	Kelerence           I         KCA 6.3.5/01           -1         KCA 6.3.5/02           -1         KCA 6.3.5/03           -1         KCA 6.3.5/04           -1         KCA 6.3.5/05           -1         KCA 6.3.5/06
	NEU	<b>V</b> o <b>2012</b> 11 7	egetatic 2013 -	on perio 2017 4	2018 2018 √ - α √ - α ↓ 4 Ω	<b>No.</b> 12,2130 5 12,2163 217-2055 12,2035 12,2035 12,2035 12,2035 12,2035 12,2035 12,2004	Formul BIX+FLU+P FLU+PTZ FLU+ISY BIX+FLU+P BIX+CUU+P2	TZ EC260 8E250 TZ EC234 TZ EC234 TZ EC260 TZ EC260 TZ EC260	number M-4420081-00 M-472556-02- M-655225-01- M-474260-04- M-479739-01-	Kelerence           I         KCA 6.3.5/01           -1         KCA 6.3.5/02           -1         KCA 6.3.5/03           -1         KCA 6.3.5/04           -1         KCA 6.3.5/05           -1         KCA 6.3.5/06

In the <u>Northern zone</u>, three trials were conducted according to the GAP in 2012. Twelve residue trials were conducted in the 2012 and 2017 growing seasons with a higher dose rate compared to the supported GAP. As all other GAP parameter respect the GAP, a downscaling factor is applied to the residue results. According to EFSA Technical Report (EFSA supporting publication 2018-EN-1503), *the proportionality concept fun be applied foresidite data from field trials conducted within a dose rate range of between 0.3x and 4x the GAP dose rate.* Thus, a proportionality factor is applied to the results of the northern residue studies (12-2163 and 17-2017) to be with the intended GAP.

Table 6.3.5-37 Scaling factors to be applied on barley total residues of fluopyram (northern residue r

Study	Triâl number	Dose rate (g ai/ha)	BBCH at application	Scaling factor
4	×12-2163-01	125	61	0.62
01	12-2163-00	©25	61	0.62
	<u></u> 2-216€03 ~	§ Q 125	61	0.62
12 242	12-2963-04	125	61	0.62
	12-2163-03	¥ 125	61	0.62
	2-2169-06	125	61	0.62
12-2163 x ² ⁵ ⁴ 4 ⁵ ⁴ x ⁵ ⁴	0 12 2163-07	125	61	0.62
ČO ^{S.}	12-2163-08	125	61	0.62



Study number	Trial number	Dose rate (g ai/ha)		BBCH at oplication	Scali	ng factor	
	17-2017-01	101		61	Ś	0.77	
17-2017	17-2017-02	101		61	O.Y	0.77 🔗	
17-2017	17-2017-03	101	<u>_</u>	61	7	0.770	
	17-2017-04	101	de la companya de la	61			
			Å	, 6 ⁹	@	, <u>3</u> 9	

In the Southern zone, eight trials were conducted according to the GAP in 2012 and 2013. Eight residue trials were conducted in the 2017 and 2018 growing seasons with a higher dose rate compared to the supported GAP. As all other GAP parameter are respected, a downscaking factor is applied to the residue results. According to EFSA Technical Report (EFSA supporting publication 2018-EN-1503), the proportionality concept can be applied to restaue date from field trais conducted within dose fate range of between 0.3x and 4x the GAP dose rate Thus, a propertionative factor is applied to the results of the northern residue studies (17-2018 and 18-2101) to fit with the intended GAP . O⁵ ~~~ *m* 

Table 6.3.5- 4:	Scaling factors to	be appl	ied on	barley	total	esidices	of fluð	pyram (	southern
	residue regions)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		, Cr	5	J O	~O~	õ	°~~

				A 8	×0 /. *Y
Study number	<b>Trial number</b>	Done wata		BBCH an pplication	Scaling factor           0.77           0.77           0.77           0.77
	17-2018-01	<u>\$ 19</u>	<u>o</u> r sr`	61 2	<u>م</u> م 0.77
17-2018	17-2018-02	2 0 ⁴ 2 101 2 101		61 61 61 61 61 61 61 61 61 61	0.77
	<u>,</u> 3 ³ 17-20 <b>0</b> 8-03 ³ √	<u> </u>		61	
	170018-04 ×	× 101 × 201 × 103 ¢		61 ° 61 °	0.77
18-2,01	P8-2101-01	1030		6b 761 0 59 61	0.75
18-2001	18-2101-02	<u>ر</u> 190		<u>_</u> 761	0.78
10 00 01	18-2101-03	* <u>````````````````````````````````````</u>		©″ 59	0.77
	218-2101-04			61	0.77
GAP 1 norther	18-2)101-02 18-2101-04 18-2101-04 18-2101-04 n zone				
	18-2101-02 18-2101-02 18-2101-02 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 18-2101-04 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 19-10 10				



Data Point:	KCA 6.3.5/01
Report Author:	
Report Year:	
Report Title:	Amendment No. 2 to Final Report No: 12-2130 - Determination of the residues of
	AE C656948, BYF 00587 and prothioconazole in/on spring barley and winter barley
	after spray application of bixafen & fluopyram & prothjoeonazole EC 260 in the field
	in northern France, the United Kingdom, Belgium and Germany
Report No:	12-2130
Document No:	<u>M-475081-03-1</u>
Guideline(s) followed in	Regulation (EC) No 1107/2009 of the European Parliament and of the Quncil of 21
study:	October 2009 concerning the placing of plant protection products on the market and
	repealing Council Directive 79/117/EEC and 91/444/EEC V
	EC Guidance working document 029/Vb95 rev 5 (1997/07-22)
	OECD 509 Adopted 2009-09-09, OECP GUIDELINE FOR THE TESTING OF
	CHEMICALS, Crop Field Total
	US EPA OCSPP foundeline No. 869.1500
Deviations from current	US EPA OCSPP (Trideline No. 860/1500, 1, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2,
test guideline:	
Previous evaluation:	yes, evaluated and accepted v v v v v v v
	Study was not found in DAR/RAR and the Addenda
GLP/Officially recognised	Yes, conducted under @LP/Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	

## Materials and Method

Four supervised rials on barley were conducted in northern Europe (in northern France, Belgium, the United Kingdom in Germany) during the 2012 season

One-spray applications was conducted with BDX+FLU+PTZ EC 260, an EC (emulsifiable concentrate) formulation containing 130 gP profile concazole, 65 g/L of fluopyram and 65 g/L of bixafen. For the purpose of this renewal, only results for fluopyram and its metabolite fluopyram-benzamide will be discussed.

The applications were conducted at the BBCH of 61 and at the application rates of 1.2 L/ha corresponding to the single application 0.048 kg as /ha. Water application rates were at 200 - 300 L/ha.

Samples of barley green materin were collected at BOCH 61, 65, 71, 83, and barley grain and straw at BBCH 89. Due to a bir attack ho sample of grain and straw was taken from trial 12-2130-03.

Each field sample was placed in doublet labeled bags and stored deep-frozen within 24 hours after sampling and until dispatch. All tield samples were shipped deep-frozen (at -18 °C or lower temperatures) under monitored conditions during shipment and arrived in good condition, except for the shipment of some samples from the trial 12-22/30-01 which were shipped in two shipments at higher average shipment temperatures. Nevertheless, also these samples arrived in good and frozen condition. A short term storage stability study was conducted to show that this deviation has no impact on the stability of the residues (see CA 6 1, KCA 6.1/10, M-400441-06-1).

The field samples were stored in a freezer at  $\leq$ -18 °C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field samples were shredded and homogenized with dry iceOn a cutter. Representative parts of the shredded samples were transferred into polystyrene boxes



and stored at  $\leq$ -18°C. For each field sample, one or several examination samples were prepared for analysis and one examination sample was prepared as a reserve sample.

Samples were analysed according to the analytical method 00984/M003 (2015, M-467, 23-03-1, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues were extracted from 5 g of sample material by extraction using a chaker (15 min) with a mixture of acetonitrile:water (4:1, v:v). After filtration the extracts of the solutions were made up to volume. The solutions were centrifuged, and the extract volume was adjusted. The extracts were colluted by adding the internal standard. An aliquot of the extracts was injected into a HPLC-(MS/MS).

The linearity was demonstrated in each analytical batch with a 1/2 weighted calibration curve established with at least 5 concentration levels.

The quantification was done by internal standardization using sotopically stable labelled internal standards.

The Limit of Quantification (LOQ), expressed as Duopyram, defined as the lowest validated fortification level, was 0.01 mg/kg.

All final extracts were analysed within 2 days after extraction. Fluopyram and fluopyram benzamide were found to be stable in extracts of matrices of plant origin for at least four weeks at  $A \pm 3$ , which was tested within the validation of method 00984/M003.

#### Findings

In order to check the performance of the method, recovery determinations were included in each set of analyses. Control samples from the study were fortified to be used as the recovery samples. All the recovery determinations were performed concirrently to the malyses of control and treated samples from the study. The apparent residues in the control sample used for the determination of recoveries were below 30 % of the LOQ. Recoveries were not corrected for apparent residues in the control samples used for the determination of recoveries were below 30 % of the LOQ. Recoveries were not corrected for apparent residues in the control samples used for these determinations.

The mean recoveries per fortification level were within the acceptable range of 70 % – 110 % and with the RSDs < 20 %. The overall mean concurrent recoveries were also in the acceptable range of 70 % and 110 %, with the RSD < 20 %.

The storage period of deep trozen samples interfield for the analysis of fluopyram and its metabolite fluopyram-benzamide ranged between 322 and 429 days.

The detailed results obtained for barley samples in northern Europe are summarized in the Table 6.3.5-6

## Conclusion

Four supervised residue trials on barley were conducted in northern Europe with the application of BIX+FLQ+PTZ EC 260 at the required rates and according to GLP. Samples of barley were analyzed for the residues of fluopy am and its metabolite fluopy am-benzamide. The results of the trials presented above show the following residues in grain at barvest

- Fluopyram residues range between < 0.01 and 0.02 mg/kg.
- Fluopyram-benzamide residues were <0.01 mg/kg
- The total residue of fluopyram (sum of FLU + FLU-benzamide, expressed as fluopyram) range between 0.02 and 0.035 mg/kg.

## Residues in straw at harvest?

- Etaopyram residues range between 0.03 and 0.06 mg/kg.
- O^Pluopyram-benzamide residues were <0.01 mg/kg



betwee	en 0.04 and 0.07	uopyram (sum of FLU + mg/kg.			,p200	^{\$}	
Assessment ar	nd conclusion by	applicant:			Ô	7	
The study is ac	ceptable.		Ď		A A	7 & .	
able 6.3.5- 5	: Concurrent r	ecovery data for Fluop	çam (stu	dy 1022	\$ 130)		opyram) range
Portion	Fortification	X	ecovery (				
analysed	level (mg/kg)	Individua recoveries	Miô	Max	Afean a	RSD.	
Fluopyram (AE	C 656948)		$\sim$		1 S	0*	
	0.01	86; 90@4; 94°95	86 4	95	. M	×#.1 8	
Barley / grain	0.10	102003; 103, 104, 5	MQ	104	2103 296 296 296 296 296 296 296 297 297 297 297 297 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010 2010	U 0.8	
Lancy / gran	0.80	Q 90; 99; 100	90	2100	y 96 v	S.	×?
		Oferall recovery (nº 12)			~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	6.2	×
	0.01	88; 88; 93; 98000; 100	88	<u>din</u>	6 95 C	6.0	
Daulary ( ano an	0.10	096; 96; 98; 102	796	[~] 102	y 98	2.9	
material	0.80	A 95; 97; 99; 100 101	95	101	× 98	2.4	
	4.0	\$ \$93; 93; 94	×93	×94	93.0	0.6	
	×	Overall recovery (n=18)	¢~	0	96	4.3	
	<u>Č</u> 0.01	73;95;96;96	7302	26	Ø90	12.6	
Barley / straw		04: 07: 100	2 ⁹⁴	\$97	<b>√</b> [¥] 96	1.6	
~^?	45	94, 97, 100	© 94 €	100©	97	3.1	
		Overall (ocovery (n= 10)		L.Or	94	8.0	
Fluopyram-be				0' M			
-	\$9.01 ×	45×85; 8796; 97499 4		0,000,000	93	6.8	
Barley / grain	<u>~ 0.18</u> ⊘ 890 ℃	9 <b>3</b> 99; 10 <b>2</b> ; 103 88; <b>0</b> , 98	<b>8</b> 8	103	101	2.4	
Barley / straw				98	94	5.8	
		$e^{12}$		109	<b>96</b> 99	6.1	
	0.00	~ 91; 90; 98; 99; 100 ~ 90; 98; 99; 100	91 90	108 100	99 97	6.6 4.7	
Barley / green		96; 92 101; 105, 108	90	100	102	4.7	
material	0.80 5 V	86; 87, 90	86	90	88	2.4	
		Overall recovery (n = 18)	00		97	6.9	
	0.01	2 95; 97; 98	92	98	96	2.8	
	0.19	89; 92; 94	89	94	92	2.3	
Barley Straw	A15 .28	104; 108; 110	104	110	107	2.8	
N N		Overall recovery (n = 10)			98	7.3	

RSD = Replive standard deviation, LOQ = Practical limit of quantification Fortified with fluopyram, determined as fluopyram and calculated as fluopyram



Proceeding of the operation of the second of A construction of the state of

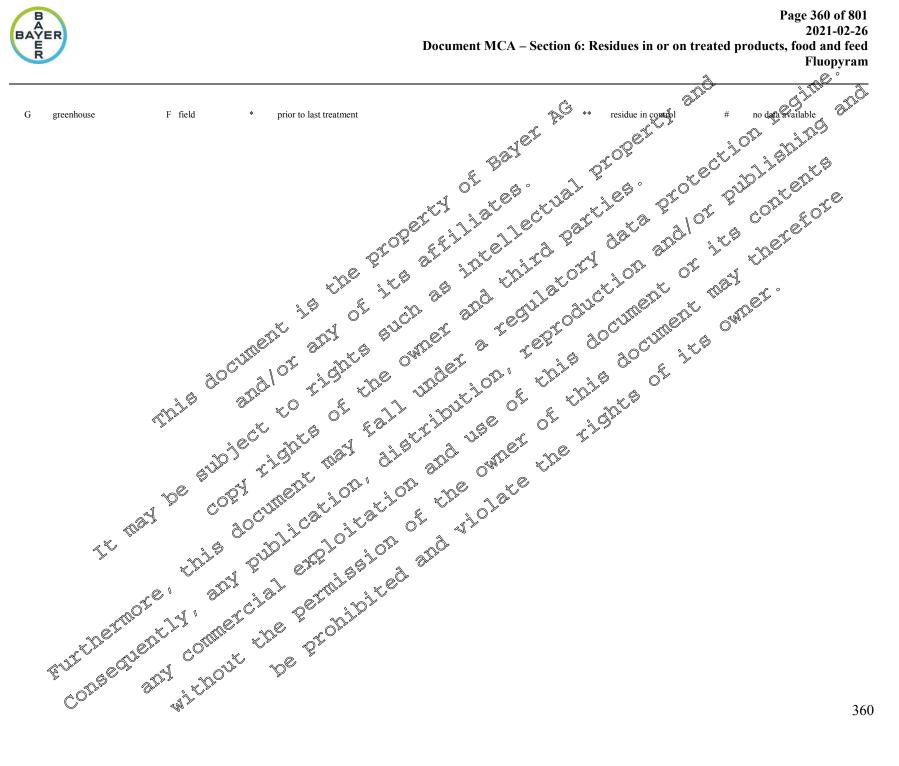
BAYER

Page 359 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

		Transplanting			ation rate per eatment Dates of treatment / Application interval Growth stage at last treatment		stage at-last treatment	agaalyzed Stage at Gampling					PH (day ©
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL			110	C (d)	Baopyram as AE C656948	benzamide as AF-C656948	Total cesidue	(e)
2-2130-01 Barle rance, north Wintu 5710 Volu haussy Barle wintu	ter 2) 1 ume; -2 ley 3) 1	04.10.2011 14.05.2012 25.05.2012 17.07.2012 20.07.2012	78	300	2800 OF	14.95 \$012/0	al and a	green x material		1.0 0.23 0.16 00055	-0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01 -0.01	1.0 0.24 0.47 0.045	0 7 14 28
)12		ć	JURCE	, J		S OWL		grain	89 d.O	0.015-7 ^{1,71}	<0.01 \$ <0.01	<u>0.025</u> 0.064	64 64
2-2130-02 Barle elgium sprin 495 Marbais Quer urope, North Malt varie	ng 2) 2 nch; - 2 ting 30	08.08.2012	78 Jul			22.06.2012 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2		green XX material grain		1.3 O 0.025	<0.01 <0.01	1.31 <u>0.035</u>	0 47
2-2130-03 Barle nited winte ingdom Carra B22 5EU Winte ambridge barle	ley, 1) ( ter 2) 2 rat; 3) 7 ter - f	07.09.2011 21.05.2022 15.07.2012 105.2012		200 200 RED ^{EC}	NOD 1	2005.2012/0- 2005.2012/0-		green S material	89 61 69 71 83	0.058 1.7 0.86 0.28 0.080	<0.01 <0.01 0.029 0.016 <0.01	0.068 1.7 0.89 0.30 0.090	47 0 7 14 27
urope, North 2012 2-2130-04 Bary ermany sprin 1399 Simb	ng 2) (	16.03.2012 05.06 2012 1.06.2012	30 78 1 1	300 61-5	26	0.06.201240	2 ²	green material	61	1.8	<0.01	1.8	0
urscheid typic urope, North regio	cal of the 3	10.08.2012 4.08.2012		, P ^{et}		×°°		grain straw	89 89	<0.01 0.024	<0.01 0.017	<u>&lt;0.02</u> 0.041	69 69

Page 360 of 801 2021-02-26







Data Point:	KCA 6.3.5/02
Report Author:	
Report Year:	2014
Report Title:	Determination of the residues of AE C656948 and protheconazole in/on pring barley and winter barley after spray application of AEC656948 & JAC 6476 SE 250 in the field in northern France, Germany, the Netherlands, Belgium and United
Report No:	Kingdom
Document No:	<u>M-472556-02-1</u>
Guideline(s) followed in	Regulation (EC) No 1107/2009 of the European Parhament and of the Council of
study:	October 2009 concerning the placing of plant protection of oduction the market and repealing Council Directives 79/117/FFC and 91/414/6EC EC Guidance working document 7029/VI/9 Prev.5 (1997-07-22) OECD 509 Adopted 2009-09-07, OECD GUIDEDINE FOR THE TESTING OF CHEMICALS Crop Field Trial
Deviations from current test guideline:	none
Previous evaluation:	yes veraluated and accepted Study was not found in DAR/RAB and the Addenda
GLP/Officially recognised	Yes, conducted@nder GPP/Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability	$Ye \Phi^{T} \xrightarrow{\downarrow T} \qquad $

Materials and Methods

Eight supervised residue triak on battey were conducted in northern Europe (in northern France, in Germany, in the Netherlands, in Belgium, in the United Kangdom) during the 2012 season.

One-spray applications was conducted with FLUFPTZ SE 250 a suspo-emulsion formulation containing 125 g/L of fluopyram and 125 g/L of prothioconazole. For the purpose of this renewal, only results for fluopyram and us metabolite fluopyram-bergamide will be discussed.

The applications were conducted at the BBCH of 61 and at the application rates of 1.0 L/ha corresponding to the single application 0.125 kg a.s./be. Water application rates were at 200 - 300 L/ha. As the dose rate is higher than the intended GQP (1x125g as ha Vs 1x78g), the residues are downscaled according to the scaling factors calculated and presented in Table 0.3.5-3.

Samples of barley green material were collected at BBCH 61, 65, 71, 73, 75, 83, barley grain and straw at BBCH of 89.

Each field sample was placed in doubled labelled bags and stored deep-frozen within 24 hours after sampling and until dispatch. All field samples were shipped deep-frozen under monitored conditions during shipment and arrived in good condition. Some temperature problems occurred during the transport of the samples from the trials [2+2163-01 and 12-2163-02. A short term storage stability study was conducted to show that this deviation has no impact on the stability of the residues (see MCA 6.1.2, <u>M-480441-06-1</u>).

The field samples were stored in a freezer at  $\leq$ -18 °C until preparation of the examination samples.



For the preparation of examination samples, the deep-frozen field samples were shredded and homogenized with dry ice in a cutter. Representative parts of the shredded samples were transferred into polystore boxes and stored at  $\leq$ -18 °C.

Samples were analysed according to the analytical method 00984/M003 (**Mathematical**, 2015, <u>M-467323-692</u> <u>1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU, regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues were extracted from 5 g of sample material by extraction using a shaker (15 turn) with a mixture of acetonitrile:water (4:1, v:v). After filtration the extracts of the solutions were made up to volume. The solutions were centrifuged, and the extract volume was adjusted. The extracts were diluted by adding the internal standard. An aliquot of the extracts was injected into a HPEC-(MS/MS).

The linearity was demonstrated in each analytice batch with a Tx weighted calibration curve established with at least 5 concentration levels.

The quantification was done by internal standardization using isotopically stable abelled internal standards. The Limit of Quantification (LOQ), expressed as fluoryram, defined as the lowest validated fortification level, was 0.01 mg/kg.

All final extracts were analysed within 2 days after extraction. Etopyran and fluopyran benzamide were found to be stable in extracts of matrices of plant origin for at least four weeks at  $4 \pm 3^{\circ}$ C which was tested within the validation of method 00984/M003

## Findings

In order to check the performance of the method, recovery determinations were included in each set of analyses. Control samples from the study were fortified to be used of the recovery samples. All the recovery determinations were performed condurrently to the analyses of control and treated samples from the study. The apparent residues in the control sample used for the determination of recoveries were below 30 % of the LOQ. Recoveries were not corrected, for apparent residues on the control samples used for these determinations.

The mean recoveries per fortification level were within the acceptable range of 70 % – 110 % and with the RSDs  $\ll 20$  %. The overall mean concurrent recoveries were also in the acceptable range of 70 % and 110 %, with the RSD < 20 %

The storage period of deep-frozen samples intende Ofor the analysis of fluopyram and its metabolite fluopyram-benzamide anged between 246 and 331 days.

The detailed results obtained for barley samples in northern Europe are summarized in the Table 6.3.5-8

Eight supervised residue trials on barley were conducted in northern Europe with the application of FLU+PTZ SE 250 at a higher rate than equired in the supported GAP (1x125g as/ha Vs 1x78g), and according to GLP. Samples of barley were analyzed for the residues of fluopyram and its metabolite fluopyram-ben amide. The results of the trials presented above show the following residues after donwscaling of grain at harvest.

- Floopyram residues range between <0.01 and 0.02 mg/kg.
- Puopyram-berdamide residues were <0.01 mg/kg

• The otal residue of fluopyram (sum of FLU + FLU-benzamide, expressed as fluopyram) after downscaling to the right dose (1x125g as/ha Vs 1x78g), range between <0.02 and 0.03 mg/kg.

Residues after downscaling in straw at harvest :



- Fluopyram residues range between 0.01 and 0.11 mg/kg. •
- Fluopyram-benzamide residues were between <0.01 mg/kg and 0.02 mg/kg
- The total residue of fluopyram (sum of FLU + FLU-benzamide, expressed as fluopyram) downscaling to the right dose (1x125g as/ha Vs 1x78g), range between 0 Az and 0.11 ms

Co Br

#### Assessment and conclusion by applicant:

The study is acceptable.

The residue level in these GLP trials was corrected with a proportionality actor according to Report (EFSA supporting publication 2018-EN-1503).

report (Dr Sr)			/	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		) A	Á
		ч. Ф.	ra° (	O ^Y J	Y m		
able 6.3.5- 7	7: Concurrent r	ecovery data for Duopy	am (stu	dy 12-2	163)		· % ~
		A . Op.	covery (	0/20	ð,	o de	A.
Portion	Fortification		Covery (		<u> </u>		
analysed	level (mg/kg)	Indevidual	Min	Max	Mean	RSD	
Fluopyram (A)	E C656948)	- A COVERCY	s S		Mean		' O
	0.01	98; 105; 108 9	D 98 &	0 108 0	100		
Barley / green	1.0	\$\$ \$\$\$;92;93	9,4°	SO.		Q ^{1.0} Q 1.1∢	$\sim$
material			0 ⁹⁸	2.99 s	0 00		
	3.0	Overall recovery (188)	0		99 980	· · · · · · · · · · · · · · · · · · ·	
	0.01/		.10	¢106	×104 %	3.1	
Barley / grain	020	~~101; 1 <b>0</b> ; 102, ~~	×101	0102	× 102×	0.6	
Durie) / Brunn	J. Or	Overall recovery (n=6)	°.¢		103	2.3	
	. 0 0.02	\$105; 110; 113		. Ør3	×\$109	3.7	
Barley / straw		89; 94, 95	89		S.	3.3	
Surrey / Surrey	×		y C	×,	101	10.1	
Fluopyram-b	enzamid			- Co			
r nopja gin o	Q.01 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	78 69 91 2	78 5	91	86	8.1	
Barley / green	6 1.0 A	\$3,95;97 O	23	97	95	2.1	
material	U 30 P	93:*** {\$	23	94	94		
~	$\sim \sim \sim \sim$	Qverall recovery (by= 8)	°O'	a contra a para	91	6.4	
- A	0.01	\$ 96,103; 098	96	108	102	5.9	
Barley grain	0.01		98	105	101	3.8	
L.	~~~~	Øverall @coverv (n =6)			102	4.5	
¥	0.01 ⁰	74, 80; M	74	101	85	16.7	
Barley / straw	(1.0 C	~ 85; 0, 97	85	97	91	6.6	
		Overall pecovery (n = 6)			88	11.7	
SD = Relative sta	indard deviation LOO	Practical Unit of quantification					

#### Q Ro

RSD = Relative standard deviation, LOQ Practical smit of quantification Fortified with fluor with, determined as puopyram and calculated as fluopyram Fortified with fluor ram-benzamide covernined as fluopyram-benzamide and calculated as fluopyram These secoveries were performed during the conduct of the study12-2163

A



Page 364 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

2-2163-01 rance, north 5710Barley, winter Volume2-2163-02 bermany 9377 Vechta Langförden turope, lorthBarley, winter012Barley, winter2-2163-02 bermany burope, lorthBarley, winter012Barley, winter012Barley, winter012Barley, winter012Barley, winter012Barley, winter012Barley, winter	y, 1 r 2 ne - 3 y, 1 r 2 lian; -	(b) ) 04.10.2011 ) 14.05.2012 - 25.05.2012 ) 16.07.2012 - 19.07.2012 ) 30.09 2011 ) 30.09 2011 ) 30.09 2011 ) 30.09 2012	125	300 CD ^C		14.052012/0 14.052012/0 14.052012/0 14.052012/0 14.052012/0 14.052012/0 14.052012/0	Ch.		61 71 83 89 89 61 71 83 70 83 70 83 70 83 70 83 70 83 70 83 70 83 70 83 70 80 70 83 70 80 70 70 70 70 70 70 70 70 70 7	fluopyram as AE co56948 0.256948 0.256948 0.250 0.043 0.043		Calc. 4 Calc. 4 1.8 0.27 0.20 0.055 0.055	Scaling factor	Scaled residue	(e) 0 7 14 28 64
rance, north 5710 winter 5710 Volume haussy burope, forth 012 2-2163-02 Barley, winter 9377 Vechta Langförden Jorth 012 2-2163-03 Barley, winter	r 2 ne - 3 - y, 1 r 2 lian; -	) 14.05.2012 - 25.05.2012 ) 16.07.2012 - 19.07.2012 ) 30.022011 ) 30.022011 ) 30.022011	OCUIR	Ø1 ₀₄		14.0\$2012/0	Ch.	material	83 g	1.8 0 25 0 25 0.19 0.043 0 0.043	<0.01 C0.01 <0.01 <0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0.01 C0	1 & 0.27 0.20 0.053	N COL	0.17 0.12 0.033	7 14 28
0122-2163-02Barley, winter9377 VechtaMeridia Meridia multilir high haCurope, lorthhigh ha0122-2163-03 Winter	r 2 lian; -	1×2×1.05.2012	125 02	300×C	- Line	AL & DE	JJL OL	grain	89	0.018	<0.01	0.028		<u>0.017</u>	64
iermany winter 9377 Vechta Meridia Langförden multilir urope, forth 012 2-2163-03 Barley, ketherlands winter	r 2 lian; -	1×2×1.05.2012	125	300	Dia.			SILAW	896	0.14	0.012	0.15		0.093	64
letherlands winter	narvest -	- 04.06.2012 - 05.07.2012 - 25.07.2012	p ^{jed}			\$2.05.20120 E		materia	73 75 80	1.8 0.95 0.31 0.44 0.025 0.066	<ul> <li>0.01</li> <li>0.01</li> <li>0.01</li> <li>0.01</li> <li>&lt;0.01</li> <li>&lt;0.01</li> <li>&lt;0.01</li> </ul>	1.8 0.96 0.32 0.15 0.035 0.076	0.62	1.1 0.60 0.20 0.093 <u>0.022</u> 0.047	0 7 14 28 62 62
lootdorp 🔍 👋	r Mart - 3	14.10.2011 01.06.2012 - 15.06.2012 ) 22.07.2012 - 02.08.2042	ĝ Ĉ	Qr.	42 00 0 0 0 0	01.06.2012/0		green	61 65 65 83 89	2.6 0.62 0.30 0.062 0.027	<0.01 <0.01 <0.01 <0.01 <0.01	2.6 0.63 0.31 0.072 0.037	0.62	1.6 0.39 0.19 0.045 <u>0.023</u>	0 7 14 28 54
urope, forth 012 EUIE ^{TIDE} COILSE	e que		D ^{DT}	197 196 196	P ^{TC}	philoit.		straw	89	0.057	<0.01	0.067		0.042	54



Page 365 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

												à		e	, °
										Ĉs		O.D.		O'L'ILL	- Car
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting		cation ra reatmen		Dates of treatment / Application interval	Growth stage at last treatment	Portion analyzet	Growth Ostage at sampling	Dat 2	OP Resi	dues (mg/fy)	) ^{(),1,4}	COLLE	PHI (days)
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	(c) 2 ^{°°°}		L'IA		fluopyram As AE C656948	FI2- benzamide as AE C656948	a	Scaling factor	Sealed Fesidue	(e)
12-2163-04 Netherlands 9076 PP Sint Annaparochie Europe,	Barley, winter Winter Malt	1) 10.10.2011 2) 30.05.2012 - 18.06.2012 3) 15.07.2012 - 01.08.2012	125	300	42 ***	0 ⁴		Oppe	65 65 83 9 9	2,10 9.25 0.088 0.030	*001 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.	0.26 0.098 0.040	9.62	1.3 0.16 0.061 0.025	0 7 14 28
North F 2012			AUT	CLA	OID		OWLEY	grain Straw	89 89	0.014 0.0		0.024		<u>&lt;0.02</u> 0.022	56 56
12-2163-05 France, north 37310 Chambourg sur Indre	Barley, spring Sebastian	1) 02.03.2012 2) 01.06.2012 - 08.06.2012 3) 20 97.2012 - 25.07.2012	P25 DI	Nor Nor	42 5 0	01.06.201 <b>20</b> 5 5 6 7 7 7 7 7 7 7 7 7 7		green material grain			<0.01 0*	1.9 0.028	0.62	1.2 <u>0.017</u>	0 53
Europe, North F, 2012		- 23.07.2012	o ^{jec}		J ^{ED} T	0 ⁴ )	G ^{t'l}	straw w	8875 S	0.014	0.020	0.034		0.021	53
12-2163-06	Barley, spring Ouench;	1) 15.03 2012 2) 22.06.2012 - 26.06.2012 3) 08.08.2012	125 J			22.06.2012/0		green material	et e P	2.2	<0.01	2.2	0.62	1.4	0
Europe, North	Malting variety	3) 08.08.2012 - 17.08.2012	20		Ċ	, to	of	grain	89	0.026	< 0.01	0.036		<u>0.022</u>	47
F 2012	J.		¢ ¢	NOL			and	straw	89	0.081	<0.01	0.091		0.056	47
E VI	onsequ	2) 22,092012 -26.06.2012 -108.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.08.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.09.2012 -17.		200 100 200	PETO PETO		ġ>								365



Page 366 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

												a		e	, o , ,
										Ĉa		O.D.		O'L'LL	a Dide
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting		cation ra reatmen		Dates of treatment / Application interval	Growth stage at last treatment	Portion analyzet	samping ©	. Out	COPECTO Resi	dues (mg/kg		E COLE	PHI (days)
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	(c)				C656948	benzamide as AE C656948	cale	factor		(e)
12-2163-07 United Kingdom CB22 5EU Little	Barley, spring Propino	1) 23.03.2012 2) 25.06.2012 - 09.07.2012 3) 06.08.2012 - 20.08.2012	125	200	63	25.96.2012/0		green material	880JU		2007 0.037 CUTO 0.057 CUTO	2.4 000	0.62 NDC ^C		0 46
Shelford Farm Europe, North F, 2012		6	OCUL	810 ³	- 1 - 1	M ^{t 9} ne	OWLE'	straw _o ,	89 50		0.037 UIN 200 OF	0.17	9	0.11	46
12-2163-08 Germany 51399	Barley, spring Simba	1) 16.03.2012 2) 05.06.2012 - 11.06.2012	125 🖓	300 K	)#2 () () ()	\$5,06.2012/0 \$5,06.2012/0		gram		2.6	Star Star	2.6	0.62	1.6	0
Burscheid Europe, North F, 2012		3) 10.08.2012 - 24.08.2012		7. ³ . O		9. J.	- OIL	straw	8975 89 ×	2.6 0.016 0.11	<0.01 0.029	0.017 0.14		<u>&lt;0.02</u> 0.087	69 69
(a) Accord (b) Only it	ding to CODEX f relevant	Classification / Guid	le (f	e) Der	after last narks may	application (Isab	Opre-harvest conditions B	overval, PHI eference to a	underline)	(h) nod (i)	Formulation typ Application met			d validation e (max)	1
(c) Year n (d) Either G greenh	nust be indicated growth stage de iouser	Classification / Guid Scription or BBCH ( F field F field Chit L V ( CON DAN WITCH		red C info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info info	ritignon wi y reference r to last the CAP	hich meadolites a alment of	are Fided			(j) (k) **	Method informa LOQ residue in contro		P based	l on date of an d on productic a available	
Ċ	OTRE	Or. Pr	~												366



Data Point:	KCA 6.3.5/03
Report Author:	
Report Year:	2019
Report Title:	Determination of the residues of BCS-CN88460, prothioconazole and Ab C656948 in/on spring barley after spray application of FLU & RCS-CN88460 & PTZ EC 234 in Germany, Denmark, the United Kingdom and nothern France
Report No:	17-2017 <u>A</u> O [×] <u>U</u> <del>A</del> A
Document No:	<u>M-655225-01-1</u>
Guideline(s) followed in	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21
study:	October 2009 concerning the placing of plant protection products on the market OECD Guideline for the Testing of Chemicals on Croop Field Trial (TG 509 published in September 2009) US EPA OCSPE 860.1500, Croop Field Trial
Deviations from current test guideline:	none $(\mathcal{A}^{*}, \mathcal{A}^{*}, \mathcal{A}^{*}$
Previous evaluation:	Study sas not found in DAR/RAR and the Addenda
GLP/Officially recognised	Yes conducted under GLP/Officially recognised testing factities
testing facilities:	
Acceptability/Reliability:	Yes Q Q L Q Q Q
Materials an	Yes Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q

#### Materials and Methods «

Four supervised residue trials on barley were conducted on northern Europe (Germany, Denmark, in the United Kingdom, northern France during the 2017 season. 2)

One-spray applications were conducted with FIGH+ISX PTZ FC 234 an emulsfiable concentrate formulation containing 67 g/1z of fluopyram, 42 g/C of isoffucyptam, and 125 g/L of prothioconazole. For the purpose of this renewal, only results for floopyrant and its metabolite fluopyram benzamide will be discussed. ≪.

The applications were conducted at the BBOH of of and of the application rates of 1.5 L/ha corresponding to the single application fare of 011 kg a.s./ha Water application rates were at 200 – 250 L/ha. As the dose rate is higher than the intended GAP (1x101g as the Vs 1x78g), the residues are downscaled according to the scaling factors calculated and presented in Table 6.3.5-3.

Samples of barley green material were collected at BBCH 61, 65, 73, 75, 77, 83, 85, 87, barley grain and straw at BBCH of 89.

Each field sample was placed in double labelled bags and stored deep-frozen at ≤-18 °C or below, within 24 hours after sampling and until dispatch. All field samples were shipped deep-frozen under monitored conditions during shipment and arriverOn good condition. The field samples were stored in a freezer at ≤-18°C word preparation of the examination samples, except for trial 17-2017-02 and trial 17-2017-03 where temperature deviated over a short period during the field storage (trial 17-2017-03) or during shipment (trial 17-2017-02). However, these deviations were considered acceptable.



For the preparation of examination samples, the deep-frozen field samples were shredded and homogenized with dry ice in a cutter. Representative parts of the shredded samples were transferred into polystypene boxes and stored at  $\leq$ -18°C.

Samples were analysed according to the analytical method 00984/M003 (**Mathematical Science**, 2015, <u>M-467323-692</u>), see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outfined within SANCO/3029/99 rev 4.

Residues were extracted from 5 g of sample material (additionally 2.5 g for the sample material straw) by extraction using a shaker (15 min) with a mixture of acconitrile:water 4:1, v:v).

The filtering procedure under low vacuum was replaced by a centrifugation step. Then 05 mL of internal standard solution (1 mg/L) was added to the extract followed by 5 min centrifugation at 4000 rom at 10 °C. An 0.1 mL aliquot of this extract was diluted with 0.9 mL of Milli-Q water and ther proceeded to MPLC-MS/MS analysis.

The linearity was demonstrated in each analytical batch with a fox weighted carbration curves stablished with at least 5 concentration levels.

The quantification was done by internal standardization using isotopically stable labelled internal standards. The Limit of Quantification (LOQ), expressed as fluopyram, defined as the lowest validated fortification level, was 0.01 mg/kg.

All final extracts were analysed within 7 days after extraction. Fluopyram and fluopyram benzamide were found to be stable in extracts of matrices of plant origin for at least four, weeks at  $4 \pm 3$  °C which was tested within the validation of method 00984/M003.

## Findings

In order to check the performance of the method, recovery determinations were included in each set of analyses. Control samples from the study were fortified to be used as the recovery samples. All the recovery determinations were performed concurrently to the analyses of control and treated samples from the study. The apparent residues in the control sample used for the determination of recoveries were below 30 % of the LOQ Recoveries were not corrected for apparent residues in the control samples used for these determinations.

The mean recoveries of fluopyrate and is metabolite the properties of receptable range of  $\frac{1}{20}$  %  $\frac{1}{20}$  % and with the RSDs < 20 % (when applicable). The overall mean concurrent recoveries were also in the acceptable range of 70 % and 110 %, with the RSD < 20 %.

The storage period of deep-frozen samples intended for the analysis of fluopyram and its metabolite fluopyram benzamide ranged between 432 and 341 days.

The detailed results obtained for barley samples in porthern Europe are summarized in the Table 6.3.5-10.

## Conclusion

Ľ

Four supervised residue trials on barley were conducted in northern Europe with the application of FLU+ISY+PTZ EC-234 at higher rate than required in the supported GAP (1x101g as/ha Vs 1x78g), and according to GLP. Samples of barley were analyzed for the residues of fluopyram and its metabolite fluopyram-benzamide. The results of the trials presented above show the following residues after donwscaling in grain at harvest.

Fluopyram residues range between 0.02 and 0.08 mg/kg.

• Fuopyram-benzamide residues were <0.01 mg/kg



• The total residue of fluopyram (sum of FLU + FLU-benzamide, expressed as fluopyram) after downscaling to the right dose (1x78 g ai/ha Vs 1x101 g ai/ha), range between 0.03 and 0.08 mg/kg.

Residues after downscaling in straw at harvest :

- Fluopyram residues range between 0.04 and 0.28 mg/kg.
- Fluopyram-benzamide residues were between <0.01 mg/kg and 0.01 mg/kg
- The total residue of fluopyram (sum of FLU + Fkb-benzamide expressed as fluopyram) after downscaling to the right dose (1x101g as/ha Vs 1x78g ha), range between 0.05 and 0.29 mg/kg.

#### Assessment and conclusion by applicant:

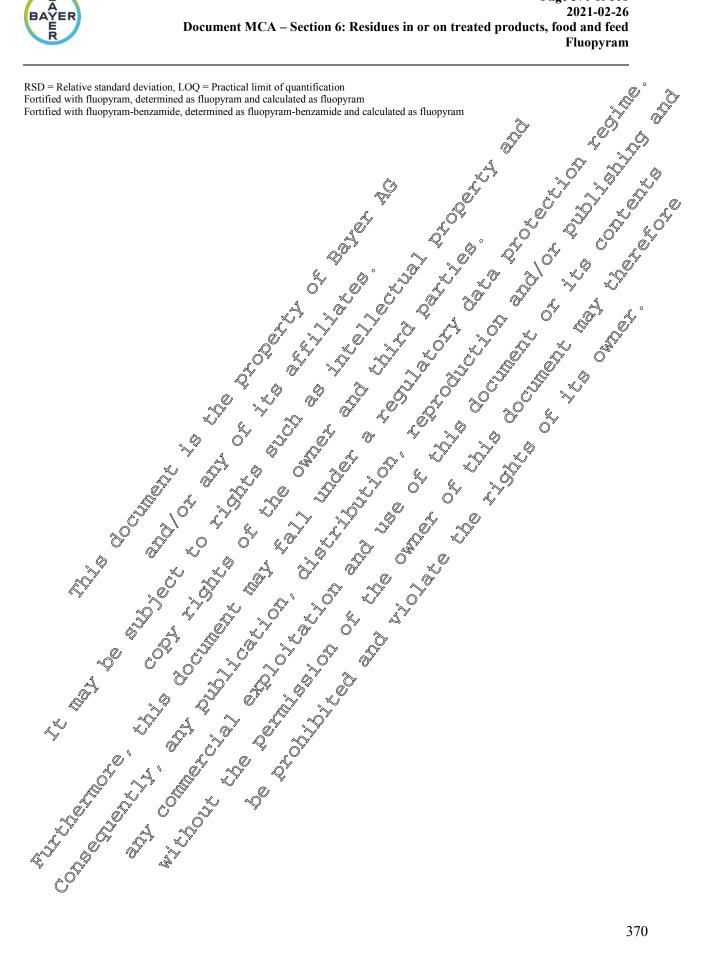
The study is acceptable.

The residue level in these GLP trials was corrected with a proportionality factor according to EFSA Technical Report (EFSA supporting publication 2018-EN-1503).

Portion	Fortification		ecovery (			
analysed	level (mg/kg)	Individual & tecoveries	Min	Max	Mean	RSD
Fluopyram (Al	E C656948)		•	e v	ĝ (	) or
	0.01	O 87; 95 O	87	95	91	A.4
Spring barley / grain	1.0	25; 99; 10 ¹	955	101	28 ~	3.1
Brunn		Overall/recovery (n=60		o ^y §	95	5.3
	\$9.01 J	82,95; 90	⁶ 82 @	90 C	867	4.7
Spring barley / green		~ 104; 106; 107 ×	100	1014	~~ ⁹ 06	1.4
material	0° <b>x9</b> ° (0	86; <b>@</b> 1; 94; <b>@</b> 5, 102; <b>*0</b> 4	86	\$104	95	7.1
\$ \$		Overall recovery (n=12)	Ç C		96	9.3
<u> </u>	0.010	95; 96; 98 ₍₅		~ <b>98</b>	96	1.6
Spring barley	Č. 10 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	96; <b>96</b> ; <b>1</b> 02 . O	₩96 №	O ₁₀₂	98	3.5
/ straw	30.40	93;94;100	93 2	100	96	4.0
		Overall recovery (n=9)			97	3.0
Fluopyram-k	onzamide C		- Or			
4		\$92; 92; 9 ²	87	93	91	3.5
Spring bartery / grain	0,10	Ø94; 96, 98 . V	94	98	96	2.1
, Srum	1 V 1	Overall recovery (1)=6)			93	4.0
Y	0.01	× • • • • • • • • • • • • • • • • • • •	81	89	84	4.9
Spring barley	© 5.0	@99; 104; 103	99	103	101	2.0
/ green material	~ 8.0	<b>4</b> , 89; 94; 96; 97; 115	81	115	96	11.7
		OveralOrecovery (n =12)			94	10.6
	0.01	89; 97; 101	89	101	96	6.4
Spring barles	\$0.10 × ×	92; 96; 100	92	100	96	4.2
Catraw S	0.40	92; 94; 96	92	96	94	2.1
°0°		Overall recovery (n = 9)			95	4.1

#### Table 6.3.5- 9: Concurrent recovery data for Fluopy Ram (study 17 2017)





BAYER ER

Page 371 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Table 6.3 Total residue	<b>3.5- 10:</b> e calculated : su	Summary m of fluopyram+F	<b>y of the</b> LU-benzar	<b>17-201</b> nide	7 ( <u>M-6</u>	55225-01-3	) study	·		Ĵ	perty	and <u>and</u> <u>tectio</u>	A A C	JING .	9.D.Or
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting		cation ra treatmen		Dates of treatment / Application interval	Growth stage at last preatment	Portion@ analyzed	Growth stage a sampling	Parting of the second s	Residues Quig/k	B) C C C C C C C C C C C C C C C C C C C		ent of et of e	PHI (days)
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL		(d)	J.D.C.		fluo <del>ps</del> ram Oas AE C656948	FLU- bouzamide ac AE C656948	residue cato	factor	Scaled residue	(f)
17-2017- 01 Germany 16818 Kränzlin Europe,	Barley, spring Simba	1) 30.03.2017 2) 14.06.2017 - 17.06.2017 3) 09.08.2017 - 09.08.2017	100.5	200	58325 D	14,96.2017/0	61 Or	gree® Daterial	61) 73 75 770 83		0.016 0.016 0.016 0.016	3.9 2.3 1⊕ 0.20 € <0.02	¢.77	3.0 1.8 0.85 0.15 <0.02	0 7 14 22 30
North F 2017		M ² S	Joc July	. (	~ ¹	* * ² 2° * * ² 2°	UIDDe UIDDe	grain traw	89°L1.	0.098 0.12	<0.04 <0.04 \$\$ 0.012	0.10 0.13		<u>0.077</u> 0.10	55 55
17-2017- 02 Denmark 6360 Tinglev Europe,	Barley, spring OVERTURE	1) 31.03.2017 2) 26.06.2017 - 28.06.2017 3) 15.08.2017 - 15.08.2017			5025 5025		9100	green material	60 73 75 72 83 6 83 6 85	M. 17	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	1.8 0.60 0.24 0.20 0.12 0.087	0.77	1.4 0.46 0.19 0.15 0.092 0.067	0 7 9 15 21 28
North F 2017		10.1 V	0×		C ^{3,5,2}	J. C.	0 ^f	grain straw	89 89	0.040 0.065	<0.01 <0.01	0.041 0.066		<u>0.032</u> 0.051	50 50
\$	LCORECT		any south	ye ye	PET OF	LiDite	, Officer						·		371



Page 372 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

														riuop	° °
									Þ	Ĵ	* 1	<u>A</u>	~L ^{©C}	riuop 3 ^{1/100}	O.D.O.
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting		ication ra treatment		Dates of treatment / Application interval	Growth stage at last treatment	- 80	Growth stage at sampling		es et	Kecting Section			PHI (days)
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	(c) 0	(d){ }		(d)	floopyran as AE C656948	n FLU- benzamiceas AE C6 <b>5</b> 6948	Total residue calc.	Scaling factor	Scaled residue	(f)
17-2017-03 United Kingdom OX15 6EP Banbury, Oxfordshire	Barley, spring Octavia	1) 27.04.2017 2) 27.04.2017 - 04.07.2017 3) 28.08.2017 - 10.09.2017	100.5	250	40.2	0607.2017/0 5 5		steen material *		1.5 0.76 0.23 0.15		9 1.5 0.80 0.23 0.16 0.16	0.77 Ç [®]	3.0 1.2 0.62 0.18 0.12	0 7 13 21 27
Europe, North F, 2017			CUI	10 ⁵	9. C.J.		WILLE F	graigs straw	89 O *	0.0200 0.096	<0.01 0.011	0.034 0.11		<u>0.026</u> 0.085	57 57
17-2017-04 France, north 02190 Juvincourt et Dammary	Barley, spring IRINA	1) 01.04.2017 2) 20.06.2017 - 30.06.2017 3) 09 98.2017 - 09.08.2017	00.5 0	$\sim$	59 <u>(2</u> 3)	29,08,2917/0	6450	green that are a straw	61 83 87 75	3.2 *.1 0.52 0.22 0.50	<0.01 0.0218 0.020 0.011 0.013	3.2 1.1 0.54 0.23 0.52	0.77	2.5 0.85 0.42 0.18 0.40	0 7 20 28 14
Europe, North F, 2017		Ģ	20 ) 00 )	T ^{jy}			20 3.00	grain O straw	89 x x x	0.049 0.34	<0.01 0.025	0.059 0.37		<u>0.045</u> 0.29	41 41
(a) Acc (b) Onl	ording to CODE y if relevant	X Classification / Gu	ideo 2 "(	e) <b>Rem</b> a	after last ar arks may in	plication (Label clude: Clinoatic c	pre-harvest in onditions; Ref	terval, PHI, and	aderline) ytical method	(h) (i)	Formulation type Application method	(l) (m)	Method va Storage (m		
(c) Yea (d) Eith G gree	ar must be indice her growth stage enhouse	description or BBCH F field	Code (	g) prior	nation which y referenced to largireat	chrynetabolites ard ment 10 ¹⁰	e Acluded	J ^Ż		(j) (k) **	Method information LOQ residue in control	#		date of anal production ailable	
-	LE THEIR	Jeft L J	and the formation of th	ye the	PETON PETON		<i>y</i>								
	<b>S</b>	Ma													372



#### GAP 1 southern zone

Data Point:	KCA 6.3.5/04
Report Author:	
Report Year:	
Report Title:	Amendment no. 3 to report no: 12-2132 - Determination of the residues of AE C656948, BYF 00587 and prothiceonazole in/on Darleyafter spray application of bixafen & fluopyram & prothiceonazole EC 260 in the field in Southern France
	C656948, BYF 00587 and prothioeonazole in/on Darleyafter spray application of
	bixafen & fluopyram & prothioconazole EC 260 in the field in Southern France
	Spain, Italy, Portugal and Grace
Report No:	
Document No:	<u>M-474260-04-1</u>
Guideline(s) followed in	Regulation (EC) No 1107/2009 of the European Parbanent and of the Council of 21
study:	October 2009 concerning the placing of plant protection products on the one of the
	market and repeating Coupcil Directives @9/117/EEC and 91/414/EEC, 🖉 🖉
	market and repeating Council Directives @/117/EEC an 91/414/EEC, EC Guidance working document 7029/91/95 ro.5 (1997-07-22),
	OECD 509 Adopted 2009-09-07, OECD GLIDELINE FOR THE TESTING OF CHEMICAES, Crop Field Prial,
	CHEMICALS, Crop Field Prial, N N N N N
	US EPA OCSPPGGuideltae No 860.1590
Deviations from current	none is in the second s
test guideline:	
Previous evaluation:	yes, evaluated and accepted Or A to the second accepted
	Study was not found in DAR/RAR and the Addenda
GLP/Officially recognised	Yes conducted under GLP Officiall recognised testing factures
testing facilities:	
Acceptability/Reliability:	Ales of the state
Č [×] "\	

## Materials and Methods

Seven supervised residue tria on barley were conducted in southern Europe (in southern France, Spain, Italy, Portugal, and Greece) during the 2002 season.

One-spray applications was conducted with with BIX+FLU+OTZ EC 260, an EC (emulsifiable concentrate) formulation containing 130 c/L prothioconazole 65 g/L of fluopyram and 65 g/L of bixafen. For the purpose of this renewal, only results for fluopyram and its metabolite fluopyram-benzamide will be discussed.

The applications were conducted at the BBCH of 61 (BBCH 65 for the trial 12-2132-08) and at the application rates of 1.2 L the corresponding to the single application 0.078 kg a.s./ha. Water application rates were at 282 - 400 l/bha.

Samples of barley green material were collected at BBCH 61, 69, 73, 77, 83, 85, 87, barley grain and straw at BBCH of 89.

Each field sample was placed in doubled labelled bags and stored deep-frozen within 24 hours after sampling and until dispatch. All field samples were shipped deep-frozen under monitored conditions during shipment and arrived in good condition. The field samples were stored in a freezer at  $\leq$ -18 °C until preparation of the examination samples. Temperature above -18°C were recorded during shipment in 4 trials. Ashort term storage stability study was conducted to show that this deviation has no impact on the stability of the residues (see MCA 6.1.2, M-480441-06-1).



For the preparation of examination samples, the deep-frozen field samples were shredded and homogenized with dry ice in a cutter. Representative parts of the shredded samples were transferred into polystypene sboxes and stored at  $\leq$ -18 °C. All examination samples for analysis were stored deep frozen until analysis or further shipment.

Samples were analysed according to the analytical method 00984/M003 (**Method 2015**, <u>Method 2323-03-</u><u>1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the Etheregulatory requirements outlined without SANCO/3029/99 rev 4.

Residues were extracted from 5 g of sample material by using a shaker (15 min) with a mix one of acetonitrile/water (4:1; v.v). After filtration the extracts of the solutions were made up to volume. The solutions were centrifuged, and the extract volume was adjusted. The extracts were divided by adding the internal standard. An aliquot of the extracts was injected into a HPLC (MS/MS).

The linearity was demonstrated in each analytical batch with a 1/x seighted calibration curve established with at least 5 concentration levels.

The quantification was done by internal standardization using isotopically stable labelled internal standards. The Limit of Quantification (LOQ), expressed as fluopyrant defined as the lowest validated fortification level, was 0.01 mg/kg.

All final extracts were analysed within 2 days after extraction Phuopytam and Iluopytam-berzamide were found to be stable in extracts of plant origin for at least four weeks at 4 3 °C which was tested within the validation of method 00984/M009

### Findings

In order to check the performance of the method, pecovery determinations were included in each set of analyses. Control samples from the budy were fortified to be used as the pecovery samples. All the recovery determinations were performed concurrently to the analyses of control and treated samples from the study. The apparent residues in the control sample used for the determination of recoveries were below 30 % of the LOQ. Recoveries were not corrected for apparent residues in the control samples used for these determinations.

The mean recoveries of fluor and its metabolic fluor yram benzamide per fortification level were within the acceptable range of 70 % -110% and with the RSDs < 20 % (when applicable). The overall mean concurrent recoveries were also in the acceptable range of 70 % and 110 %, with the RSD < 20 %.

The storage period of deep-thozen amples intended for the analysis of fluopyram and its metabolite fluopyram-benzamide ranged between 369 and 449 days.

The detailed results obtained for parley samples in southern Europe are summarized in the Table 6.3.5-12

## Conclusion

Seven supervised residue trials on barley were conducted in southern Europe with the application of BIX+FLU+PTZ EC 260 at the required rates and according to GLP. Samples of barley were analyzed for the residues of fluopyram and its metabolite fluopyram-benzamide. The results of the trials presented above show the following vesidues in grain at harvest.

- From residues range between <0.01 and 0.11 mg/kg.
- Fluopyram-benzamide residues between <0.01 mg/kg and 0.01 mg/kg.

The fotal residue of fluopyram (sum of FLU + FLU-benzamide, expressed as fluopyram) range between <0.02 and 0.12 mg/kg.



- •
- .
- •

Residues in st	raw at harvest :						
		nge between 0.03 and 1.1	mg/kg.				
• Fluop	yram-benzamide	residues were from <0.01	l mg/kg	to 0.06 r	ng/kg	ð	
• The to	otal residue of fl	uopyram (sum of FLU +	FLU-be	enzamide	e, express	d as flu	opyram) range
betwe	en 0.04 and 1.2 1	ng/kg.			A		
			Ô		Å.	la l	Y NY XY
Assessment a	nd conclusion by	applicant:	( Yr		Q,	Ö	
The study is a	cceptable.	4	Ũ	4	) ^v	×	
			>	Q		<del>\</del>	
		urrent recovery data for	s °		$\langle 0 \rangle \sim \langle \gamma \rangle$	× \ ⁰	
Table 6.3.5- 1	1: Concu	irrent recovery data for	Fluon	am (stu	dy 12-213	20	N W
		A. Op	ecovery (	0/Q	ð,	Or A	opyram) range opyram) range opyram (1) (1) (1) (1) (1) (1) (1) (1)
Portion	Fortification		ecovery (	70)*	\$. 6 ^{\$}	<u> </u>	
analysed	level (mg/kg)	Indevidual S	Min	Max	Mean	RSD	
Fluopyram (Al	E C656948)	Coverses ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	×,		5 \$	Ő	
Theopyrum (Th	0.01	93; 94; 98; 97; 197	D 93 6	107,0	27 N	28	K.
	0.10	\$ \$\$\$; 90; 20 °	4			0.0%	۶. Y
Barley / grain	0.80	\$99; 10,0102	099	£102 va	\$ 100g	1.9	
	×~*	Overall recovery (1)		- S	.96	3.7	
	0.0	\$80; 80; \$4; 89; 90, 93; 190	.80%	<u>¢100</u>	1088	8.4	
	200	2 90; <b>90</b> , 92	\$30	0 92	× 91 ×	1.1	
Barley / green	, NO.80, O	98; 49; 99; 100	980		29	1.0	
material	0 150	× 89; 91; 93 L	89	<b>G</b> 3	<b>\$</b> 91	2.2	
	O O V	Overall recovery (n=07)	è ć	SY a.	92	6.8	
	0.01 👟	× 89; gt 93; 9098 0	89,	28	94	4.1	
R.	0 00	\$86; 94; 99	× \$6	299	93	7.1	
Barley / straw	20.3 K	98; 98; 102, 7 (	98	102	100	2.1	
		Q .92; 95; 99 O	22 -57	99	95	3.7	
	O OY A	Overal recovery (n=14)	Ś		95	4.8	
Fluopyram-b	enzamide 🔊		,		N. 70		
<i>A</i>	0.01	392; 9€ 100; 1€7; 110 €	92	110	101	7.1	
Barley/ grain	Č. Š.	90; 96, 96	90	96	92	3.5	
Santon gram	\$0.80	30 [™] 1010/03; 108 [™]	101	108	104	3.5	
		Overall recov (n=11)			100	7.0	
	A.O1 0	84, 90; 97; 97; 101; 102;	84	106	97	7.8	
	× 0.105	× 100 × × × × × × × × × × × × × × × × × × ×	90	94	92	2.3	
Barley / green materia	0 0.80	102; 104; 105; 108	102	108	105	2.4	
	A15 25	94; 97; 101	94	101	97	3.6	
G ST	O A	Overall recovery (n=17)			98	6.8	
BarleyOstraw	0.01	82; 92; 95; 108; 108	82	108	97	11.5	
		,,,,,					Į



							°
Portion	Fortification	R	ecovery (	%)			. 4
analysed	level (mg/kg)	Individual recoveries	Min	Max	Mean	RSD	
	0.10	92; 101; 103	92	103	99_	5.9	
	1.5	93; 94; 97	93	97	<u>95</u>	2.2 💊	Ô° ô° g
	15	86; 90; 94	807	94	¢90	4.4 %	
		Overall recovery (n=14)	L,	_	<b>9</b> 5 <b>9</b> 5	.79	\$ × ×
SD = Relative standa Fortified with fluop Fortified with fluop Fhese recoveries we	and deviation, LOQ = Pract yram, determined as fly yram-benzamide, deter ere performed during the second	Reverses 92; 101; 103 93; 94; 97 86; 90; 94 Overall recovery (n=14) ical limit of quantification copyram and calculated as fluopyram-benzamides and the conduct of the study 12;2132					
		≫ ^v					

BAYER

Page 377 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting		cation ra reatmen		Dates of treatment / Application interval	Growth stage at lat	Portion analyzed	Growth stage at sampling		Residues (mg/kg	BODINE CONT	ې PHI (day
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	OT OP		e ^{22e}		C656948	Benzamide as AE C656948	alc.	(e)
2-2132-01 Trance, south	Barley Queen;	1) 14.10.2011 2) 07.05.2012	78	300	26 * De	07.05.2012/0		green material		1.30 ⁵	<0.01 <0.01	1.3	0 7
1620 Bouloc urope, South	Winter Barley	- 14.05.2012 3) 20.06.2012 - 01.07.2012		1¢		, da	OLD OLD	dy.	85 JU	1.30 ¹² 20.11 0.042 0.042 0.072 0.092 0.092		an lot a a	14 28
012			UIRCIA	0		GV MP	e ⁷ 7	grain straw	Ç	0.093	0.01 0.01	0.022	49
2-2132-02	Barley	1) 14.10.201 h 2) 03.05.201	78	300	20)D	03.05.2012/0	de ^r .	green		Ġ1.5	0.0.1	0.12	49 0
rance, south 6200 Pouant urope, South	Cervoise; Winter variety	- 10.05.2012 - 10.05.2012 3) 20.06.2012 - 20.06.2012	78 J.L.D.							BON D	<0.01	<0.02	57
012			ecv		, A			straw	89 %. 	0.025	< 0.01	0.035	57
2-2132-03 pain	Barley Gomera;	1) 23.01.2012 2) 15.05.2022	73.3	282.01	20:0	16.95.2012/07			61 73	2.0 0.58	<0.01 0.010	2.0 0.59	0 7
7184 Salitja urope, South	winter barley	- 25 08 2012 3) 19 06.2012 4 07.07.2012		PCTU-	K JOIL	t 10 ¹¹	z ^{De} J ²	LO. T.	77 85	0.17 0.10	0.010 <0.01	0.18 0.11	15 28
012	TAD .	₩ 07.07.2012	30 ⁰ °	j c ^e			J.	grain	89	0.028	<0.01	0.038	42
	J.C	1 P	JUC	-	o ^y e	10 ²	20×	straw	89	0.18	0.015	0.20	42
2-2132-04 pain	Barley Graphic;	1) 01.02.2012 2) 14 05 2012	78	300 70	26	14.05.2012/0	61	green material	61 77	2.0 0.71	<0.01 0.010	2.0 0.72	0 7
3520 Les	summer	@22.05.2012	· · ·		o Ball	, K		material	83	0.55	0.016	0.57	14
anqueses el Valles -	barley	3) 15.06.2012	~C ²	-0 ^ë		<b>1</b> 2			87	0.32	0.011	0.33	28
larata	DETTHE	- 01.042012	*.D		CORT			grain	89	0.034	<0.01	0.044	42
Marata Europe, South F 2012	t here are	1) 01.02 2012 2) 14.05 2012 3) 15.06.2012 - 07.04 2012 -	t Di	, Ś	¢0».	14.05.2012/0		grain straw	89 89	0.034	<0.01 0.028	0.044 0.80	4



Page 378 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

											2		<u>¢°</u>
									Ĉ		O.D.	d'il	"" and
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting		cation ra reatmen		Dates of treatment / Application interval	Growth stage at last treatment	Poction autivityzed	Growth stage at sampling	er opert	Residues (ng)	i de la comercia de l	
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	(c)	(d) \$			fluopyram « as AF C6 <b>56948</b>	FLU- benzamide as		^с (е)
12-2132-05 Italy 01016 Tarquinia Europe, South F 2012	Barley Quench; Distich	1) 21.12.2011 2) 24.04.2012 - 04.05.2012 3) 15.06.2012 - 15.07.2012	78	300	26		O.S. J.D.	grain	61 69 73 84 89 89	0.079 0.079	20.01 <0.01 0.045 0.019 0.019 0.018 0.018 0.018 0.018 0.018 0.018 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.019 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.018 0.	0990	0 7 14 28 56
12-2132-07 Portugal 2580-230- Meca Alenquer	Barley scarlet; Cevada	1) 03.01.2012 2) 24.04.2012 - 27.04.2012 3) 15.06.2012 - 21.06.2012	78000	400 8 0 ⁵⁵ 0 ⁵	1 June	24.04.2012 24.04.2012 2000 - 50		stbaw green material Dgrain		Q 2.1 0 0.01 0 0 0 0 0	<0.01 <0.01	1.2 2.1 <0.02	56 0 55
Europe, South F 2012		The size		¢° ∑¢	of	Early ra	10000	stra® [¥]		OLOGIE I	0.021	0.12	55
12-2132-08 Greece GR-61100	Barley Lutes; Six lines ear	1) 20.12.2011 2) 03.05.2012 - 09.12.2003	\% _{^ [^] →	300	26 51	09.05.2072/0		green waterial ×	65C	2.0	<0.01	2.0	0
Kastanies, Kilkis		3) 13.05,2012 - f\$07.2012	PI .	1010	10 ¹⁰	101	* De	graine C	89	0.11	< 0.01	0.12	35
Europe, South F 2012	The second		90000	, jol		Pri of	J ¹ C	straw	89	0.40	0.020	0.42	35
<ul> <li>(a) Accord</li> <li>(b) Only i</li> <li>(c) Year r</li> </ul>	ding to CODEX C f relevant		and de la constant	Days after Remarks r	last applicat navouerude:	ion (Labébare-ha Clinade conditio	ns; Reference t	PHI, underline) o analytical me	thod (i)	Formulation r Application r Method info	nethod (m)	Method validatio Storage (max) ! based on date o	
(d) Either G greenh	growth star desc ouse the entre	lassification Guide		Studyse fe Brior to las	st toment	goones are inclu			() (k) **	LOQ residue in con		P based on produ P based on produ no data available	ction date



Data Point:	KCA 6.3.5/05
Report Author:	
Report Year:	2014
Report Title:	Determination of the residues of AE C656948, BYF 00587 and prothio@nazol@n/on barley after spray application of bixaten & fluopyram& prothioconazote EC 260 in Italy
Report No:	13-2004
Document No:	<u>M-479739-01-1</u>
Guideline(s) followed in	Regulation (EC) No 1107/2009 of the European Parlament and of the Council of 21
study:	October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79 41 7/EEO and 94 414/EEO EC Guidance working document 7029 VI/95 eV.5 (1997-07-22) OECD 509 Adopted 2009-00-07, OCCD GUDELINE FOR THE HISTING OF CHEMICALS, Crop Field Trial
Deviations from current test guideline:	
Previous evaluation:	yes, evaluated and accepted Study as not found in DAR/RAR and the Addenda
GLP/Officially recognised	Yes conducted under GLP/Officially recognised testing factities
testing facilities:	
Acceptability/Reliability:	Yes Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q

#### Materials and Methods

One supervised residue trial on barley were conducted in Southern Europe (Italy) during the 2013 season. One-spray applications was conducted with BX+FLO+PTZ EC 260, an EC (emulsifiable concentrate) formulation containing 130 gV protoconazole, 65 g/L of fluopyram and 65 g/L of bixafen. For the purpose of this renewal, only results for fluopyram and its metabolite fluopyram-benzamide will be discussed.

The applications were conducted at the BBC/P of 61 and at the application rates of 1.2 L/ha corresponding to the single application 0.078 kg a s/ha. Water application rate was at 300 L/ha.

Samples of barley green material were collected at BBCH 83, samples of barley grain and straw at BBCH 80

Each field sample was placed in doubled labelled bags and stored deep-frozen within 24 hours after sampling and until dispatch. All field samples were shipped deep-frozen under monitored conditions during shipment and arrived in good condition. The field samples were stored in a freezer at  $\leq$ -18 °C until preparation of the examination samples Q

For the preparation of examination samples, the deep-frozen field samples were shredded and homogenized with dry ice in a cutter. Representative parts of the shredded samples were transferred into polystyrene boxes and prored at  $\geq$  -18 °C. For each field sample, one or several examination samples were prepared for analysis and one examination sample was prepared as a reserve sample.

¢°



Samples were analysed according to the analytical method 00984/M003 (**Mathematical**, 2015, <u>M-467323-02-</u><u>1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues were extracted from 5 g of sample material with a mixture of acetonitrile:water (4:1;v:v) using a shaker (15 min). After filtration, the internal standards were added, and the extracts made up to volume. Ap aliquot of the extract was injected into an HPLC-(MS/MS).

Slight modifications on the extraction procedure were made during analysis of fluopyram and fluopyrambenzamide recovery samples (for barley grain at the fortification level of 0.1 mg/kg). After shaking, the sample was centrifuged, an 0.1 mL aliquot of the sample was filled up with 0.9 mb water and subjected (of HPLC-(MS/MS) analysis. These modifications have no impact on the quality of the analytical method.

The linearity was demonstrated in each analytic batch with at 1/x weighted salibration curve established with at least 5 concentration levels.

The quantification was done by internal standardization using isotopically stable abelled internal standards. The Limit of Quantification (LOQ), expressed as fluory ram, defined as the lowest validated fortification

level, was 0.01 mg/kg.

All final extracts were analysed within 4 days after extraction. For opyrain and for opyrain-benzamide were found to be stable in extracts of matrices of plant origin for at least four weeks at  $4 \pm 5^{\circ}$ C which was tested within the validation of method 00984/M003

#### Findings

In order to check the performance of the method, recovery determinations were picluded in each set of analyses. Control samples from the study were fortified to be used of the recovery samples. All the recovery determinations were performed concurrently to the analyses of control and treated samples from the study. The apparent residues in the control sample used for the determination of recoveries were below 30 % of the LOQ. Recoveries were not corrected for apparent residues in the control sample used for the determination of recoveries were below 30 % of the LOQ. Recoveries were not corrected for apparent residues in the control samples used for these recoveries with one ocception: One recovery of the opyramile at LOQ in barley / green material was corrected by the inherent anount of residues in the corresponding control sample (22.4 % of LOQ; 0.00224 mg/kg).

The overall mean concurrent recoveries were also in the acceptable range of 70 % and 110 %, with the RSD < 20 % (when applicable).

The storage period of deep-frozen samples intended for the analysis of fluopyram and its metabolite fluopyram-benzamide anged between 224 and 249 days.

The detailed results obtained for barley samples in southern Europe are summarized in the Table 6.3.5-14

## Conclusion

One supervised residue trials on barley were conducted in southern Europe with the application of BIX+FLU+PTZ EC 260 at the required rates and according to GLP. Samples of barley were analyzed for the residues of fluopyram and is metabolite fluopyram-benzamide. The results of the trials presented above show the following residues of grain at harvest.

- Fluepyram residues were 0.02 mg/kg.
- Fluopyrum-benzamide residues were <0.01 mg/kg
- The total residue of thopyram (sum of FLU + FLU-benzamide, expressed as fluopyram) were 0.03

Residues in straw at harvest :

• Fluopyram residues were 0.81 mg/kg.



- Fluopyram-benzamide residues were 0.04 mg/kg •
- r luopyram-benzamide residues were 0.04 mg/kg The total residue of fluopyram (sum of FLU + FLU-benzamide, expressed as fluopyram) were 9.85 mg/kg. ment and conclusion by applicant: idy is acceptable.

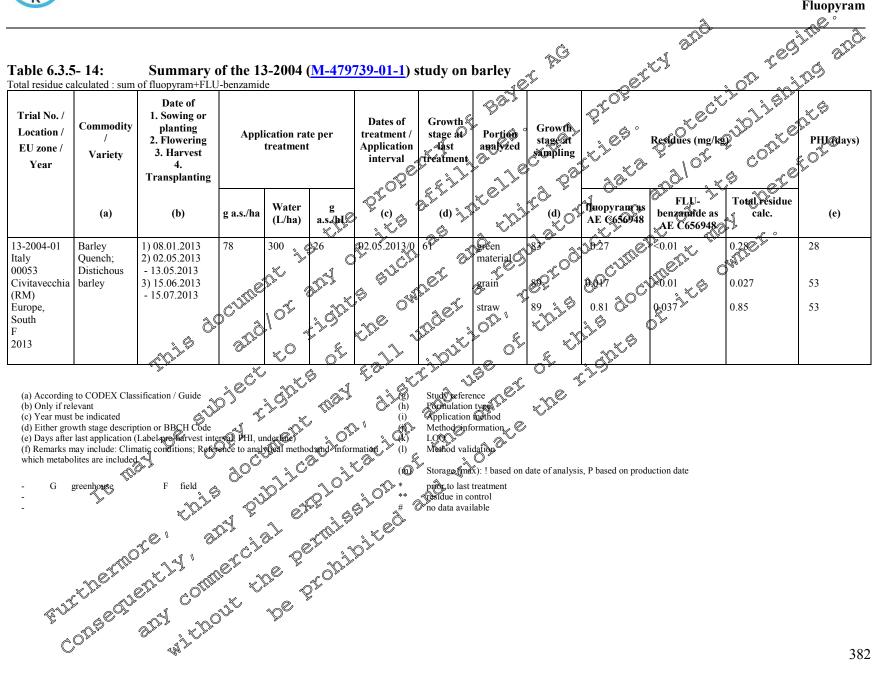
Assessment and conclusion by applicant: The study is acceptable.

		nrent recovery data &	Renver			2	
Portion	Fortification		Recover	S. (0)			
analysed	level (mg/kg)	recoveries	Mity	yrang (st y (%) Max	⊿ Mean~	RSD	
Fluopyram (AH	E C656948)			Å Ó		~	
	0.01		× - ~	L* ~/	0,02	¢ - \$	
Barley / green material	2.0		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		3 ² 99 5 ³		, L
inaterial		O@rall recovery (n=2)		$O_{A} = e^{i}$			×
	0.01			Í "Ö ^v	g 113 (	× - ×	
Barley / grain	0.10	0100*; 193*	100	103	× 102 ℃		
	0.10 V	Official and the second (42)	é é		105	6.5	
				s s	100 Ô 984	-	
Barley / straw			1 Alexandre	- -	O [™] 98√√	-	
		Overall recovery (m=2) >				-	
Fluopyram-b	anide C		, ~ 		K)Y		
	0.01	83* (130*) - 2 83* (130*) - 2 5 5 5 5 5 5 5 5 5 5 5 5 5	<i>S</i>	0-0	02* (120*)	124	
Barley / green	2.0 5	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		-0	95	-	
		Overall recovery (n=0)			89	-0	
	9.01 ×	Overall recovery (n=2)	% -	3 ⁷ -	108	-	
Barley / grain	0.10	\$9*; 10Q*	99	100	100	-	
~		Oversall recordery (n=3)	0 99 S		102	4.8	
A	0.01		<b>∂</b> -	н	100	-	
Barley / storw	2.0	D 65 95 5 1	<i>v</i> -	-	95	-	
*		Overall recovery (n-2) Protical ling of quanty ficatio			98	-	

RSDA Relative standard deviation (SQ = Protical line) of quantification Fortified with fluopyram, determined as fluopyram and salculated as fluopyram Fortified with fluopyram-benzamide, determined as fluopyram benzamide and calculated as fluopyram *For the extraction of these samples, the analytical method 00984/M003 was slightly modified



Page 382 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram





Data Point:	KCA 6.3.5/06
Report Author:	
Report Year:	2019
Report Title:	Determination of the residues of BCS-CN88460, prothioconazole and AS C656978 in/on barley after spray application of BLU & BCS-CN88460 & PTZ EC 234 in southern France, Italy, Spain and Greece
Report No:	17-2018
Document No:	<u>M-656993-01-1</u>
Guideline(s) followed in	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21
study:	October 2009 concerning the placing of plant protection products on the market OECD Guideline for the Testing of Chemicals on Crop Pield Total (TG 509 published in September 2009) US EPA OCSPP 869.1500/2Crop Field Tria
Deviations from current test guideline:	none
Previous evaluation:	No, not previously submitted with the Addendar S
GLP/Officially recognised testing facilities:	Yes, conducted under GCP/Officially recognise resting facilities
Acceptability/Reliability:	Yest a a a a a a a a a a a a a a a a a a a

Materials and Methods United Kingdom, northern France) during the 2017 season.

One-spray applications were conducted with PLU+1SY+PTZ EC@234 an emulsfiable concentrate formulation containing 6% g/L of fluopyram, 42 g/L of soflueypram, and 125 g/L of prothioconazole. For the purpose of this renewal, only results for fluopy an and its metabolite fluopyram-benzamide will be discussed. Ô

The applications were conducted at the BBCH of 61 and at the application rates of 1.5 L/ha corresponding to the single application rate of 0.10 long as the Water application rates were at 250 - 400 L/ha. As the dose rate is how he was a constant of a start of a star according to the scaling factors calculated and presented in Table 6.3.5-4.

Samples of barley green material were collected at several growth stages, barley grain and straw at BBCH of 89,

Each field sample was placed in double abelled bags and stored deep-frozen at ≤-18 °C or below, within 24 hours after sampling and until dispatch. Al field samples were shipped deep-frozen under monitored conditions during shipment and arrived in good condition. The field samples were stored in a freezer at  $\leq$ -18°C until preparation of the examination samples.

For the preparation of examination samples, the deep-frozen field samples were shredded and homogenized with dry ice in a cutter. Representative parts of the shredded samples were transferred into polystyrene boxes and stored at 18°C

Samples were analysed according to the analytical method 00984/M003 (Mathematical, 2015, M-467323-03-1, see ACA section 4.1.2). Full details and acceptable validation data to support this method are presented



within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues were extracted from 5 g of sample material (additionally 2.5 g for the sample material straw) by extraction using a shaker (15 min) with a mixture of acetonitrile:water (4:1, v:v).

The filtering procedure under low vacuum was replaced by a centrifugation step. Then 0.5 mC of internal standard solution (1 mg/L) was added to the extract followed by 5 min centrifugation at 4000 rpm at 40 °C f

An 0.1 mL aliquot of this extract was diluted with 0.9 mL of Milli-Q-water and then proceeded to HPIC-MS/MS analysis.

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established with at least 5 concentration levels.

The quantification was done by internal standardization using isotopically stable Pabelled internal standards.

The Limit of Quantification (LOQ), expressed as fluopyram defined as the flowest validated fortification level, was 0.01 mg/kg.

All final extracts were analysed within 12 days after extraction. Fluopyram and fluopyram benzamide were found to be stable in extracts of matrices of plant origin for at least four weeks at 4 +3 °C which was tested within the validation of method 00984/M0030

#### Findings

In order to check the performance of the method, recovery determinations were included in each set of analyses. Control samples from the study were fortified to be used as the recovery samples. All the recovery determinations were performed concurrently to the analyses of control and treated samples from the study. The apparent residues in the control sample used for the determination of recoveries were below 30 % of the LOQ. Recoveries were not concerted for apparent residues in the control samples used for the determinations.

The mean recoveries of fluopyram and its metabolite fluopyram-benzamide per fortification level were within the acceptable range of 70 %  $^{\circ}$  110 % (with few exceptions) see Table 6.3.5-15) and with the RSDs < 20 % (when applicable). The overall mean concurrent percoveries were also in the acceptable range of 70 % and 110%, with the RSD < 20%.

The storage period of deep frozen samples intended for the analysis of fluopyram and its metabolite fluopyram-benzamine ranged between 459 and 663 days,

The detailed results obtained for barley samples in northern Europe are summarized in the Table 6.3.5-16

# Conclusion

Four supervised residue trials on barley were conducted in northern Europe with the application of FLU+ISS+PTZ EC 234 at a higher rate than required in the supported GAP (1x101g as/ha Vs 1x78g as/ha), and according to GDP. Samples of barley were analyzed for the residues of fluopyram and its metabolite fluopyram-benzamide. The results of the trials presented above show the following residues after donwscaling ingrain at harvest.

- Fluopyram residues were between 0.01 mg/kg and 0.03 mg/kg
- Fluopyram-benzabilde residues@vere <0.01 mg/kg
- The total residue of thiopyram (sum of FLU + FLU-benzamide, expressed as fluopyram) after downsealing to the right dose (1x101g as/ha Vs 1x78g as/ha), range between <0.02 and 0.04 mg/kg.

Residues after downscaling in straw at harvest :

• The provide the second secon



- Fluopyram-benzamide residues were between <0.01 mg/kg and 0.02 mg/kg •
- The total residue of fluopyram (sum of FLU + FLU-benzamide, expressed as fluopyram) after downscaling to the right dose (1x101g as/ha Vs 1x78g as/ha), range between 0.02 and 0.92 mg/kg. •

					Ô	Ŭ.	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
Assessment a	nd conclusion by	applicant: trials was corrected with a ation 2018-EN-1503). urrent recovery data for			A		
The study is a	cceptable.		Č5		a second	s,	
The residue le	evel in these GLP	trials was corrected with a	proportio	onality fa	cor accord	ling to El	FSAJechnica
Report (EFSA	supporting public	ation 2018-EN-1503).	Ũ ^Y		)`		
		rrent recovery data for	<i>b</i>	 ►	Ô° É	5 . 5	í Oĭ "Ø'
Table 6.3.5- 1	5: Concu	irrent recovery data for	Fluopyr	ani (stu	dv 17-201	8)	
Portion	Fortification	O R	kover k	%)		n c	FSA Pechnical C
analysed	level (mg/kg)	Individual	Min	Max A	Mean	RSD	
Fluopyram (A)	E C656948)			, O ^Y		\$ ×	
Spring barley / grain	0.01	5-91; 91@8 ~~ ⁵	- AGA	<b>3</b> 98	2 93 5	4.2	, O 6
Ų	0.10	94; 94; 96; 98	94 6	98,0	[®] ®	2.0	
	0.50	\$ \$117* O	4	ŝ	<u> </u>	° - 4	·
	Ó	Overall recovery (n = 8)	Ø		970	8.6	
Spring barley / green material	0.01	24;96;98 ⁴	.945 ³⁷	99 ⁵ 9	236 A	2.6	
	eio d	\$ 96; \$ 98 \$	\$ 96	98	97	1.0	
	6 ³ 4.0 0	× 110,4111; №2 . S	1100	112	b.1**	0.9	
	20 100° 705 ×	95; 95, 97	<u>9</u> 3	<b>3</b> 7	96	1.2	
Ô	05 V	109 . 9	ç» - ć		-	-	
	, All All All All All All All All All Al	Overall recovery () = 13)	, O		101	6.9	
Spring barley / straw	all in	Tos; 141, 120 0		0120	113***	5.5	
	≥ ³ 0.10	93; 96; 96; 100	93.~	100	96	3.0	
	0.20 0.50	<b>200</b> ; 100, 401	JOO	101	100	0.6	
~			- O ^y -	-	( <b>.</b> =)		
	1.0 0	Q ⁷ 97Q103; 100 O	97	104	101	3.7	
		Overall/recovery (n = 14)			101	7.5	
Fluopyram-b	enzamide				ř		
Spring barley / grain		e ^y \$\$; 91; 8	85	93	90	4.6	
	Q.10 Q	~~************************************	87	98	93	5.0	
	0.10 0.50 0.50	¢ 107	-	-	-	-0	
, Û ^V	Ô ^{\$} O Å	Overall recovery (n = 8)			94	7.3	
Spring Varley / green material		97; 102; 103	97	103	101	3.2	
	0.10	96; 100; 100	96	100	99	2.3	
G							â.



Portion	Fortification	Re	Recovery (%)									
analysed	level (mg/kg)	Individual recoveries	Min	Max	Mean	RSD						
	4.0	105; 106; 107	105	107	106 "0	0.9						
	10	93; 94; 96	93	96	<b>94</b>	1.6 💊	0° 68 8					
	15	104		-	Ĵ.	- 🕺						
		Overall recovery (n = 13)	L.		S [©] 100	49	\$ \$ 4					
Spring barley / straw	0.01	83; 89; 95	, 83	95Q	89	6.7 L						
	0.10	82*; 90; 92; 92	82	<b>392</b> v	© 89 ~	5,30						
	0.20	95; 97; 99	95 _x ^	کر 99 ^{عر}	×,	Q.1						
	0.50	94			8 <b>-</b>							
	1.0	93; 98, 101	<b>3</b> 93	101 🔎	97	4.2						
		Overall recovery (n = 14)	V , S		 	6.0						

Fortified with fluopyram, determined as fluopyram and calculated as fluopyram Fortification level. RSD = Relative standard d

FL = Fortification level, RSD = Relative standard develtion, LOQ = Practical limit of quantification Fortified with fluopyram, determined as fluopyram benzamide and calculated as fluopyram benzamide, determined as fluopyram benzamide and calculated as fluopyram benzamide as fluopyram benzamide and calculated as fluopyram benzamide as fluopyram benzamide as fluopyram benzamide and calculated as fluopyram benzamide as flu This value at the fortification level of 0.50 meVe was very ted versus this fortification level 0 not the most relevant to the residue levels for fluopyram found in the study samples (the highest residue for fluoryram is definition level 0 not the most relevant to the residue levels for fluoryram is definition level 0 not the most relevant to the residue levels for fluoryram is definition level 0 not the most relevant to the residue levels for fluoryram is definition level 0 not the most relevant to the residue levels for fluoryram is definition level 0 not the most relevant to the residue levels for fluoryram is definition levels in the most relevant to the residue levels for fluoryram is definition of the most relevant to the residue levels for fluoryram is definition of the most relevant to the residue levels for fluoryram is defined as the fortification levels for



Page 387 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

														- 1TGP	, 
<b>Fable 6.3</b> Fotal residue	<b>3.5- 16:</b>	Summai um of fluopyram+	r <b>y of th</b> FLU-benz	e 17-2 amide	017 ( <u>M</u>	<u> -655225-0</u>	<u>1-1</u> ) stud	ly on ba	rley	P.C	at the	"Or"	s s		Offe
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Appli	cation ra reatmen	1	Dates of treatment / Application interval	Growth stage at last treatment	1,220	Growth state [°] at sampling	UR R	estătuës (mg/kg	10"	C° a		PHI S(days)
	(a)	(b)	g a.s./ha	Water (L/ha)		(c) °2 [°]	(d)) G	/	( <b>d</b> ) 7	fluopyram as AE 6556948	FL benzamide as C656948	calc.	Seating Factor	Scaled residue	(f)
17-2018- 01 France, south 26120 Upie	Barley Maltesse, winter	1) 17.11.2016 2) 14.05.2017 - 30.05.2017 3) 23.06.2017	101	300	33.5 1	¥5.05.2017/0		400	75 .	2.7 c 0.58 0.37 c 0.3 c		calc. 20 0.59 0.60 0.38 20.32	C.C.T.	2.1 0.45 0.46 0.29 0.25	0 7 14 22 28
Europe, South F 2017		This	9.0CV		р ^с ,0 ,0			straw	89 89 E	0.467643**	<0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0			<u>&lt;0.02</u> 0.023	38 38
17-2018- 02 Italy 20090 Settala	Barley Concerto	1) 21.03.2017 2) 28.06.2017 - 04.07.2017 3) 11.08.2017	101 50000	<b>đồ</b> ơ ~5 ^{° D}	25,2 9 ))))) ))))	28.06.2017/0		green 9 material	61 650 75 83	40 0.63 0.30 0.19 0.19	0.010 0.017 <0.01 0.010 0.014	4.1 0.65 0.31 0.20 0.20	0.77	3.2 0.50 0.24 0.15 0.15	0 7 14 22 28
Europe, South F 2017		ROA DO			2.02×			grain straw	89 89	<0.01 <0.01	<0.01 <0.01	<0.02 <0.02		<u>&lt;0.02</u> <0.02	44 44
¢,	JIT THEFT	- 04.07.2017 3) 11.08.2017 3) 11.08.2017 0 0 0 0 0 0 0 0 0 0 0 0 0	and aner poner	En 2 Je 2 Je 2 Je	ets per	dit son it of	s _Q r. Dr.								38



Page 388 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram

											2				_
									Ĉa		9. De		<u>dj</u>	ju ali	>
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting		cation ra reatmen		Dates of treatment / Application interval	Growth stage at last treatment	Portián	Growth stage at sampling	P ¹ O ^P Ra	esidues (mg/kg)	ki0 ²⁰			PHI (days)
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	(c) E	(d)) (d))			Auopyram as AC Co50948	FLU- benzantide @AE @C656948	residne Calc.	Scaling factor	Scaled residue	(f)
17-2018-03 Spain 08717 Montmaneu Europe, South F 2017	Barley Meseta; Winter	1) 21.11.2016 2) 04.05.2017 - 12.05.2017 3) 21.06.2017	101	250		04.05.2017/0 5 5 5 6 0 0 0 0 0 0 0 0 0 0 0 0 0	en ja	green material	61 ( 490) 73 75 83 75 83 75 89 89 89 89 89 89 89 89 89 89	2.4 5 5 5 6 6 6 6 6 6 6 6 6 6 6 6 6	0.020 0.022 0.022 0.029 0.029 0.029 0.029 0.029 0.029 0.029 0.029	2.4 1.5 1.1 0.90 0 1.1	0.77 °	1.8 1.2 0.85 0.74 0.69 0.85 <u>0.038</u> 0.92	0 8 14 20 27 18 48 48
17-2018-04 Greece GR 54500 Drymos Europe, South F 2017	Barley Hyvito	- 05052017 3) 01.06.2017 - 10.06.2017			¢ 607	La di St.	A DOUN	green mater@F	61 71 73 73 75 89 89	6.8 2.2 1.7 1.8 1.6 0.019 0.38	<0.01 0.31 0.040 0.016 0.017 0.011 <0.01 <0.01	6.8 2.7 2.2 1.7 1.8 1.6 0.029 0.39	0.77	5.2 2.1 1.7 1.3 1.4 1.2 0.022 0.30	0 7 14 21 23 27 43 43.
(a) Acc (b) Only (c) Yea (d) Eith G gree	ording to QODEX y if relevant r must be indicate er growth stage de nhouse	Classification / Guide cclassification / Guide d cclassification / Guide cclassification / Guide cclas		Arys at Remark Study r Prior to	ter last opli s. @vincluc tion which eference last reatmer	cation (Affeel pre- le: Elimatic condi actabolites action nt	harvækinterva tigter Referenc	I, PHI, underlin	ne) (h method (i (j (k **	) Applicatio ) Method ir x) LOQ	on method	(m) Sto ! b P t	ethod validati rage (max) ased on date ( aased on prod data available	of analysis uction date	
(		N I I I												38	8



Data Point:	KCA 6.3.5/07
Report Author:	
Report Year:	
Report Title:	Determination of the residues of BYF 00587 and AE C656948 in/on barley after spraying of bixafen & fluopyram EC 200 in the field in France (south), Italy and Greece
Report No:	18-2101
Document No:	<u>M-668264-01-1</u>
Guideline(s) followed in	Regulation (EC) No 1107/2009 of the European Partiament and of the Council of 21
study:	October 2009 concerning the placing of plant protection products on the market
	M-668264-01-1 Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guideline for the Testing of Chemicals on Gop Field Trial
	OECD Guideline for the Testing of Chemicals on Grop Field Trial
	(TG 509 published in September 2009)
	US EPA OCSPP 860 1500, Grop Figd Trial
Deviations from current	none a A A A
test guideline:	
Previous evaluation:	No, not previously submitted and a construction of the constructio
GLP/Officially recognised	Yes, conducted under GEP/Officially recognised esting facilities
testing facilities:	
Acceptability/Reliability:	Yest y was the first of the second se

# Materials and Methods

Four supervised residue trials on barrey were conducted in southern Europe (Germany, Denmark, in the United Kingdom, porthern France, during the 2017 season.

One-spray applications were conducted with BIX+FLU EC200 and emutshable concentrate formulation containing 100 g/L of bixater and 100 g/L of fluopyram. For the purpose of this renewal, only results for fluopyram and its metabolite fluopyram benzamme will be discussed.

The applications were conducted at the BBCH of 59-61 and at the application rates of 1. L/ha corresponding to the single application rate of 0.101 kg a scha. Water application rates were at 300 L/ha. As the dose rate is higher than the intended GAP ( $x_{101g}$  as/ha  $x_{s}$  1x78g as/ha), the residues are downscaled according to the scaling factor scale that and presented in Pable 6.3.5-4.

Samples of barley green material were collected at several growth stages, barley grain and straw at BBCH of 89.

Each field sample was placed in double labelled bag and stored deep-frozen at  $\leq$ -18 °C or below, within 24 hours after sampling and until dispatch All field samples were shipped deep-frozen under monitored conditions during support and arrived in good condition. The field samples were stored in a freezer at  $\leq$ -18°C until preparation of the examination samples.

For the preparation of examination samples, the deep-frozen field samples were shredded and homogenized with dry ice in a outer. Representative parts of the shredded samples were transferred into polystyrene boxes and stored at  $\leq$ -18°C.

Samples were analysed according to the analytical method 00984/M003 (**Mathematical**, 2015, <u>M-467323-03-1</u>, see MCA section (1.2), Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO 3029/99 rev 4.



Residues were extracted from 5 g of sample material (additionally 2.5 g for the sample material straw) by extraction using a shaker (15 min) with a mixture of acetonitrile:water (4:1, *v*:*v*).

The filtering procedure under low vacuum was replaced by a centrifugation step. Then 0.5 mL of prernal standard solution (1 mg/L) was added to the extract followed by 5 min centrifugation at 4000 rpm at 10 22.

An 0.1 mL aliquot of this extract was diluted with 0.9 mL of Milli-Q-water and then proceeded to HPLC MS/MS analysis.

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established with at least 5 concentration levels.

The quantification was done by internal standardization dising isotopically stable labelled internal standards

The Limit of Quantification (LOQ), expressed as floopyram, defined as the lowest validated fortification level, was 0.01 mg/kg.

All final extracts were analysed within 4 days after extraction Fluopyram and fluopyram-benzamide were found to be stable in extracts of matrices of plant origin for a least four weeks at  $A \pm 3$  °Cwhich was tested within the validation of method 00984/M003.

#### Findings

In order to check the performance of the method, recovery determinations were included in each set of analyses. Control samples from the study were for ified to be used as the recovery samples. All the recovery determinations were performed concurrently to the analyses of control and treated samples from the study. The apparent residues in the sontrol sample used for the determination of recoveries were below 30 % of

the LOQ. Recoveries were not corrected for opparent residues in the control samples used for these determinations.

The mean recoveries of fluopyram and its metabolite fluopyram benzamide per fortification level were within the acceptable range of 70% – 110% (with few exceptions, see Table 6.3.5-15) and with the RSDs < 20% (when applicable). The overall mean concurrent recoveries were also in the acceptable range of 70% and 110%, with the RSD 020%.

The storage period of deep-frozen samples intended for the analysis of fluopyram and its metabolite fluopyram benzamide ranged between 457 and 663 days.

The detailed results obtained for barley samples in porthers Europe are summarized in the Table 6.3.5-18

## Conclusion

Four supervised residue triats on barley were conducted in northern Europe with the application of BIX+FLU EC200 at a higher rate than required in the supported GAP (1x101g as/ha Vs 1x78g as/ha), and according to GLP. Samples of Darley were analyzed for the residues of fluopyram and its metabolite fluopyram-benzamide. The results of the trials presented above show the following residues after donwscaling in grain at harvest.

Fluopyram residues were between 0.01 mg/kg and 0.03 mg/kg

- Fluopyram-benzamide residues were 0.01 mg/kg
- The total residue of thuopyram (sum of FLU + FLU-benzamide, expressed as fluopyram) after downscaling to the right dose (1x101g as/ha Vs 1x78g as/ha), range between <0.02 and 0.04 mg/kg.

Residues after downscaling jostraw at harvest :

- Fluspyramore sidues were between 0.02 mg/kg and 0.11 mg/kg
- Enopyram-benzamide residues were between <0.01 mg/kg and 0.07 mg/kg



The total residue of fluopyram (sum of FLU + FLU-benzamide, expressed as fluopyram) after downscaling to the right dose (1x101g as/ha Vs 1x78g as/ha), range between 0.04 and 0.17 mg/kg. •

	0 0	(	0		0	ð	
Assessment a	nd conclusion by	applicant:			Ő	Ş	ESA Technical
The study is a	cceptable.	trials was corrected with a ation 2018-EN-1503).			4		
The residue le	evel in these GLP	trials was corrected with a	proporti	onality fa	ctor accor	ding to E	ESA Technical
Report (EFSA	supporting public	ation 2018-EN-1503).	- T	10	<u> </u>	- N	
			Ś		5¥	, Ø	N X X
able 6.3.5- 1	7: Concu	rrent recovery data for	Fluopy			11	
				V	O ³ ⁽	2×	
Portion	Fortification	X,	covery		<u>Y</u>		
analysed	level (mg/kg)	Individua	Miô	Max	Mean	RSD	× × *
		recoveries			Spean	(ORD)	A s.°
Fluopyram (Al	· · · · · ·					<u> </u>	
G : 1 1	0.01	92:@8; 100 ~	U 92 4	1005	No.	¥.3	
Spring barley / green	0.10	Ø5, 96; 98 . S	267	- B	296	1.6	
material	5.0	Q102; 102; 105	102	105	° 103 ℃	12	K.
		O@rall recovery (n= 9)			~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Q4.1	۲
	0.01	100; 10kgk03	109	<u></u>	101	1.5	
Spring barley / grain	0.10	98; 109, 100	@98	×100 ×	× 29Q	1.2	
/ gram	- A	Querall recovery $(a = 6)$		N N	2000	₩1.6	
	0.65	91 (1) ( [*] ; 97 (122)*; 10)	~%1	¥00 §	96 °	4.8	
		(120)*	*		y 90%	4.0	
Spring barley	50.10 0	<b>99999997969991971111111111111</b>	96 C	97	26	0.6	
/ straw		206: 11 2 .	106	12	×110	2.9	
æ.		Overall recovery (n 99)	Ô,	, Ø	101	7.3	
Fluonvramb	enzamide 🐥 💡			~~~~			
	Q. Q.	98; 101; 105		105	101	3.5	
Spring barley	Q.10 4	101;003; 107 %	101	10	104	2.9	
/ green	6 5.04	103; 103; 196 O	101	107	104	1.7	
material	a or a	Overall receivery (n 39)		100	104	2.7	
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			102	112	CONTRACTOR CONTRACTOR	5.4	
Spring barley	0.01	7 102 Y11; 1137 7 109; 411	102 106	113 111	109 109	2.3	
/ grain		Overall receivery (n = 6)	100	111	109	3.7	
	\$0.01	103@108; 113	103	113	109	4.6	
×-	0.10	103, 103, 103 09					
Spring barley / straw		~~~103; 103 <u>0</u> 89	103	109	105	3.3	
nou aw	0.50		104	111	109	3.7	
		Overall recovery (n = 9)	1		107	3.8	

FL = Fortification level RSD = Wative standard devation, LOQ = Practical limit of quantification Fortified with fluop/fam-bergamide determined as fluopyram and calculated as fluopyram Fortified with fluop/fam-bergamide determined as fluopyram-bengamide and calculated as fluopyram * These recovered were background corrected since the control sample used for spiking (18-2101-01-0006E) was found to contain (apparent) residues at a local of 0.00254 mg/ty. The uncorrected recovery is shown in brackets.

BAYER

Page 392 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

(a) (b) g a.s./ha Water (L/ha) g a.s./hI (L/ha) (c)	Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	App	lication ra treatmer		Dates of treatment / Application interval	Growth stage at last treatment	Portion analyzed	Growth stage at samoling	P ^{LOP}			- MA-		PHI (days
18-2101-01-01-T Barley 1) 25.10.2017 103 308 38.3 92.05.20180 90 90 0.032 0.014 0.046 0.75 0.035 1 13-2101-01-T Cassia 3) 25.06.2018 -05.07.2018 0.17 1 10.17 10.17 10.17 10.17 10.17 10.17 10.17 10.17 10.17 10.17 10.17 10.17 10.17 10.18 10.17 10.18 10.17 10.18 10.17 10.18 10.17 </th <th></th> <th>(a)</th> <th>(b)</th> <th></th> <th></th> <th>g a.s./hI</th> <th></th> <th></th> <th>re^riñ</th> <th>¢°</th> <th>fluopyram</th> <th>BEU- benzamide as AFO C656948</th> <th>Total residue cale_1</th> <th></th> <th></th> <th>(f)</th>		(a)	(b)			g a.s./hI			re ^r iñ	¢°	fluopyram	BEU- benzamide as AFO C656948	Total residue cale_1			(f)
$\frac{18-2101-02}{18-2101-02-T} Race south 84170 Augusta = 0.010 1.12 2017 2018 0.01 1.2 2017 2018 0.01 0.036 0.028 0.01 0.036 0.028 0.01 0.038 0.030 0.066 0.028 0.01 0.038 0.030 0.066 0.028 0.01 0.038 0.030 0.044 0.0066 0.01 0.056 0.004 0.004 0.006 0.004 0.004 0.004 0.006 0.004 0.004 0.006 0.004 0.004 0.004 0.004 0.004 0.006 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.006 0.004 0.004 0.004 0.006 0.004 0.004 0.004 0.006 0.004 0.006 0.004 0.006 0.004 0.006 0.004 0.006 0.004 0.006 0.004 0.006 0.004 0.006 0.004 0.006 0.004 0.004 0.006 0.004 0.006 0.004 0.004 0.006 0.004 0.0$	18-2101-01-T France, south 31330 St Caprais Europe, South F 2018	Cassia	2) 01.05.2018 - 10.05.2018 3) 25.06.2018 - 05.07.2018	CUIR	10 ²	, JD ^{it}	P OW	2ef				C 0.014 K	0.046 0.046	0.75		57 57
Tt may control and	18-2101-02 18-2101-02-T France, south 84170 Monteux Europe, South F 2018	Barley Augusta	1) 11.12.2017 2) 01.052018 -06.05.2018 3) 18.06.2018 - 22.06.2018			ST.4 OF TOOT	92.05.2018/0 E D L E	EI JUNE	green material	61 × 69 × 77 ×	0.028	< 0.01 0.011 < 0.01 < 0.01 < 0.01 < 0.01	1.2 0.36 0.17 0.084 0.038	0.78	0.94 0.28 0.13 0.066 <u>0.030</u>	0 7 14 21 28 48 48
	EUT	Tt Mermo	A CONTRACT		DD L L C DD L L C D L D L D L C D L D L D L D L D L D L D L D L D L D L	er on it		I UN		07	0.040	~0.01	0.030	1	0.044	48



Page 393 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

												2		<u> </u>	>
									Ĉa		Ċ.		a C	JI THE	a Do
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Арр	lication r treatme		Dates of treatment / Application interval	Growth stage at last treatment	Portion analyzed	Growth stage at sampling	P ^{TOR}	esidues (mg/l	(g) C ^T		JING C	PHI (days)
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	-Q ¹ 00Q	C. C. C.		(d) P	Duopyrant as AB C656948	OFLU- benzamide as AP C656948	Total residue cate.	Scaling factor	Scaled	(f)
18-2101-03 18-2101-03-T Italy 44123 Boara Ferrara Europe, South		1) 19.10.2017 2) 02.05.2018 - 16.05.2018 3) 11.06.2018 - 25.06.2018	101	302		30.04.20 BO	59 59 Du ⁰ Ou ⁰	Grain	89x C 3×89	~~ <i>~</i>		0.948 0.16 0.16	0.77	<u>0.037</u> 0.12	44 44
F, 2018 18-2101-04 18-2101-04-T Greece 50100 Thymaria, Kozanis Europe, South	Barley Explorer	1) 09.12.2017 2) 03.05.2018 - 07.05.2018 3) 14.06.2018 - 49.06.2018	do un		33.2 JU		n n	green material	51 73 75 89	1,3 • 0,91 • 0,16 • 0,047	<pre></pre> <001 <001 <001 <001 <001 <001 <001 <001	1.3 0.42 0.17 0.057 0.037 0.024	0.77	1.0 0.32 0.13 0.044 0.028 <u>0.018</u>	0 7 14 21 28 42
F 2018 (a) Accord	ing to CODEX	Classification / Ruide		Davsa	Thet last applie	ation (Label pros-	barvest interv	stal	Rine)	0.038	<0.01 sulation type	0.048	Method val	0.037	42
(d) Accord (b) Only if (c) Year n (d) Either G greenh	The code of the co	Classification / Guide Classification / Guide Protection or BBCH Co F field Classification / Guide Classification / Guide		Robert Robert Junform Study Ariopt D C C C C C C C C C C C C C	ks max approved a transfer and a tra	e: Climatic@ndi netabuttes are in n	auded		al method	 (i) Form (i) Appli (j) Meth (k) LOQ ** residu 	ication method od information	(m) #	Storage (m	ax) date of analy production	
Ĉ)*)														393



Based on the residue definition for risk assessment, the sum of fluopyram and fluopyram-benzapide expressed as fluopyram, the total residues for barley are summarized in the Table 6.3.5-19

Table 6.3.5- 19:	Summary of fluopyram total residue data for	barley trials supporting	GAP 1
	(after results scaling)	1	\$~~C

				<u> </u>	
Сгор	Commodity	Region/Indoor (a)	Trial results relevant to the critical GAP (mg/kg)	STMR (b)	HR C
		NEU		0.023	0.0770
	Grain	SEU	$ \begin{array}{c} & 4x < 0.02 ; 0.012 ; 0.018 ; 2x 0.022 ; \\ & 0.027 ; 0.030 ; 0.035 ; 0.037 ; 2x 0.038 ; \\ & & & & & & & \\ & & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & $	0.025 j	0.090 °
		NET SEU O	$\begin{array}{c} 5x < 0.02; 0.011; 0.022; 0.015; 2x \\ 0.017; 0.018; 4x 0.022; 0.023; 0.025; \\ 0.026; 0.027; 0.029; 0.030; 0.032; 2x \\ \end{array}$	0.023	
Barley	5		0.035 ; 0.037 ; 2.00.038 0.044 0.045 0.077 ; 0.090 0.021 ; 0.022 ; 0.041 ; 0.042 ; 0.047 : 0		
		ONEU S	20.051; 0.056; 0.064, 0.068; 0.085; 0.087; 0.093; 0.14, 0.19; 0.29	0.064	0.29
	E Straw	SEU C	<0.02; 0.023; 0.037; 0.0442; 3x 022; 0.157; 0.20; 0.30; 042; 0.42; 0.80 ; 0.85; 0.92; 1.2	0.145	1.2
	Straw	NEU DU	\$0.02; 0.021; 0.022; 0.023; 0.035; 0.037; 0.041; 0.042; 0.044; 0.047; 0.056; 0.056; 0.064; 0.068; 0.085;	0.087	1.2
		autoor tricks in EU, m	0.087; 0.093, 0.11, 3x 0.12; 0.17; 0.19 0.20; 0.29; 0.30, 0.42; 0.80; 0.85; 0.92; 1.2		

(a) NEU or SEU for nothern or southern gendoor trials in EU member states, (b) STMR: Supervised Trials Matian Residue (c) HR: Highest residue



Kegron Vegetation period E (Formulation) number Kedrence Barley NEU 4 4 E19R8074, (FLU SC250) Marcistr5-01-1 KCACA5/5/08 Barley SEU 4 4 E09RP109, GEU SC250) Marcistr5-01-1 KCACA5/5/08 U = northern EU field SEU = southern EU field SEU = southern EU field KCA 6.3.5/09 KCA 6.3.5/09 AP 2 northern zone SEU = southern EU field SEU = southern EU field KCA 6.3.5/08 KCA 6.3.5/08 eport Author: 2021 SEU = southern EU field SEU = southern EU field SEU = southern EU field eport Author: 2021 SEU = southern EU field SEU = southern EU field SEU = southern EU field eport Year: 2021 SEU = southern EU field SEU = southern EU field SEU = southern EU field eport Nuthor: IDetermination of the residues of frothioconazole, BYF-00587 and AE C656948 in/on Barley after a spray appreciatory of bixatch & fluopyrantex protucoconazole EC 260 in Gernary, nothern Eance and the Naherlands SEU = southern EU field eport No: E19RP074 SEU = southern EV field Trial (TG 509) SEU = southern EV field Trial (TG 509) uideline(s) followed in Actematy and the council of 210	Kergion Vegetation period Σ (Formulation) number Rederence Barley NEU 4 4 E19R0974, (FULV SC250) Math 1575-01-1 KCA 6.3,5708 Barley SEU 4 4 E00R0109, (FULV SC250) Math 1575-01-1 KCA 6.3,5708 U = northern EU field SEU = southern EU field SEU = southern EU field KCA 6.3,5708 KCA 6.3,5709 AP 2 northern zone SEU = southern EU field SEU = southern EU field KCA 6.3,5708 KCA 6.3,5708 ata Point: KCA 6.3,5708 KCA 6.3,5708 KCA 6.3,5708 KCA 6.3,5708 apport Author: 2021 Seu = southern EU field Seu = southern EU field KCA 6.3,5708 apport Author: 2021 Seu = southern EU field Seu = southern Eu field Seu = southern Eu field sport Tautor: 2021 Seu = southern Eu field Seu = southern Eu field Seu = southern Eu field sport No: E19R074 Math 20087 and AE C656948 in/on Barley affer a spray appreation of bix fern & fluopyram & protectoconazole EC 260 in Gergany, nothern Eance aff the Notherlands Secure of the Setting of the Setting of plant protection products on the market QECD Guideline for the Setting of plant protection products on the market QECD Guid			No. of independent	t trials			
NEU 4 4 E19R074, (FLU SC250) Mz81575-01-1 CCA 63/5/08 SEU 4 4 E00RP109, EDU SC250) Mz81575-01-0 KCA 63/5/08 SU = northern EU field SEU = southern EU field SEU = southern EU field Mz81575-01-0 KCA 63/5/09 AP 2 northern zone SEU = southern EU field SEU = southern EU field Mz81575-01-0 KCA 63/5/09 Data Point: KCA 63/5/08 KCA 63/5/08 Mz81/5/05/01-0 KCA 63/5/09 Data Point: KCA 63/5/08 KCA 63/5/08 Mz81/5/05/01-0 KCA 63/5/09 Leport Author: 2021 Mz81/5/05/01-0 KCA 63/5/08 Mz81/5/05/01-0 Leport Year: 2021 Z021 KCA 63/5/08 Mz81/5/05/01-0 Leport No: Determination of the residues of prothioconazole, BYF-0/5/87 and AE C656948 in/on Barley after a spray application of bixaten & filopyrame protucioconazole EC 260 in Gerpfany, nothern Rance and the Natherlands Report No: E19RP074 Mz761/5/011-0 Mz761/5/011-0 Jouideline(s) followed in Regulation (EC) No T107/2009 of the European Parliament and of the Council of 21 October 2009 coupering the placing of Plant protection products on the market 0ECD Guideline for the esting of Chemicals on Crop Field Trial (TG 509 <	Barley NEU 4 4 E19R0974, (FLU SC250) M=#1575-01-1 XCA.6.7.5/08 3U = northern EU field SEU 4 4 E09RP109, EPU SC250) X1-761576-01-0 KCA.6.3.5/09 AP 2 northern zone SEU = southern EU field SEU = southern EU field KCA 6.3.5/08 KCA 6.3.5/08 Data Point: KCA 6.3.5/08 KCA 6.3.5/08 KCA 6.3.5/08 KCA 6.3.5/08 Leport Author: 2021 KCA 6.3.5/08 KCA 6.3.5/08 KCA 6.3.5/08 Leport Year: 2021 KCA 6.3.5/08 KCA 6.3.5/08 KCA 6.3.5/08 Leport Year: 2021 KCA 6.3.5/08 KCA 6.3.5/08 KCA 6.3.5/08 Leport Year: 2021 KCA 6.3.5/08 KCA 6.3.5/08 KCA 6.3.5/08 Leport No: Beremination of the residues of prothioconazole BYF-00587 and AE C656948 in/on Barley after a spray application of bixaten & fluopyrant & protucoconazole EC 260 in Gerefiany, nothern Fance and the Notherlands Keport No: Kegulation (EC) No T107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market GECD Guideline for the desting of Plant protection products on the market GECD Guideline for the desting of Chemicals on Crop Field Trial (TG 509	Crop	Region	Vegetation period	-	Report No.	Document	Reference
SEU 4 4 HORP109, GEU SC250 XI-761576-01-P KCX 6.3,009 EU = northern EU field SEU = southern EU field SEU = southern EU field KCX 6.3,009 AP 2 northern zone AP 2 northern zone AP 2 northern zone AP 2 northern zone Data Point: KCA 6.3,5/08 AP 2 northern zone AP 2 northern zone Data Point: KCA 6.3,5/08 AP 2 northern zone AP 2 northern zone Data Point: KCA 6.3,5/08 AP 2 northern zone AP 2 northern zone Data Point: KCA 6.3,5/08 AP 2 northern zone AP 2 northern zone Data Point: KCA 6.3,5/08 AP 2 northern zone AP 2 northern zone Data Point: KCA 6.3,5/08 AP 2 northern zone AP 2 northern zone Data Point: KCA 6.3,5/08 AP 2 northern zone AP 2 northern zone Data Point: KCA 6.3,5/08 AP 2 northern zone AP 2 northern zone Determination of the residues of prothioconazole, BYF-00587 and AE C656948 in/on barley after a spray application of bixaten & fluopyram & protuoconazole EC 260 in Gernfany, nothern Rance and the Natherlands AP 2 2000 no 200	SEU 4 4 EVENP109, EU = northern EU field KCX 6.3, 209 EU = northern EU field SEU = southern EU field SEU = southern EU field KCX 6.3, 209 AP 2 northern zone AP 2 northern zone AP 2 northern zone AP 2 northern zone Data Point: KCA 6.3, 5/08 AP 2 northern zone AP 2 northern zone Data Point: KCA 6.3, 5/08 AP 2 northern zone AP 2 northern zone Data Point: KCA 6.3, 5/08 AP 2 northern zone AP 2 northern zone Data Point: KCA 6.3, 5/08 AP 2 northern zone AP 2 northern zone Data Point: KCA 6.3, 5/08 AP 2 northern zone AP 2 northern zone Data Point: KCA 6.3, 5/08 AP 2 northern zone AP 2 northern zone Determination of the residues of prothioconazole, BYF-00587 and AE C656948 in/on Barley after a spray appreation of bixaten & fluopyram& protoconazole EC 260 in Gerpfany, nothern Kance and the Natherlands AP 2 200 Document No: M-76157-01-7 AP 2 2009 AP 2 2009 Deviation(S) followed in Regulation (EC) No 1107/2009 of the Euroncan Parliament and of the Council of 21 October 2009 concepting the placing of plant protection products on the market QECD Guideline for the 2 sting of Chemicals on Crop Field Trial (TG 509 published in Schember 2009) Deviations from current esting facilities: No, nor previolisis submitted No, nor previolisi s			2019	Σ	(Formulation)	number	
SEU 4 4 EVPRP109, GEU SC250 XL-761576-01-P KCX 6.3, 609 3U = northern EU field SEU = southern EU field SEU = southern EU field KCX 6.3, 609 AP 2 northern zone 4 4 4 4 Pata Point: KCA 6.3, 508 KCA 6.3, 508 teport Author: 1 1 1 teport Year: 2021 2021 teport Year: 2021 2021 teport Title: Determination of the residues of prothioconazole, BYF-00587 and AE C656948 in/on barlex after a spray appreciator of bixaten & fluopyram & protuoconazole EC 260 in Germany, nothern Rance and the Natherlands ceport No: E19RP074 2 occument No: M-76159-01-F biuideline(s) followed in Regulation (EC) No 1107/2009 of the Euroncan Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market ØECD Guideline for the Setting of Cherticals on Crop Field Trial (TG 509 published in Schember 2009) US-EPA OCSPP 860.1500, Crop Field Trial No, nor previoisly submitted No, nor previoisly submitted No, nor previoisly submitted	SEU 4 4 HURP109, GEU SC250 KL-761576-01P KCX 6.3,009 3U = northern EU field SEU = southern EU field SEU = southern EU field KCX 6.3,009 AP 2 northern zone AP 2 northern zone AP 2 northern zone AP 2 northern zone ata Point: KCA 6.3,5/08 KCA 6.3,5/08 teport Author: Determination of the residues of prothioconazole, BYF-00587 and AE C656948 in/on barley after a spray appreation of bixaten & fluopyrande protuoconazole EC 260 in Gernary, nothern Rance and the Nutherlands ceport No: E19RP074 AP 2 occument No: M-76159-01-1 biudeline(s) followed in Regulation (EC) No 1107/2009 of the Euronean Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market ØECD Guideline for the desting of Cherticals on Crop Field Trial (TG 509 published in Schernber 2009) Vulsiphed in Schernber 2009) Vulsiphe		NEU	4	4	E19R7074, (FLU SC250)	<u>M-81575-01-1</u>	KCA 57.5/08
Barley after a spray apprication of bixaten & filippyram & protoconazole EC 260 in Germany, nothern Fonce and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in tudy: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the desting of Chermicals on Crop Field Trial (TG 509 published in September 2009) Deviations from current est guideline: No, no previously submitted Oreviations from current esting facilities: No, no previously submitted	Barley after a spray apprication of bixaten & fillopyrant & protuoconazole EC 260 in Germany, nothern France and the Notherlands Report No: E19RP074 Occument No: M-76159-01-1 Guideline(s) folloved in Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the festing of Chernicals on Crop Field Trial (TG 509 published in September 2009) US-EPA OC SPP 860.1500, Crop Field Trial October 2009 supervisition of the feature of the fe	Barley	SEU	4	4	EPRP109,	Q <u>M-761576-01</u>	KCX 6.3 \$ 09
Barley after a spray apprication of bixaten & filippyram & protoconazole EC 260 in Germany, nothern Fonce and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in tudy: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the desting of Chermicals on Crop Field Trial (TG 509 published in September 2009) Deviations from current est guideline: No, no previously submitted Oreviations from current esting facilities: No, no previously submitted	Barley after a spray apprication of bixaten & fillopyrant & protuoconazole EC 260 in Germany, nothern France and the Notherlands Report No: E19RP074 Occument No: M-76159-01-1 Guideline(s) folloved in Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the festing of Chernicals on Crop Field Trial (TG 509 published in September 2009) US-EPA OC SPP 860.1500, Crop Field Trial October 2009 supervisition of the feature of the fe	EU = northern I	EU field	SEU = southern EU field				
Barley after a spray application of bixaten & filupyram & protoconazole EC 260 in Germany, nothern France and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in tudy: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the setting of Chemicals on Crop Field Trial (TG 509 published in September 2009) Deviations from current est guideline: No, nor previously submitted Orevious evaluation Ves, conducted under GLD/Officially recognised testing facilities	Barley after a spray application of bixaten & filospyrant & protuoconazole EC 260 in Germany, nothern Kance and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in tudy: Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the festing of Chermicals on Crop Field Trial (TG 509 published in September 2009) Deviations from current est guideline: No, nor previously submitted Orevious evaluation No, nor previously submitted GLP/Officially recognized esting facilities: Vestor of the facilities				×		N N C	
Barley after a spray application of bixaten & filupyram & protoconazole EC 260 in Germany, nothern France and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in tudy: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the setting of Chemicals on Crop Field Trial (TG 509 published in September 2009) Deviations from current est guideline: No, nor previously submitted Orevious evaluation Ves, conducted under GLD/Officially recognised testing facilities	Barley after a spray application of bixaten & filospyrant & protuoconazole EC 260 in Germany, nothern Kance and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in tudy: Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the festing of Chermicals on Crop Field Trial (TG 509 published in September 2009) Deviations from current est guideline: No, nor previously submitted Orevious evaluation No, nor previously submitted GLP/Officially recognized esting facilities: Vestor of the facilities				Ő		\$ \$ \$	
Barley after a spray apprication of bixaten & fluopyram & protoconazole EC 260 in Germany, nothern France and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in tudy: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the setting of Chemicals on Crop Field Trial (TG 509 published in September 2009) Deviations from current est guideline: No, no previously submitted Orevious evaluation Ves, conducted under GLD/Officially recognised testing facilities OLP/Officially recognised Ves, conducted under GLD/Officially recognised testing facilities	Barley after a spray apprication of bixaten & filopyram & protectionazole EC 260 in Gernany, nothern France and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in tudy: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the Jesting of Chemicals on Crop Field Trial (TG 509 published in Septembel 2009) Deviations from current nobe Previous evaluation No, nor previously submitted GLP/Officially recognised Ves, conducted under GLD/Officially recognised testing facilities	AP 2 nor	thern zor	Ie	× A			or the co
Barley after a spray application of bixaten & filupyram & protoconazole EC 260 in Germany, nothern France and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in tudy: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the setting of Chemicals on Crop Field Trial (TG 509 published in September 2009) Deviations from current est guideline: No, nor previously submitted Orevious evaluation Ves, conducted under GLD/Officially recognised testing facilities	Barley after a spray application of bixaten & filospyrant & protuoconazole EC 260 in Germany, nothern Kance and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in tudy: Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the festing of Chermicals on Crop Field Trial (TG 509 published in September 2009) Deviations from current est guideline: No, nor previously submitted Orevious evaluation No, nor previously submitted GLP/Officially recognized esting facilities: Vestor of the facilities				Ś .^	y y ð	A. Ör «	
Barley after a spray application of bixaten & filupyram & protoconazole EC 260 in Germany, nothern France and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in tudy: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the setting of Chemicals on Crop Field Trial (TG 509 published in September 2009) Deviations from current est guideline: No, nor previously submitted Orevious evaluation Ves, conducted under GLD/Officially recognised testing facilities	Barley after a spray application of bixaten & filospyrant & protuoconazole EC 260 in Germany, nothern Kance and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in tudy: Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the Setting of Chermicals on Crop Field Trial (TG 509 published in September 2009) Deviations from current est guideline: No, nor previously submitted Orevious evaluation No, nor previously submitted GLP/Officially recognized esting facilities: Vestor of the Council of CD/Officially recognised testing facilities			Q,				
Barley after a spray apprication of bixaten & fluopyrant & protoconazole EC 260 in Gernany, nothern France and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in study: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the resting of Chemicals on Crop Field Trial (TG 509 published in September 2009) US CPA OC SPP 860.1500, Crop Field Trial (CG 509 published in September 2009) Deviations from current none Vestor Conduction of the Council of 2009 (Crop Field Trial (CG 509 published in September 2009) GLP/Officially recognised Vestor conducted under GLD/Officially recognised testing facilities Accord to 100/0000000000000000000000000000000000	Barley after a spray apprication of bixaten & fluopyrant & protetoconazole EC 260 in Gernány, northern France and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in study: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the Jesting of Chemicals on Crop Field Trial (TG 509 published in Septembel 2009) Deviations from current est guideline: No, nor previously submitted Orevious evaluation No, nor previously submitted GLP/Officially recognised Yes, conducted under GLD/Officially recognised testing facilities			L ^O *	and the second s			Ĩ,
Barley after a spray apprication of bixaten & fluopyrant & protoconazole EC 260 in Gernany, nothern France and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in study: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the resting of Chemicals on Crop Field Trial (TG 509 published in September 2009) US CPA OC SPP 860.1500, Crop Field Trial (CG 509 published in September 2009) Deviations from current none Vestor Conduction of the Council of 2009 (Crop Field Trial (CG 509 published in September 2009) GLP/Officially recognised Vestor conducted under GLD/Officially recognised testing facilities Accord to 100/0000000000000000000000000000000000	Barley after a spray apprication of bixaten & fluopyrant & protetoconazole EC 260 in Gernány, northern France and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in study: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the Jesting of Chemicals on Crop Field Trial (TG 509 published in Septembel 2009) Deviations from current est guideline: No, nor previously submitted Orevious evaluation No, nor previously submitted GLP/Officially recognised Yes, conducted under GLD/Officially recognised testing facilities	Net a D i t						<u>Si v</u>
Barley after a spray apprication of bixaten & fluopyrant & protoconazole EC 260 in Gernany, nothern France and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in study: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the resting of Chemicals on Crop Field Trial (TG 509 published in September 2009) US CPA OC SPP 860.1500, Crop Field Trial (CG 509 published in September 2009) Deviations from current none Vestor Conduction of the Council of 2009 (Crop Field Trial (CG 509 published in September 2009) GLP/Officially recognised Vestor conducted under GLD/Officially recognised testing facilities Accord to 100/0000000000000000000000000000000000	Barley after a spray apprication of bixaten & fluopyrant & protetoconazole EC 260 in Gernány, northern France and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in study: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the Jesting of Chemicals on Crop Field Trial (TG 509 published in Septembel 2009) Deviations from current est guideline: No, nor previously submitted Orevious evaluation No, nor previously submitted GLP/Officially recognised Yes, conducted under GLD/Officially recognised testing facilities			KCA 63.5/08				~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
Barley after a spray apprication of bixaten & fluopyrant & protoconazole EC 260 in Gernany, nothern France and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in study: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the resting of Chemicals on Crop Field Trial (TG 509 published in September 2009) US CPA OC SPP 860.1500, Crop Field Trial (CG 509 published in September 2009) Deviations from current none Vestor Conduction of the Council of 2009 (Crop Field Trial (CG 509 published in September 2009) GLP/Officially recognised Vestor conducted under GLD/Officially recognised testing facilities Accord to 100/0000000000000000000000000000000000	Barley after a spray apprication of bixaten & fluopyrant & protetoconazole EC 260 in Gernány, northern France and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in study: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the Jesting of Chemicals on Crop Field Trial (TG 509 published in Septembel 2009) Deviations from current est guideline: No, nor previously submitted Orevious evaluation No, nor previously submitted GLP/Officially recognised Yes, conducted under GLD/Officially recognised testing facilities		01.	202 0	NO N			
Barley after a spray apprication of bixaten & fluopyrant & protoconazole EC 260 in Gernany, nothern France and the Netherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in study: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the resting of Chemicals on Crop Field Trial (TG 509 published in September 2009) US CPA OC SPP 860.1500, Crop Field Trial (CG 509 published in September 2009) Deviations from current none Vestor Conduction of the Council of 2009 (Crop Field Trial (CG 509 published in September 2009) GLP/Officially recognised Vestor conducted under GLD/Officially recognised testing facilities Accord to 100/0000000000000000000000000000000000	Barley after a spray apprication of bixaten & fluopyrant & protutoconazole EC 260 in Germany, northern Krance and the Notherlands Report No: E19RP074 Document No: M-76159-01-1 Guideline(s) followed in study: Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the Jesting of Chemicals on Crop Field Trial (TG 509 published in September 2009) Deviations from current note Previous evaluation No, nor previously submitted GLP/Officially recognized Yes, conducted under GLD/Officially recognised testing facilities			Digtermination of	The resid	Ries of prothioconaz	role BVE 01887 an	 d AF C656948 in/on
Gerrany, nothern Rance and the Notherlands Report No: E19RP074 Document No: M-76159-01-19 Guideline(s) followed in study: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QFCD Guideline for the setting of Chernicals on Crop Field Trial (TG 509 published in September 2009) Deviations from current none Previous evaluation No, not previously submitted GLP/Officially recognised Ves, conducted under GICP/Officially recognised testing facilities	Germany, nothern Kance and the Notherlands Report No: E19RP024 Document No: M-76159-01- Guideline(s) followed in study: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QFCD Guideline for the Sesting of Chemicals on Crop Field Trial (TG 509 published in September 2009) Deviations from current est guideline: No, not previously submitted Orrevious evaluation No, not previously submitted GLP/Officially recognised Ves, conducted under GLD/Officially recognised testing facilities	ceport rule.						
Document No: M-761592-01-1 Guideline(s) followed in study: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market Octuber 2009 concerning the placing of plant protection products on the market OECD Guideline for the Sesting of Chemicals on Crop Field Trial (TG 509 published in September 2009) Oeviations from current Deviations from current Previous evaluation An opport October 2009 concerning the placing of chemicals on Crop Field Trial (TG 509 published in September 2009) October 2009 concerning the placing of chemicals on Crop Field Trial (TG 509 published in September 2009) Opport Concerning the placing of Chemicals on Crop Field Trial (TG 509 published in September 2009) Opport Concerning the placing of Chemicals on Crop Field Trial (TG 509 published in September 2009) Opport Concerning the placing of Chemicals on Crop Field Trial (TG 509 published in September 2009) Opport Concerning the placing of Chemicals on Crop Field Trial (TG 509 published in September 2009) Opport Concerning the placing of Chemicals on Crop Field Trial (TG 509 published in September 2009) Opport Concerning the placing of Chemicals on Crop Field Trial (TG 509 published in September 2009) Opport Concerning the place of Chemical September 2009 published in September 2009 published in September 2009 published in September 2009 published Sep	Document No: M-76159-01-1 Guideline(s) followed in study: Regulation (EC) No 1007/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market Study: October 2009 concerning the placing of plant protection products on the market Deviations from current Deviations from current No, not previously submitted No, not previously submitted GLP/Officially recognised Xes, conducted under GLD/Officially recognised testing facilities							
Guideline(s) followed in study: Regulation (EC) No 107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OFCD Guideline for the setting of Chemicals on Crop Field Trial (TG 509 published in September 2009) Very transmission of the setting of chemicals on Crop Field Trial (TG 509 published in September 2009) Very transmission of Crop Field Trial (TG 509 published in September 2009) Deviations from current none Very transmission of Crop Field Trial Previous evaluation No, nor previously submitted Very transmission of Clark previously submitted GLP/Officially recognised Very transmission of Clark previously recognised testing facilities	Guideline(s) followed in study: Regulation (EC) No.107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market QECD Guideline for the desting of Chernicals on Crop Field Trial (TG 509 published in September 2009) V USEPA OC SPP 860.1500, Crop Field Trial Deviations from current none Previous evaluation No, not previously submitted GLP/Officially recognised Xes, conducted under GLD/Officially recognised testing facilities	Report No:	Ő		Ø i	S LY O	× ×	
study: October 2009 concerning the placing of plant protection products on the market OCD Guideline for the zesting of Chemicals on Crop Field Trial (TG 509 published in September 2009) US-EPA OCSPP 860.1500, Crop Field Trial Deviations from current est guideline: Previous evaluation Deviations from current Schemer (State Construction) No, not previously submitted Schemer (State Construction) Schemer (State Construction) October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market opposite the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market opposite the placing of plant protection products on the market opposite the placing of plant protection products on the market opposite the placing of plant protection products on the market opposite the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market opposite the place of the place	study: October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of plant protection products on the market October 2009 concerning the placing of the place of th	Document No	o: 🖓				0 🍫	
Operations Conduction Conduction <td>GLP/Officially recognised Xes, conducted under GLD/Officially recognised testing facilities</td> <td></td> <td>folloved in</td> <td>Regulation (EC)</td> <td></td> <td></td> <td></td> <td></td>	GLP/Officially recognised Xes, conducted under GLD/Officially recognised testing facilities		folloved in	Regulation (EC)				
Operations Conduction Conduction <td>GLP/Officially recognised Xes, conducted under GLD/Officially recognised testing facilities</td> <td>tudy:</td> <td>~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~</td> <td>October 2009 co</td> <td>poophing</td> <td>the placing of plant</td> <td>protection products</td> <td>on the market</td>	GLP/Officially recognised Xes, conducted under GLD/Officially recognised testing facilities	tudy:	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	October 2009 co	poophing	the placing of plant	protection products	on the market
US EPA OC SPP 860.1500, Crop Field Trial® Deviations from current note est guideline: Previous evaluation No, n@ previously submitted GLP/Officially recognised testing facilities esting facilities: Accorded and the field of the field	US EPA OC PP 860.7500, Crop Field Trial® Deviations from current not v v v v v v v v v v v v v v v v v v v	(s O	@ECD Guideline	for the	Festing of Chernical	s on Crop Field Tria	al (TG 509
Deviations from current none est guideline: Previous evaluation No, nor previously submitted GLP/Officially recognised Ves, conducted under GIO/Officially recognised testing facilities esting facilities:	Deviations from current none est guideline: Previous evaluation No, nor previously submitted GLP/Officially recognised Ves, conducted under GIO/Officeally recognised testing facilities esting facilities:	<u>`</u>	, ,	published in Sept	tember 2	009)	٧ ٢	
est guideline: Previous evaluation GLP/Officially recognised esting facilities: No, nor previously submitted GLP/Officially recognised testing facilities (CDL) (CDL) (C	est guideline: Previous evaluation No, nor previously submitted GLP/Officially recognised Xes, conducted under GLD/Officially recognised testing facilities esting facilities:			US US CPA OC SPP	<u>860.T50</u>	U, Crop Field Trial	Jr	
Previous evaluation No, nor previously submitted	Previous evaluation No, not previously submitted	veviations fr	om current	- nome	\$°` %			
GLP/Officially recognised testing facilities	GLP/Officially recognised Ves, conducted under GLO/Officially recognised testing facilities			A No not provide		<u> </u>		
esting facilities:	esting facilities:	ievious eval	iualiog					
esting facilities:	esting facilities:	GLP/Official	lo recognis	ed Yes, conducted u	Deder GI	D/Offically recogni	sed testing facilities	5
A second a list of the list of the second se	A second at 12 (De that hitter and Ward and A	esting facilit	ies:			- · · · · · · · · · · · · · · · · · · ·	<i>8</i>	
				Yes Yes	<u>, 6</u> °			
		" `	. 🚿	1. Y' . 'U	_`¥			

Materials and Methods

Ô.

Four supervised residue trails on barley were conducted in northern Europe (in northern France, Germany and the Verherlands) during the 2019 season. One-spray applications was conducted with BIX+FLU+PTZ EC 260, an EC (emulsifiable concentrate) formulation containing 100 g/L prothioconazole, 65 g/L of fluopyram and 65 g/L of bixafen. For the purpose of this renewal, only results for fluopyram and its metabolites fluopyram-benzamide, fluopyramĉ



pyridyl-carboxylic-acid, fluopyram-pyridyl-acetic-acid),fluopyram-7-hydroxy and fluopyram-methyl sulfoxide will be discussed.

The applications were conducted at the BBCH of 61 and at the application rates of the L/ha corresponding to the single application 0.039 kg a.s./ha. Water application rates were at 300 L/ha

Samples of barley green material were collected at BBCH 61 and barley grain and straw at havest BBCH 89.

Each field sample was placed in doubled labelled bags and stored deep-frozen within 24 hours after sampling and until dispatch. All field samples were shipped deep-frozen at -18 °C or lower temperatures) of under monitored conditions during shipment and arrived in good combined.

The field samples were stored in a freezer at \leq -18 °C antil preparation of the examination samples. For the preparation of examination samples, the deep-frozen field samples were shredded and homogenized with dry ice in a cutter. Representative parts of the shredded samples were transferred into polystyrene boxes and stored at \leq -18°C. For each field sample, one or several examination samples were prepared for analysis and one examination sample was prepared as a reserve sample.

Residues of fluopyram and its metabolites (FkU-benzamide, FLU-PCA, FLU-PAA, FLU-7-OH, FLUmethyl-sulfoxide), were determined by CC-MS/MS according to method 00984 (1990) 05/02/2007, M-<u>283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the OU regulatory equirements outlined within SANCO/3029/99 rev 4.

Residues were extracted from 10 gof sample material botwo successive extractions using a high-speed blender with a mixture of acetonitrile:water (80.20; *x*:*v*). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards

- One dilution was performed under acidic conditions: this extract flowed the determination of FLU-PCA and FDU-methyl-suffoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed the determination of fluopyram, PLU-bonzamide and FLU-200H.

An aliquot of the extracts was injected in LCMS/MS operated in Electrospray Ionization mode:

- One injection in positive electrospray ionization for the determination of fluopyram, FLUbenzamide and FLU-7-OH
- Another injection in negative electrospery ionization for the determination of FLU-PCA and FLUmethyl_sulfoxide under different conditions

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established with at least 5 concentration level. For each calibration curve, the correlation coefficient R was above 0.99. The quadrification was done bounternal standardization using isotopically stable labelled internal standards. The Einit of Quantification (LOQ), expressed as fluopyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat straw and 0.05 mg/kg for all other matrices.

Full details and acceptable variation data to support this method are presented within document M-CA 4, which composite the EUsegulatory requirements outlined within SANCO/3029/99 rev 4.

Conditions used on this study: The method was used as described in the original method with some minor modifications, which have no impact on the validity of the study:

Residues were extracted from 5 g of sample material of grain and green material and from 2.5 g of straw. Extraction was done with only 30 mL (straw 40 mL) acetonitrile/water (80/20 v/v). The blender is washed with 5 mL acetonitrile/water (80/20 v/v). The internal standard concentrations were changed from 0.01 mg/L to 10 mg/L and the dilution step after filtration was omitted. The adjustment to pH= 8 was done with



ammonium chloride/ammonia buffer followed by the dilution with acetonitrile/water (4/1, v/v) to get Extract A. The determination was done from an aliquot of Extract A in the positive ion mode.

The time between the beginning of the sample preparation and the sample analysis did not exceed 24 hours for grain and straw and 4 days for samples of the matrix green material. The stability of analyses in extracts of green material, grain and straw of barley were investigated in this study. Extracts of green material, grain and straw were found to be stable for at least 5 days when stored at < 6 °C

Findings

In order to check the performance of the method, recovery determinations were included a each set of analyses. Control samples from the study were fortificato be used as the recovery samples. All the recovery determinations were performed concurrently to the analyses of control and treated samples from the stady. The apparent residues in the control sample used for the determination of recoveries were below 30% of the LOQ. Recoveries were not corrected for apparent residues in the courtrol somples used for these determinations.

The mean recoveries per fortification level were within the acceptable range of 00 % 110 % and with the RSDs < 20 %. The overall mean concurrent recoveries were also in the acceptable range of 70% and 10 %, with the RSD < 20 %. Ô

The storage period of deep-frozen samples intended for the analysis of fluopyram and its metabolites ranged between 311 and 375 days. Ô

The detailed results obtained for barley samples in northern Europe de summarizer in the Table 6.3.5-21 ç, Ŋ

Conclusion

Four supervised residue trials on barley were conducted in northern Europe with the application of BIX+FLU+PTZ EC 250 at the required rates and according to GLP. Samples of Barley were analyzed for the residues of fluops am and its metabolite fluops am-ben zamide. The results of the trials presented above show the following residues in grain at harvest.

- Fluopyram residues range between 0.01 and 0.11 mg/kg. According to Dixon's test the highest value can be considered as an outlier.
- Fluopyram-benzamide residues were < 0.01 mg/kg •
- The total residue of floopyram (sum of FLN + FLC -benzamide, expressed as fluopyram) range between < 0.02 and $0 \pm 2 \text{ mg/kg}$.
- Fluopyram pyridyl-carboxylic-acid residues range between <0.01 and 0.01 mg/kg •
- Fluopyram-pyriovl-acedic-acid residues were <0.01 mg/kg •
- Fluopstam-7-pydroxy residues wer <0.06 mg/kg
- Fluopyram-methylsulfoxide residues were <0.01 mg/kg

Residues in straw at harvest :

Fluopyram residues range between <0.05 and 0.808 mg/kg.

- Fluopyram-benzomide residues were 70.05 mg/kg
- The total residue of Auopyram (such of FLU + FLU-benzamide, expressed as fluopyram) range bety@en <Q.f. and @858 mg/kg.
- Fluopyram-pyrio carboxylic ocid residues were <0.05 mg/kg
- Huopyram-pyridyl-acetic-acid residues were <0.05 mg/kg
- Fluopyram, hydroxy residues between <0.05 and 0.068 mg/kg.
- Fhiopyram² methylsulfoxide residues were <0.05 mg/kg



Assessment a	nd conclusion by	applicant:					
The study is a							A C C C C C C C C C C C C C C C C C C C
		ghest value of fluopyram in grai	in can be	consider	ed as an w	lier.	
					- Or	C	
Table 6.3.5- 2	1: Concu	irrent recovery data for Flu	lopyran	n (study	E19RP07	4) 0	
			overy (?			<u>4)</u>	
Portion analysed	Fortification level (mg/kg)	Individual	, over j ()		8		
anaryseu	lever (ing/kg)	recoveries	Min	Max	∘Mean	RŞD	
Fluopyram (AI	E C656948)			Y . 0		RSD	o or
	0.01	97; 102; 102; 102; 106	20	196		3.1%	, S
Barley / grain	0.2	95; 95; 97; 99; 102 🗸	Č95	2102 2	98 0	3:0 3.7	4
		Overall recovery (n=10)		× A	100	9.7	
Doulary / anoon	0.01	95; 90096; 101,102	. 95	502	× 98	3.3	
Barley / green material	1.20	9608; 98; 400; 1000	\$96	100	<u>۶ 98 کر ا</u>	<u>a</u>	0
		Over a recovery (n= 10)	, sr		38	§ 2.6	<i>Q</i>
(201 - 201 - 10 - 10	0.05	Q 94; 25; 96; 97; 98	840	~98 ~	96 930	1.6	
Barley / straw	0.9	85; 89; 9 6 ,97; 99	* 85	2 ⁵⁴ 99	930*		
12021 1211	·	Ove@ll recovery (n=00)			\$95	4.6	
Fluopyram-b	enzamide	\$7,93;98;98;100 *				1.6	
D 1 / .		5 91; 92; 94; 98; 100 5	× ~~ 0	103	.90) ~95	4.6	
Barley / grain		0,91; 96,94; 98; 401 5	91	1Q″	· ·	4.2	
		Overall recovery (n= 10) 84; 96; 90; 94; 96; 97; 98; 101	29 29 20	10K	96 94	4.2	
Barley / green	0.00 C P.20	96; 96; 96; 98; 900	84 96		94	5.8 1.8	
material	1.20	Overall (ocovery (n= 13)		W.	97 95	4.9	
		77; 80; 80; 80; 0 ×	Ø 77 O		81	4.6	
Barley / straw	30.9 5 30.9 5	\$ 78; \$9, 80; 82; 83 K	770 18	83	80	2.6	
Darrey / Sala //	Q A	Overall recovery (n= 10)	A	00	81	3.5	
Fluopyram-py	sdyl-carboxilic-ici		7				
1. 1.	0.01	92; 99, 103; 104; 114	92	114	102	7.8	
Barley / again	0.2	96, 97; 98; 100; 101	96	101	98	2.1	
		Overall recovery (n=10)			100	5.9	
	0.01	•90, 95; 97, 100; 100, 102; 102;	90	106	99	5.0	
Barley / green	1.20	<u>⊘</u> ″	99	101	100	0.7	
material		Overall recovery (n = 13)		101	99	3.8	
	0.05	98,99; 105; 105; 111	98	111	104	5.1	
Barley Straw	€ [¥] 40.9	91; 95; 96; 96; 100	91	100	96	3.4	
S O		Overall recovery (n= 10)			100	5.9	
Fluopyram-py	ridyl-acetic acid						
Barle grain	0.01	93; 97; 100; 102; 113	93	113	101	7.4	
		10 Sector Sec			1000 APR 101	and the Association	



Portion	Fortification	Rec	overy (%	(0)		
analysed	level (mg/kg)	Individual recoveries	Min	Max	Mean	RSD 5.9 6.3 7 4.2 6.3 6.3 7 6.3 6 7 6 3.8 7 5.6 5 6 3.8 7 6 4.3
	0.2	96; 97; 100; 101; 111	96	111	101	5.9
		Overall recovery (n = 10)	(Pr)		×7101	6.3 0
Barley / green	0.01	92; 96; 98; 99; 101; 103; 106; 114	₹ 92	114 102	101	Č.
material	1.20	92; 93; 95; 98; 102	92	102 *	96 🕱	¥.2
		Overall recovery (n = 13)		Ŷ,	° 99 🎸	623
	0.05	99; 100; 101; 102; 110	99	110	102	Q.3
Barley / straw	0.9	91; 93; 97; 99	200	105	× 97) 5.6%
		Overall recovery (n = 10)		6 0	ح 100 €	5 (5
Fluopyram-7-h	ydroxy		× »	A	Â,	0
	0.01	95; 96 100; 103, 103 V	~95	003	2 99 S	3.&
Barley / grain	0.2	9 2 ,95; 95; 1 01; 102	\$ ⁹²	102	976	¢Å
		Overal recovery (n = 10)	, A	, de la compañía de	Ø8 .	يَ 4.1 ₹
_	0.01	89; 92; 94; 95; 99; 100; 491		<i>√</i> ¥01	8 ⁰ 95 °	5.0
Barley / green material	1.20	86; 89; 9 5; 95	× 86	95	.92 [©]	Å.3
		Overall recovery (n 413)	· · · · · · · · · · · · · · · · · · ·		°∼ 9 4 (4.9
	0.05	87; 87; 92; 94	\$ ⁸⁷	×94 ×	90 ×	3.6
Barley / straw		\$2; 87; 88; 91; 95 \$2; 87; 88; 91; 95	× 82 ×	95	~ <u>8</u> 9)	5.4
		Qverall recovery (n 210)	 	0"	∛90	4.4
Fluopyram-met				a $\sim a$	Ø	
	0.07 () () 90; 94 ; 93 ; 97; 98)	90	98	95	3.3
Barley / grąin	0.2	90; 96; 97; 28, 105	90°	× 1015	97	5.5
		Overall ecovery (n = 10)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Ø	96	4.5
	(A.6) >>	87; 92; 8 8; 106; 1 99 ×	× 870	109	98	9.4
Barley / green material	Jr1.2 ↓	96; 102, 103; 105 ; 112	496	112	104	5.6
		Overall recovery (n = 10)	ð		101	7.7
~	6 05 0	87; 87 088; 89; 9 0	87	90	88	1.5
Barley / straw	0.9	86Q2; 92; 93; 97	86	97	92	4.3
	adard darban LOO	Overal Precovery (n = 10)			90	3.8

RSD = Relative standard derivation, LOQ = Practical limit of quantification Fortified with fluopyram, determined as fluopyram and acculated as fluopyram Fortified with fluopyram-benzamide, determined as fluopyram-benzamide and calculated as fluopyram Fortified with fluopyram-pyridyl-acetic acid, determined as fluopyram-pyridyl-acetic-acid and calculated as fluopyram Fortified with fluopyram-pyridyl-acetic acid, determined as fluopyram-pyridyl-acetic-acid and calculated as fluopyram Fortified with fluopyram-pyridyl-acetic acid, determined as fluopyram-pyridyl-acetic-acid and calculated as fluopyram Fortified with fluopyram-pyridyl-acetic acid, determined as fluopyram-pyridyl-acetic-acid and calculated as fluopyram Fortified with fluopyram-pyridyl-acetic acid, determined as fluopyram-pyridyl-acetic-acid and calculated as fluopyram Fortified with fluopyram-pyridyl-acetic acid, determined as fluopyram-rethyloxy and calculated as fluopyram Fortified with fluopyram-pyridyl-acetic acid, determined as fluopyram-rethyloxy and calculated as fluopyram Fortified with fluopyram-pyridyl-acetic acid, determined as fluopyram-rethyloxy and calculated as fluopyram Fortified with fluopyram-pyridyl-acetic acid, determined as fluopyram-methylsulfoxide and calculated as fluopyram Fortified with fluopyram-pyridyl-acetic acid and calculated as fluopyram Fortified with fluopyram acetic acid and calculated as fluopyram Fortified with fluopyram acetic acid and calc

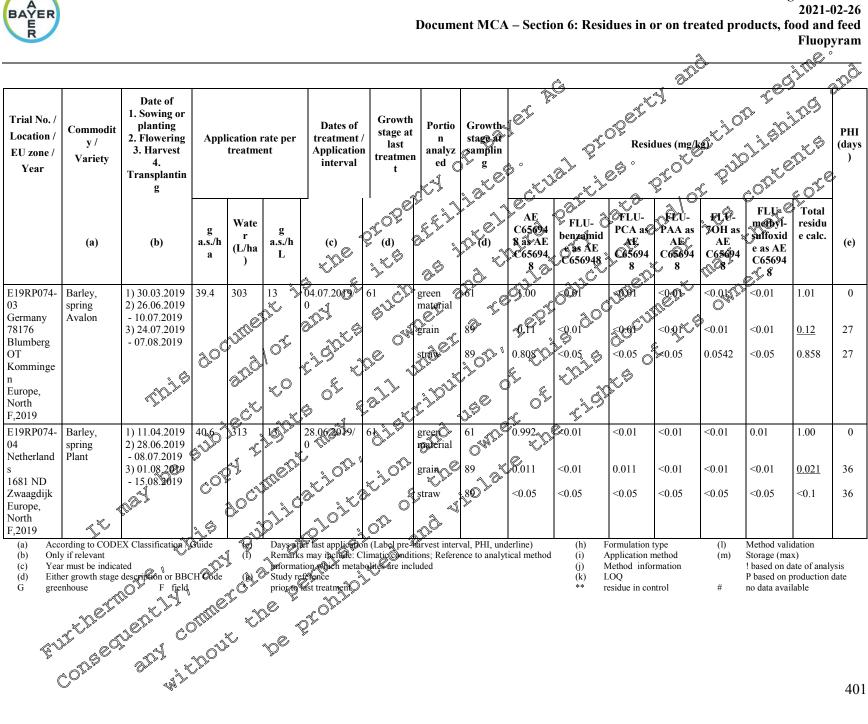


Page 400 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

		nmary of the				<u>575-01-1</u>) st	udy on b	arley		P	Ç	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	4 II	}	~Leo	J. T. C. C.	<u>).</u> Lifor
Trial No. / Location / EU zone / Year	Commodit y / Variety	um of fluopyram- Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplantin g	Appl		rate per	Dates of treatment / Application interval	Growth stage at last treatmen t	n (analyz	Growth stage at sample		Part's	Gr.	lugg fing/k			A ^{ts}	PHI (days)
	(a)	(b)	g a.s./h a	Wate r (L/ha)	g a.s./h L	5 05 05 05 05 05 05 05 05 05 05 05 05 05				AE C65694 8 as AB C65694 C65694 8	e as OF COS6948	PCA as PCA as AE C65694	FLEC PAA as AE C65694	FLU- 7 QfF as	FLU- methyl- sulfoxid Cas AE C65694 8	Total residu e calc.	(e)
E19RP074- 01 Germany 51399 Burscheid Europe, North F,2019	Barley, spring Avalon	1) 01.04.2019 2) 11.06.2019 - 15.06.2019 3) 01.08.2019 - 31.08.2019	38.1	294 C ULD QLD QLD		2000-2019/ 5-1-0-1-5- 5-1-0-5-5-5-5-5-5-5-5-5-5-5-5-5-5-5-5-5-		straw	6% 890 ⁵⁰ ¹ 789	1.00 ~0.00 0.058	<0.010 \$ <0.014 \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	<0.01 <0.01	<0.01 <0.01 <0.05	<0.01 <0.01 0.068	<0.01 <0.01 <0.05	1.12 <u><0.02</u> 0.108	0 57 57
E19RP074- 02 France, north 37270 Athée sur Cher Europe, North	Barley, spring Sebastian	1) 18.02.2019 2) 26.05.2019 - 01.06.2019 3) 05.07.2019 - 15.07.2009	39.5 ×			27.05.2019/ 0 100 100 100 100 100 100 100 100 100 1		green maretuil grain straw	89 89 89 20 5	€9.872 ⊗9.01 0.224	<0.01 <0.01 <0.05	<0.01 <0.01 <0.05	<0.01 <0.01 <0.05	<0.01 <0.01 0.050	<0.01 <0.01 <0.05	0.88 <u><0.02</u> 0.274	0 39 39
F,2019	LET DECC	1) 11.06.2019 - 15.06.2019 3) 01.08.2019 - 31.08.2019 - 31.08.2019 - 31.08.2019 - 31.08.2019 2) 26.05.2019 - 01.06.2019 3) 05.07.2019 - 15.07.2019 - 15.07.2019 - 15.07.2019 - 15.07.2019 - 15.07.2019 - 15.07.2019 - 15.07.2019 - 01.06.2019 - 01.06.2019	June Burne	L V L V L V		er or i or	y CO	2 ² 2	<u> </u>				<u> </u>	<u> </u>			40



Page 401 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram



401



GAP 2 southern zone

Data Point:	KCA 6.3.5/09
Report Author:	
Report Year:	
Report Title:	Determination of the residues of prothioconazole, BYF 00587 and SE C656948 in 8n
-	barley after a spray application of bixafen & fluop ram & prothio conazole EC 260 in
	southern France and Italy
Report No:	E19RP109
Document No:	<u>M-761576-01-1</u>
Guideline(s) followed in	Regulation (EC) No 116/2009 of the European Parliament and of the Council of 21
study:	October 2009 concerning the placing of plant protection products on the market
	OECD Guideline for the Testing of Chemicats on Crop Field Trial (7G 50)
	OECD Guideline for the Testing of Chemicals on Crop Field Trial (7G 509) published in September 2009) US EPA OCSP 860,4500, Crop Field Trial
	US EPA OCSP 860.4500, Crop Field Frial
Deviations from current	published in September 2009) US EPA OCSPP 860.4500, Crop Field Frial
test guideline:	
Previous evaluation:	No, not previously submatted
GLP/Officially recognised	Yes, conducted under GLP/Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes A Q A A A A A A
4	

Materials and Methods

Four supervised residue trials on barley were conducted in southern Europe (in southern France, and Italy) during the 2019 season.

One-spray application was conducted with BIX (LU+PZ EC 260, an EC (emulsifiable concentrate) formulation containing 130 g/L prothioconazole 65 g/L of thropyram and 65 g/L of bixafen. For the purpose of this renewal, only results for fluopyram and its metabolites fluopyram-benzamide, fluopyram-pyridyl-carboxylic-acid, fluopyram-pyridyl-acetic acid) fluopyram-7-hydroxy and fluopyram-methyl sulfoxide with be discussed

The applications were conducted at the BBCH of 39-61 and at the application rates of 0.6 L/ha corresponding to the single application 0.032 kg a state. Water application rates were at 300-350 L/ha.

Samples of barley green material were coffected as BBCH 61 and barley grain and straw at harvest BBCH 89.

Each field sample was placed in doubled tabelled bags and stored deep-frozen within 24 hours after sampling and until dispatch All field samples were shipped deep-frozen (at -18 °C or lower temperatures) under monitored conditions during shipment and arrived in good condition except for the shipment of samples from the trial E19RP109-03 and -04 which were shipped in two shipments at higher average shipment temperatures. Nevertheless, also these samples arrived in good and frozen condition. A short term storage stability study was conducted to show that this deviation has no impact on the stability of the residues (see CA 6.1.1. KCA 6.1/10, M-480441-06-1).



The field samples were stored in a freezer at \leq -18 °C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field samples were shredded and homogenized with dry ice in a cutter. Representative parts of the shredded samples were transferred into polystyrene boxes and stored at \leq -18 °C. For each field sample, one or several examination samples were prepared for analysis and one examination sample was prepared as a reserve sample.

Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-PAA, FLU-7-OH) FLU-7 methyl-sulfoxide), were determined by LC-MS/MS according to method 00984 (2007) 2007, 20

Residues were extracted from 10 g of sample material by two successive extractions using a high-speed blender with a mixture of acetonitrile:water (80.20; 10). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal stondards.

- One dilution was performed under acidic conditions: this extract allower the determination of PLU-PCA and FLU-methyl-sulfoxide
- In parallel, another dilution was performed under basic conditions: this extract allowed the determination of fluopyram, LU-benzamide and FLU-7, OH.

An aliquot of the extracts was injected in LC-MS/MS operated in Efectrospray Ion zation mode:

- One injection in positive electrosoray ionization for the determination of Duopyram, FLUbenzamide and FLU-7-OH.
- Another injection in negative electrospery ionization for the determination of FLU-PCA and FLUmethyl-sulfoxide under different conditions

The linearity was demonstrated in orch analytical batch with a 1/x weighted calibration curve established with at least 5 concentration levels? For each calibration curve the cortelation coefficient R was above 0.99. The quantification was done by internal standardization using isotopically stable labelled internal standards. The Limit of Quantification (LOQ), expressed as fluopyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat straw and 0.01 mg/kg for all other matrices.

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU fegulatory requirements outlined within SANCO/3029/99 rev 4.

Conditions used in this study: The method was used as described in the original method with some minor modifications, which have no impact on the validity of the study:

Residues were extracted from 5 g of sample material of grain and green material and from 2.5 g of straw. Extraction was done with only 20 mL (straw 40 mL) acetonitrile/water (80/20 v/v). The blender is washed with 5 mL acetonitrile/water (80/20 v/v). The blender is washed from 0.01 mg/L to 10 mg/L and the dilution step after filtration was omitted. The adjustment to pH= 8 was done with ammonium chloride/ammonia buffer followed by the dilution with acetonitrile/water (4/1, v/v) to get Extract A. The determination was done from an aliquot of Extract A in the positive ion mode.

The time between the beginning of the sample preparation and the sample analysis did not exceed 24 hours for grain. For green material and straw longer delays were observed. The stability of analytes in extracts of green material and straw of barley were investigated in this study. Extracts were found to be stable for at lease 11 days when stored at < 6°C.

Findings



In order to check the performance of the method, recovery determinations were included in each set of analyses. Control samples from the study were fortified to be used as the recovery samples. All the recovery determinations were performed concurrently to the analyses of control and treated samples from the tudy. The apparent residues in the control sample used for the determination of recoveries were below 30 % of the LOQ. Recoveries were not corrected for apparent residues in the control samples used for these determinations.

The mean recoveries per fortification level were within the acceptable range of 70 % – 110 % and with the RSDs < 20 %. The overall mean concurrent recoveries were also in the accoptable range $\Re^2/0$ % and 1 Ω^2 with the RSD < 20 %.

The storage period of deep-frozen samples intended for the analysis of Quopyram and its metabolites range between 319 and 409 days.

The detailed results obtained for barley samples in northern Europe are summarized in the Table 6.

Conclusion

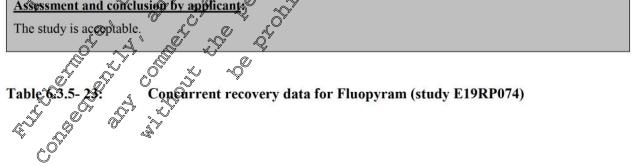
Four supervised residue trials on barley were conducted in portherp Europe with the application of BIX+FLU+PTZ EC 260 at the required rates and according to GLP. Simples of barley were analyzed for the residues of fluopyram and its metabolite fluopyram benzapride. The residus of the trials presented above show the following residues in grain at harvest.

- Fluopyram residues range between <0.01 and 0.02 mg
- •
- Fluopyram-benzamide tesidues were <0.01 mg/kg The total residue of fluopyram (sun) of FI(U + FLU-benzamide expressed as fluopyram) range between <0.02 and 0.022 mg/kg. Fluopyram-pyridyl-carboxylic-acid residues were <0.01 mg/kg Fluopyram-pyridyl-acenc-acid/residues were <0.01 mg/kg •
- .
- .
- Fluopyram-methylsulfoxide residues were <0.01 mg/kg

Residues in straw at harvest

- Fluopyram residues range between <0,85 and 10185 mg/
- Enopyram-ben amide residues were <0.05 mg/kg
- The total residue of Muopyram (som of FUU + FLU-benzamide, expressed as fluopyram) range between <01 and 0.235 mg/kg. \bigcirc
- Fluopyram-pyridyl-carboxylig acid residues were <0.05 mg/kg
- Fluop ram-pyridyl-zoetic-acid residues wore <0.65 mg/kg
- Fluopyram-7-hydroxy residues between \$0.05 and 0.078 mg/kg.
- Foropyram-methylsulforide residues were \$9.05 mg/kg

Assessment and conclusion by applicant

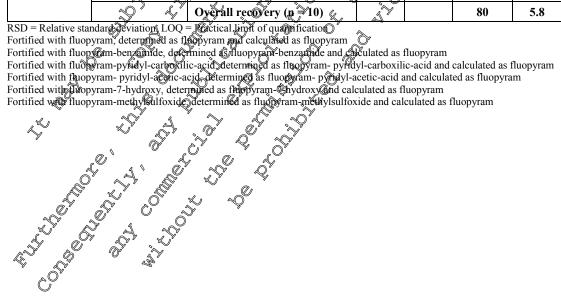




Portion	Fortification	Rec	covery (%	6)			
analysed	level (mg/kg)	Individual recoveries	Min	Max	Mean	RSD	
Fluopyram (AI	E C656948)				4	đ	
	0.01	90; 93; 96; 99; 106	90	106	\$ 97	6.3 0	
Barley / grain	0.4	94; 98; 99; 100; 102	₩ 94	102	99	3.9	
		Overall recovery (n = 10)	<i>•</i>	, ô ^ş	98	@4.8	9° × 4
	0.01	88; 94; 95; 100; 102	88	Â02	° 96 °	5.7 🖓	
Barley / green	0.4	93; 94; 95; 97; 97	93 🔊	97 Ø	95Q	, d ³⁹	
material	2.0	90; 93; 95; 98;401	93 ~ 905°	101	<i>7</i> 9 5 ^	<u>}</u> 4.5 ≪	, <u>, , , , , , , , , , , , , , , , , , </u>
		Overall recovery (n = 15)	ð	ŵ ^	Ø 95 Ø	4.0	× .4
	0.05	78; 79; 79; 80; 81	78 ^	8 81	78 	Ø.4	
Barley / straw	0.4	73; 76; 79; 83; 86	7,200	86	~ ⁹ 9 ×	¢ 6.6	
		Overall recovery (n = 10)		× (× 79 Ø	45	
Fluopyram-b	enzamide				No.	<u>,</u>	Ŷ
	0.01	96; 98 , 9 9; 102, 1 04	8	d94	0 ¹⁰⁰ ć	3.2~	p ·
Barley / grain	0.4	89,991; 92; 93; 93 °	x 89	Q 93	0° 9200	X.8	
	Ô	Overall recovery (n = 10)	, ~		<i>. 0</i> 96	O _{5.2}	
	0.01 📎	92; 92; 92; 94, 101	.92	×101	⁹⁴ 4	₹ 4.1	
Barley / green material	0.4	\$ \$ \$ 89; 90, 94	0 88 &	94	965	2.5	
inatorial		Over all recovery (n ⇒10)	, 0	Ő	ý2´	4.0	
		<i>x</i> 70,∜2; 74, ₹5; 78 <i>x</i> 0	J.	<i>"</i> € 78	ر 74	4.1	
Barley / straw		* * 2 ; 72; 74, 81; 83	~ 72	¢ 83,5	76	6.8	
Ĉ		Overall recovery (n 🗐 0)		a)	75	5.7	
Fluopyram-py	ridyl-carboxilie-aci			K) M			
R.Y.	Q.007 .	مَ [*] الْحَجَّةِ: 82; 89; 90; 1	79	117	91	16.5	
Barley / grain		88; 90 94; 95; 203	887	103	94	5.8	
		$\mathbf{G} \mathbf{v} \mathbf{e} \mathbf{r} \mathbf{a} \mathbf{l} \mathbf{x} \mathbf{e} \mathbf{c} \mathbf{o} \mathbf{v} \mathbf{e} \mathbf{r} \mathbf{y} \mathbf{h} = 10)^{\bigcirc}$	ð		93	11.6	
		89, 100; 100; 102:402	89	102	99	5.5	
Barley / green	0.4	92; 9 ¥, 95; 9 6 × 97	92	97	95	2.2	
		Overall recovery (n = 10			97	4.6	
	Å.05	86; 87; 91; 92; 96	86	96	90	4.5	
Barley / straw	×0.4	₹ <u>0</u> 70: 2 5; 79; 8 ¥, 91	70	91	79	9.9	
		Overall recover (n = 10)			85	9.8	
Fluopyram-py	vidyl-acetic-acid						
	× 0.01	93; 100; 104; 105; 112	93	112	103	6.6	
Barley / grain		95, 98; 98; 100; 101	95	101	98	2.3	
NY K	r 1 ~~	Overall recovery (n = 10)			101	5.4	
Barley / green material	0.01×	99; 101; 101; 102; 103	99	103	101	1.5	
material	0.4	94; 96; 98; 98; 103	94	103	98	3.4	



Portion	Fortification	Rec	covery (%	6)			
analysed	level (mg/kg)	Individual recoveries	Min	Max	Mean	RSD	
		Overall recovery (n = 10)			100	3.0	
	0.05	82; 82; 82; 85; 91	82 78	91	× 84	4.6 O	
Barley / straw	0.4	78; 79; 85; 87; 93	78	93	84		ST ST
		Overall recovery (n = 10)	<i>*</i>	, Ô ^v	84	,Ø5.8 🌋	9° × 4
Fluopyram-7-h	ydroxy	A		Â,		° Q	
	0.01	90; 90; 90; 94; 97	90 🔌	97 Ø	92Q	, ⁶ .5	
Barley / grain	0.4	89; 90; 90; 90, 90, 95	8950	95,7	29 1	2.6 %	× ~~~
		Overall recovery (n = 10)	õ	â s	Ø 92 Ø	3,0	~
	0.01	84; 88; 91; 92; 100	84	♀ 100		6 .5	
Barley / green material	0.4	88; 96; 91; 94; 93	880,	\$G	s ^O í ×	¢ 2.0	
		Overall recovery (n = 10)		× (^م ن 91 ب	45 45	Ő
	0.05	0; 71; 72; 76; 82 ³	^ل 70 م	82~	, De la companya de l		ÊQ
Barley / straw	0.4	69; 75; 73; 79, 88	0 0	, ^Q	0 ⁷⁶ ć	9.9~	¢
		Overall recovery (n = 10)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		°° 75⊖°	8.1	
Fluopyram-me	thyl-sulfoxide 👸		r K		Ś.	0	
	0.01 📎	84; 9f293; 100, 101	84	×1901	⁹⁴ 4	7.4	
Barley / grain	0.4	\$7 92, 92; 93, 94; 96 \$	0 ⁹ 92 &	96	93	1.8	
		Overall recovery (n ⇒10)	,″ 0	Ő	ý94 Í	5.1	
D 1 /		92; % 104; 404; 106 0	. 03 ¹²	_√ 106	ر 100	6.0	
Barley / green material		\$93; 93; 93, 97; 98 \$	≫ ₉₀ €	Ø 98, S	94	3.5	
Å	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Overall recovery (n \$10)		a,	97	5.8	
	0.05 × 0	× 75 77; 80; 88 °	@ ₁ 75	88	80	6.2	
Barley /straw	Q.C	\$5; 76; 82; 85; 8 5	75	85	81	6.0	
	<u></u>	Overall rec@ery (p ≠10) &	, AN		80	5.8	





Page 407 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No. / Location / EU zone / Year	Commodit y / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplantin g		cation ra treatmer		Dates of treatment / Application interval	Growth stage at last treatmen t	Portion analyze	Growth Stage at samplin		Parting	OP C ^P Resid	iues Ang/k	(g) 2 ⁰¹⁴ 5 1, 5	20 ² 20 ² 20 ²	sint of fore	PHI (days)
	(a)	(b)	g a.s./h a	Wate r (L/ha)		E OF				C65694	OFLU-	PCA as AE		FLU- 70ff as	FLU- methyl- sulfoxid E as AE C65694 8	Total residu e calc.	(e)
E19RP109 -01 France, south 31330 ST Caprais Europe, South F, 2019	Barley Irina	1) 20.02.2019 2) 25.05.2019 - 05.06.2019 3) 10.07.2019 - 25.07.2019	37.7	OTHE OTHE	10 ² ×0	T' O'L' X	10°	straw J	J.S ^e	0.785 0.012 00185		<0.020 20		<0.01 <0.01 0.078	<0.01 <0.01 <0.05	0.794 <u>0.022</u> 0.235	0 46 46
E19RP109 -02 France, south 13103 St Etienne du Gres Europe, South F, 2019	Barley Rafaela	1) 24.10.2018 2) 15.04.2019 - 25.04.2019 3) 17.06 2009 - 30.06.2019		200 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		15.04 2019/ 0 2 t 2 0 t 4 2 t 2 0 t 4 2 t 2 0 t 4 5 t 2 0 t 4 5 t	* ¹ 0 ²⁰		61 389 380 20 20 20 20 20 20 20 20 20 20 20 20 20	0.573 0.01 0.0913	<0.01 <0.01 <0.05	<0.01 <0.01 <0.05	<0.01 <0.01 <0.05	<0.01 <0.01 0.068	<0.01 <0.01 <0.05	0.583 <u><0.02</u> 0.141	0 64 64
Ē,	urt her consec	DOTE V DOTE V DETT C DETT C	DIALO		2 ⁰ 0 2 ⁰ 0 2 ⁰ 0	er dillo	J.C.										40



Page 408 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

														<u>}</u>			
											Ĉa		OID!		Ő	J. Lu.	a DO
Trial No. / Location / EU zone / Year	Commodit y / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplantin g		cation ra treatme		Dates of treatment / Application interval	Growth stage at last treatmen t	Portion analyze d	Growth stage of samplin g		NOT OF	OP Resid	۲) dues (mg/J	P ^{til}	COLLEC	FOIL C	PHI (days)
	(a)	(b)	g a.s./h a	Wate r (L/ha)	g a.s./h L	(c) * ² ²⁰	S ^C (d)			C65694 8 ás AE C65694 8 Ø	FLU- benzamid Oas AE C656948	ØFLU- PCA as	PAA as AE(.	FL P- TOH as AE C65694	FLU methyl- suffoxid e as AE C65694 8	Total residu e calc.	(e)
E19RP109 -03 Italy 44123	Barley Sidney	1) 25.02.2019 2) 06.05.2019 - 16.05.2019 3) 17.06.2019	39.2	353	11.1) D	14.05.2019	GUL	green material grain	890 890	0965 ~09	<0.01 ⁰	Stor J	<0.01 <0.01 ×	<0.015 0 <0.01	<0.01	0.975 <0.02	0 50
Boara Ferrara Europe, South F, 2019		· ·	9.0°		10*	TI OLI			89 2000 1	<0.05 °C 5	-0.05 G	<0.05 <0.05	×0.05	0.065	<0.05	<0.1	50
	Barley Pandora	1) 03.11.2018 2) 01.05.2019 - 15.05.2019	40	308,*C	13	05.2019/8 005.2019/8	69. J. St.	freen material	SE	1.10	<0.01) ©	<0.01	<0.01	<0.01	0.01	1.15	0
76014 Spinazzola		3) 01.06.2019 - 30.06.2019	GUD	_ ~\$		Thomas	O.	ggun	88 Wy. m.	<0.0%	<0.01	< 0.01	< 0.01	< 0.01	< 0.01	<u><0.02</u>	57
Europe, South F, 2019		90°	co		ALL CL	at 10st	D.C. J. O.S.	straw	89	~0.05	< 0.05	<0.05	<0.05	<0.05	<0.05	<0.1	57
(a) Ac (b) On (c) Ye (d) Eit G gre	cording to COD ly if relevant ar must be indic her growth stage eenhouse	Classification / ated e description or BR F field	Guide		Days Remark Inform Study a prior	fler last applicati ks max iQude: (ation) which meta elemence flast treatment	on (Label fue Climate cond both are in	harvest inter itions Reference clures	vál, PHI, un ence to analy	derline) tical method	(h) (i) (j) (k) **	Formulation Application I Method info LOQ residue in co	method rmation	(m)	Method vali Storage (ma ! based on d P based on p no data avai	x) ate of analy production	
Ę	Jut Der	1) 03.17.2018 2) 01.05.2019 - 15.05.2019 3) 01.06.2019 - 30.06.2019 - 30.06.2019			ve ve	er origin) ×										408
		v															404



Based on the residue definition for risk assessment, the sum of fluopyram and fluopyram-benzarade expressed as fluopyram, the total residues for barley are summarized in the Table 6.3.5-25

	Commodity	Region/Indoor (a)	Trial results relevant to the oritical	STMR HR (b) (c) (c)
		NEU	(10, 10, 10, 10, 10, 10, 10, 10, 10, 10,	(b) (c)
	Grain	SEU	3x<0.02,002 5x<0.02,002	0.02 0.02
Barley		NEU/SEU	5x<0.02 x0.02 0.12	0.02 0.02
Daney		NEU		0.149 49.86
	Straw	SEU 🔊	\$\$\$<0.1,\$\$14,0.2\$	0.12 0.24 °
		NEU/SEC	3x<0, 0.11, 0.14, 0.27, 0.86 ≪	0.125 0.86
HR: Highest res	Dixon's test the l	highest value of f	5 ₃ <0.02 2x0.02 0.12 0 0.1x0.11, 0.27, 0.86 2x<0.1, 0.14, 0.24 3x<0.1, 0.14, 0.24 3x<0.1, 0.14, 0.24 0 0.15 0 0.14, 0.27 0.86 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	The outlier.
			J.	

Summary of fluopyram total residue data for barley trials supporting GAP 2 Table 6.3.5- 25:



CA 6.3.7 Lettuce

Information on the intended use pattern (GAP) is summarised in Table 6.3.6-1.

Table 6.3.6-1: Use patterns (critical GAP) for the spray application of Fluxpyram in/on lettuce in European greenhouses

Formulation	F/ GH	No. of appl.	Growth stage at application (BBCH Code) Application rate per treatment (g a.s./ha) Code) Water (L/Ka) Code) Code
FLU+TFS SC500	GH	2	

 GH : greenhouse

Residue trials to support GAP were conducted in green ouse in Europe at a similar AP.

Table 6.3.6- 2:	Overview of European res	sidae trials con	deleted in green	bouse with lettuce per
	vegetation period	O A O		

		8		'¥	~ '0'	L	<i>S</i>	° ~	× «,	
Crop	Region	Vegeta	independent/ floin period 2014 2018	A 18/	Report N	ρ. 	Formulat	ion ²	O ⁷ © Document number	Reference
Lettuce	GH	54	3 3 3 4 4 5 4 5 4 5 4 5 4 5 4 5 4 5 4 5	, P	RA\$620/ 14-2026 18-20#8		FLU+TFS S	\$C500	M-308622-01-1 M-534623-01-1 M-675904-01-1	KCA 6.3.6/01 KCA 6.3.6/02 KCA 6.3.6/03
GH : greenh	, ⁿ Ç			\$ \$ \$						
Data Poin	it:	Ĵ,	€CA 6,3,6/0	l Oy	x, × «		Ý			
Report Au	uthor: 👸	2 1			r O'					
Report Ye	ear: 🦲	"Q"	200							
Report Ti		Ô	Determinatio	n of the	e residues of	F & C 65	6948 and tri	floxystro	bin in/on head lettu	ce
Report N	j. j.	\$	and lettice at in Germany RA 2620/07	ter spr	avian of AB	C65694	8 & CGA279	9202 (500	SC) in the greenho	buse
		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	A - 308622-0		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~					
Documen				- <i>//</i>	1001 7	020/3/1/0	5 mars 5 (100	7 07 22)		
	(s) Ionow		91/414/EEC	w Jury	$0^{1991}$	029/ V1/9	5 IEV. 5 (199	7-07-22)		
study: Deviation	a francisco ano		pone		~					
test guide			wone V	$\sim$						
			* 	l and a	a a a m t a d					
Previous	evaluation		yes, evaluate Yes, conduct	∦ and a	ccepted					
GLPOffi	cial reco	gmised (	Yes, conduct	ed und	er GLP/Offi	cially rec	ognised test	ing facilit	ies	
testing fac	ainties:	di si	~							
Acceptab	Mity/Relia	bility.	Yes							
ĉ,										

Ô



#### **Materials and Methods**

Four supervised residue trials on lettuce were conducted in greenhouse (in southern France, the Netherland and Germany) during the 2007 season.

Two-spray applications were conducted with FLU+TFS SC590, a SC (soluble concentrate) formalation containing 250 g/L of fluopyram and 250 g/L of trifloxystrobit. For the purgose of this renewal, only results for fluopyram and its metabolite fluopyram-benzamide will be discussed.

The applications were conducted at the BBCH of 41 to 49 and an the application rates of corresponding to the single application 0.20 kg a.s./bg/Water application rates were at 300-1000 L/ha

Samples of lettuce (head) were collected at BBC 45 to  $49^{\circ}(51)$ 

Each field sample was placed in doubled labered bags and stored deep bozen within 24 hours after sampling and until dispatch. All field samples were shipped deep-frozen (at -18 °C or lower temperatures) under monitored conditions during shipment and arrived in good condition. Č

The field samples were stored in a freezep at  $\leq$ - $48^{\circ}$ C uptil preparation of the examination samples. For the preparation of examination samples, the deep frozen field samples were shredded and homogenized with dry ice in a cutter. Representative parts of the shredded samples were transferred into polystyrene boxes and stored at  $\leq$ -18°C. For each field sample, one of several examination samples were prepared for analysis and one examination sample was prepared as a reserve sample. Å

Residues of fluopyram and its metabolites were determined by LC-MS/MS according to method , 2007, M-297145, 1, see MCA section 4.1, 2 Full details and acceptable 00984/M001 ( validation data to support this method are presented within document M-CA4, which comply with the EU regulatory requirements outlined within SA&CO/3029/9% tev 4.

Residues were extracted from 10 g of sample material by two successive extractions using a high speed blender with a solution of acetonitrile water (\$9:20; *v).

Subsequently, the raw extracts were diluted 10-ford by adding internal standard solutions:

Ope dilution performer Quinder reidic conditions (for determination of fluopyram-PCA)

 $\sim$ 

Another dilution performed under basicOconditions (Or determination of fluopyram, FLUbenzamide and FLO-PAA 1

Residues were quantified by reversed phase chromatography coupled with tandem mass spectrometry (MS/MS) with electrospray winisation. One injection in positive electrospray ionisation allowed the determination of flugpyrand FLU-benzamide and FLU-PAA. Another injection in negative electrospray ionisation allowed the determination of BLU-BCA under different conditions.

For analysis fast LC-conditions were used (0.4 to 0.8 mL on a 2 mm i.d., column with 2.5 µm material). Differing to the original method the following transitions were used: Ĩ Q.

	ÇŪ'	× ,O'	
compound ⁴	mode	QD mass [m/z]	Q3-mass [m/z]
FLU-bergamide MRM	ESI-pos	Ø 190	170
FLU-bonzamide IST	55I-pos	196	136
FLK PAAMRMA	ESI-pos	240	212
FGU-PAG ISTR	ESI-pos	244	197
FLU-REA MRM 1 🔌	ESI-neg	224	198
- A			



The quantitation was carried out by internal standardization using internal stable labelled standards. The Limit of Quantitation (LOQ, calculated and expressed as fluopyram parent equivalents for fluopyram and its metabolites), defined as the lowest validated fortification level, was 0.01 mg/kg in all matrices for all analytes. All residues are calculated as parent fluopyram.

The quantification was done by internal standardization using isotopically stable labelled internal standards.

#### Findings

In order to check the performance of the method, recovery determinations were included in each set of analyses. Control samples from the study were fortified to be used as the recovery samples. About recovery of determinations were performed concurrently to the analyses of control and treated samples from the study. The apparent residues in the control sample were below the LQQ. Recoveries were not corrected for apparent residues in the control samples used for these determinations.

The mean recoveries per fortification level were within the acceptable range of 70 % -110 % and with the RSDs < 20 %. The overall mean concurrent recoveries were also in the acceptable range of 70 % and 110 %, with the RSD < 20 %.

The storage period of deep-frozen samples interded for the analysis of Duopyram and its metabolites anged between 419 and 520 days.

The detailed results obtained for lettice samples in greenhouse are summarized in the Table 6.9.6-3

#### Conclusion

Four supervised residue trials on lettuce were conducted in greenhouse with the application of FLU+TFS SC500 at the required rates and according to GLP. Samples of lettuce were enalyzed for the residues of fluopyram and its metabolite fluopyram-benzamide, fluopyram pyridyl-acetic acid and fluopyram-pyridyl-carboxylic-acid. The results of the trials presented above show the following residues in lettuce (head) at harvest following a pre harvest interval (PLP) of 7 days.

- Fluopyrand Vesidues range between 0.23 and 2. Omg/kg
- Fluopyrun-benetimide range between <0.01/and 0.02 mg/kg
- Fluopyram-P&A and Fluopyram-P&A were <0.00mg/kg
- The total residue of fluopyram (sum of FLU FLU-benzaroude, expressed as fluopyram) range forween 0.24 and 2.1 for kg.

#### Assessment and conclusion by applicant;

The study is acceptable Q	
The study is acceptable $\bigcirc$	~
	A.

Portion	Fortification		ecovery (			
analysed	level (mg(kg)	, recoveries	Min	Max	Mean	RSD
Fluopyram (A	C656248)					
Ő	₹ 0.01	80 (69; 91; 83	69	91	81	11.3
Lettuce head	Ô ^S 1.0	71; 71; 76; 72; 72	71	76	72	2.9
Lettuces nead	\$.0 \$	77; 78	77	78	78	<u></u>
6 ⁵⁴ 60	\$1.0 \$ 0 0	Overall recovery (n= 12)			76	8.5
	enzamide(AEF14	(8815)	÷			

# Table 6.35 3: Concurrent recovery that for Flugpyram (study RA-2620/07)



Portion Fortification	Re	ecovery (	%)		
analysed level (mg/kg)	Individual recoveries	Min	Max	Mean	<b>RSD</b> 5.4 3.4 4.1 2 0 1.1
0.01	77; 75; 75; 68	68	77	74 0	5.4
Lettuce / head 1.0	70; 74; 77; 74; 73	70	77	73 ×	3.4 、
	Overall recovery (n= 12)	- CÔ		6,74	4.1
Fluopyram-pyridyl-acetic-acid	I (BCS-AA10139)	d,	(	ŝ.	.0
0.01	66; 84; 79; 85	Ø 66	85	79	ð1.1
Lettuce / head 1.0	69; 75; 75; 75; 78	69	~78	<i>2</i> 74 (	4.4
	Overall recovery (n₹12)	<i>≥</i> °		× 76	.8.2
Fluopyram-pyridyl-carboxilic	-acid (AE C657188)	<u>y</u> j			S.
0.01	79; 63; 47		Q.	073	°° 11.95
Lettuce / head 1.0	73; 77, 77; 7,3	73	م <u>77 م</u>	750	3.1
	Overall recovery (n = 12)			ĨĂ	\$7.3
Portion analysed Fortification level (mg/kg) Lettuce / head 1.0 Fluopyram-pyridyl-acetic-acid 0.01 Lettuce / head 1.0 Fluopyram-pyridyl-carboxilic Fluopyram-pyridyl-carboxilic SD = Relative standard deviation, Tinal determination as: fLU-PAA Residu Tinal determinat	73; 77, 77; 73 <b>Overall recovery u = 12</b> es calculated as: fluopyram esidues calculated as: fluopyram is calculated as: fluopyra				



Page 414 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No. / Location / EU zone / Year	Commod ity / Variety	ram+FLU-benzamic Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Appl	ication ra treatmer	1	Dates of treatment / Application interval	Growth stage at Olast treatment	Portion analyzed	Growto stage at	y ^{oper}	N Did Resid		j Glain g) Clain	, ^s	PH (da )
	(a)	(b)	g a.s./ha	Water (L/ha)	a.s./hQ	COPE'S S		1)e 1)e	P(d)		GELU- benzamide as AE C656948	FLU- PCA & as AE	FLU-	Total residues calc	(e
2007 0266/3(0266-07) ermany 42799 Leichlingen fordrhein-Westfalen) urope, North 2007	Lettuce, head Alexandr ia	1) 10.02.2007 3) 03.04.2007 - 15.04.2007	200.0 200.0 ½	600 ×	33.25 33.85 33.85	20.03.20070 27.03.2007/7 3 ^{1,0}	45 0. 0100 1	head 1 e 2 c 2 c 2 c 2	45 45 47 49 49 49 6 99	1.5 5.8 0.73 0.73 080		<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<pre>&lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01</pre>	$ \begin{array}{r} 1.51 \\ 5.81 \\ 4.71 \\ \underline{2.11} \\ 0.74 \\ 0.52 \end{array} $	14 2
2007 0642/1(0642-07) etherlands L-1693 NR ervershoof urope, North 2007	Lettuce Lolo Rosso	1) 17.043007 3) 1408.2007 31.05.2007	¥0000 >200.0 ×,0	1000 1000	20.00 20.00 \$ \$ \$	91.05.2007 08.05.2007 08.05.2007	J ^{L'ÌO}	0×	47 47 47 49 49 49 49 49	0.81 5.5 1.2 0.92 0.44 0.24	0.02 0.02 0.02 0.02 0.02 0.01 0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	0.83 5.52 1.22 <u>0.94</u> 0.45 0.25	1
2007 0644/8(0644-07) ance, south 86380 Ouzilly (Poitou- narentes) prope, South 2007	Lettuce, head Santoro	1) 16.04.2007 3) 21.052007 - 0206.2007	20000 20000		33.25 33.25 0 ¹⁰	00.05.2007/0 06.05.2007/5 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1)21 )45 ) ¹⁰ , 0) ¹⁰	Bead K	45 45 47 49 49 51	0.39 3.4 2.3 1.4 0.37 0.07	<0.01 <0.01 0.01 0.02 0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	$\begin{array}{c} 0.40 \\ 3.41 \\ 2.31 \\ \underline{1.42} \\ 0.38 \\ 0.08 \end{array}$	
2007 0645/6(0645-07) rmany 88074 Meckenberren aden-Württemberg) rope, North 2007	Alexandr ia; Butterhea d	1) 30.01.2007 1) 09.03.2007 3) 120 9.2007 0.05.2007			\$\$ ¹	18.002007/0 \$.04.2007 0 0 0	41	head	45 45 45 47 49 49	0.69 3.5 0.63 0.23 0.19 0.07	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	$\begin{array}{c} 0.70 \\ 3.51 \\ 0.64 \\ \underline{0.24} \\ 0.20 \\ 0.08 \end{array}$	1
2007 a) According to CODE b) Only if relevant c) Year must be indica d) Either growth stage G greenhouse	ted description or F	ion / Guide (e) BBCH (b) field *	Days a Remu Ofform Study prior t	ks may in ation wh	clude. Clim I metaboli	Label pre-harvest i natic conditions; Re tes are included			(h) (i) (j) (k) **	Formulation Application Method info LOQ residue in co	rmation	(m) Sto ! b P	ethod validati orage (max) oased on date based on prod data availabl	of analysis luction date	



Data Point:	KCA 6.3.6/02
Report Author:	
Report Year:	2015
Report Title:	Determination of the residues of fluopyram and trifloxystrobin in/on lettore after spray application of fluopyram & trifloxystrobin SC 500 in the greenhouse in Germany, the Netherlands, Belgium and France
Report No:	14-2028
Document No:	<u>M-534623-01-1</u>
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guideline for the Festing of Chemicals on Crop Field Trait (TG 509 published in September 2009) US EPA OCSPP Guideline too. 860@500 on Crop Field Trial
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted a strain of the
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised esting facilities
Acceptability/Reliability:	Yest of the transformed of the t

Materials and Methods Six supervised residue trials on lettuce were conducted in greenhouse (France, the Netherlands, Belgium and Germany) during the 2014 season Ø

Two-spray applications were conducted with FLU+TES SC509, a SC (soluble concentrate) formulation containing 250 g/L of flugpyram and 250 g/L of rifloxy strobig. For the purpose of this renewal, only results for fluopyram and its metaboline fluopyram-benzamide will be discussed.

The applications were conducted at the BBCH of \$9-48 and at the application rates of 0.8 L/ha corresponding to the single application 0.20 kg/a.s./ha.Water application rates were at 300 - 1000 L/ha.

Samples were collect in a manner designed to obtain representative samples. Samples of lettuce (head) were collected at BBCH 4500 49.

Each field sample was placed in doubled labelled bags and stored deep-frozen within 24 hours after sampling and until dispatch. All field samples were shipped deep-frozen (at -18 °C or lower temperatures) under monitored conditions during shipment and arrived in good condition.

The field samples were stored in a freezer at 28 °C until preparation of the examination samples. For the preparation of examination samples the deep-frozen field samples were shredded and homogenized with dry ice in a Onter Representative parts of the shredded samples were transferred into polystyrene boxes and stored  $\mathfrak{A} \leq -1 \mathfrak{C}$ . For each field sample, one or several examination samples were prepared for analysis and one examination sample was prepared as a reserve sample.

Sample's were analysed according to the analytical method 00984/M003 (Methods), 2015, M-467323-03-1, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within Socument M-CA 4, which comply with the EU regulatory requirements outlined within SANCØ/3029/99 rev 4.



Residues were extracted from 5 g of sample material by extraction using a shaker (15 min) with a mixtare of acetonitrile:water (4:1, v.v). After filtration the extracts of the solutions were made up to volume. The solutions were centrifuged, and the extract volume was adjusted. The extracts were diluted by adding the " internal standard. An aliquot of the extracts was injected into a HPLC-(MS/MS).

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established with at least 5 concentration levels.

The quantification was done by internal standardization using stoppically stable labelled internal standards The Limit of Quantification (LOQ), expressed as fluopyrum, defined a the lowest validated Portification level, was 0.01 mg/kg.

All final extracts were analysed within 20 days after extraction. Fluepyramend fluepyrame benzamide were found to be stable in extracts of matrices of plant origin for at least four weeks a 04 ± 3% which was usted N. within the validation of method 00984/M003.

#### Findings

Conclusion

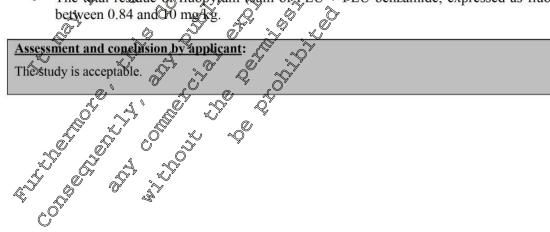
In order to check the performance of the method, recovery determinations were included in each set of analyses. Control samples from the study were tortified to be used as the recovery samples will the recovery determinations were performed concarrently to the analyses of control and treated samples from the study. The apparent residues in the control sample used for recovery experiments were below 30% of the LOQ. Recoveries were not corrected for apparent residues in the control samples used for these determinations. The mean recoveries per fortification level were within the acceptable range of 70 % - 10 % except for fluopyram (114% at LOQ level) and with the RSI < 20 %. The overall mean concurrent recoveries were also in the acceptable range of 700% and 110 % with the RSD 20 %

The storage period of deep-frozen samples intended for the analysis of fluopyram and its metabolites ranged between 127 and 369 days.

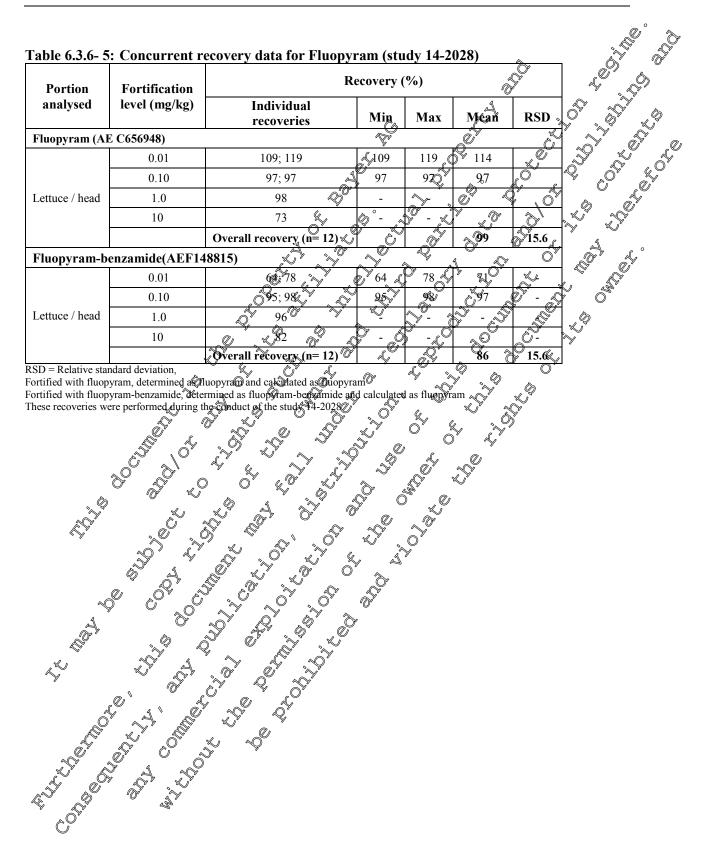
between 127 and 369 days. The detailed results brained for terrice complex in greenhouse are summarized in the Table 6.3.6-6

C Four supervised residue trials on bettuce were conducted in greenhous@with the application of FLU+TFS SC500 at the required rates and according to OLP. Samples of lettice were analyzed for the residues of fluopyram and its met bolite Duopyram-benzamide. The sesuits of the trials presented above show the following residues indettuce (head) at har ost following a pre harvest interval (PHI) of 7 days.

- Fluopyran residues range between 0.85 and 10 mg/kg
- Fluopyram-bergamide range between <0.01 and 0.08 mg/kg
- The total residue of fluopy am (sum of PU + PLU-benzamide, expressed as fluopyram) range between 0.84 and 00 mg/kg.







BAYER

Page 418 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Commodity / Variety	1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Applicati	on rate per	treatment	Dates of treatment / Application interval	Growth Stope at last treatment	Portion Vanalyzer	Growth Stage at sampling	50 ^{5,6} Ri	Rdues (mg/)	er er	PHI (days
(a)	(b)	g a.s./ha	Water (Lahar	g a.s./aL	(Å) D ^T		AL AL	Noted)	@s [*] AE C656948	FLO benzamide as AE C656948 •	Total residues calc.	(e)
ollo bionda loose leaf rariety)	gocuttu	200			21.03.2013/0 28.03.2014/7	- J		UL 47 48, UL 49	2.5 ***	0.014 0.014 <0.01 0.011 <0.01	$     \begin{array}{r}       1.61 \\       5.81 \\       2.51 \\       \underline{1.61} \\       0.85     \end{array} $	0* 0 3 <u>7</u> 14
atine; Lolla Rosso, loose leaf ariety)	×C				13052014/7 2 J.S.C.	e S	e to	67	2.0 12 4.8 3.6 1.1	0.015 0.039 0.027 0.028 0.011	2.015 12.039 4.827 <u>3.628</u> 1.111	0* 0 3 <u>7</u> 14
ettuce ansula Daklou ariety; toose leaf ariety)	P) 08.04.2004 3) 10.052014 - 05.06.2014				23042014/0 02.05.2014 02.05.2014	<b>4</b> 5	head	45 45 46 47 49	0.42 5.3 1.5 0.83 0.47	<0.01 0.014 <0.01 <0.01 <0.01	0.43 5.314 1.51 <u>0.84</u> 0.48	$ \begin{array}{c} 0^*\\ 0\\ 3\\ \underline{7}\\ 14 \end{array} $
	(a) ettuce ugano; ollo bionda oose leaf ariety) ettuce atine; Lolla oose leaf ariety)	Variety       2. Flowering 3. Harvest         Variety       2. Flowering 3. Harvest         (a)       (b)         ettuce ugano; ollo bionda oose leaf ariety)       1) 05.02.2014 3) 01.04.2014         ettuce ugano; oose leaf ariety)       1) 05.02.2014 (- 15.04.2014)         b) 15205.2014 (- 23.06.2014)       1000000000000000000000000000000000000	Variety       2. Flowering 3. Harvest 4. Transplanting       Application         (a)       (b)       g a.s./ha         (a)       (b)       g a.s./ha         ettuce ugano; ollo bionda oose leaf ariety)       1) 05.02.2014 3) 01.04.2014 - 15.04.2014       200 200 200 200         ettuce ugano; oose leaf ariety)       1) 65.02.2014 - 15.04.2014       200 200 200         ettuce atine; Loller oose leaf ariety)       1, 15.04.2014 - 23.06.2014       200 200	Variety     2. Flowering 3. Harvest 4. Transplanting     Application rate per       (a)     (b)     g a.s./ha     Water (L/har)       (a)     (b)     g a.s./ha     Water (L/har)       ettuce ugano; ollo bionda oose leaf ariety)     1) 05.02.2014 3) 01.04.2014 - 15.04.2014     200 200 300 200 200 200 200 200 200 200	Variety       2. Flowering 3. Harvest 4. Transplanting       Application rate per treatment         (a)       (b)       g a.s./ha       Water (L/har)       g a.s./ha         ettuce ugano; ollo bionda oose leaf ariety)       1) 05.02.2014 3) 01.04.2014 - 15.04.2014       200 200 300 200       300 300 300       66.7 66.7 4         ettuce ugano; ollo bionda oose leaf ariety)       1) 1905.2014 200       200 200       1000 200       20 20         ettuce atine; Lollor oose leaf ariety)       1905.2014 - 23.06.2014       200 200       1000 200       20 20	(a)       (b)       g a.s./ha       Water (Long)       g a.s./hL       Go (c)         ettuce ugano; ollo bionda oose leaf ariety)       1) 05.02.2014 3) 01.04.2014 - 15.04.2014       200 200 - 15.04.2014       300 300 66.7 - 15.04.2014       300 66.7 - 15.04.2014       300 28.03.2014/7 - 15.04.2014         ettuce ariety)       b) 1505.2014 - 23.06.2014       200 200 - 23.06.2014       1000 200 - 23.06.2014       200 200 - 23.06.2014       1000 200 - 200 - 23.06.2014       200 200 - 200 -	(a)       (b)       g a.s./ha       Water ( $l_{a}/h_{a}$ )       g a.s./hL       (c)       (c)	(a)       (b)       g a.s./ha       (la/ha)       g a.s./hl       (c)       (c)<	(a) (b) $g a.s./ha$ $(a b.ha)$ $g a.s./ha$ $(a b.ha)$ $g a.s./ha$ $(b b.ha)$ $g a.s./ha$ $(b b.ha)$	(a) (b) $g a.s./ha$ (c) $g a.$	(a)       (b)       g a.s./ha       (b)       g a.s./ha       (b)       g a.s./ha       (b)       g a.s./ha       (c)       (c)	



Page 419 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

											Fluop	y1 am
						4	, Ĝ	×A	S.L.S.	~C [@]	gi me	O.L.O
Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Applicati	on rate per	• treatment	Dates of treatment / Application interval	Growth	Dortion	Growth stage at sampling	C C C C C C C C C C C C C C C C C C C	i Or sidues (ng/k		PHI (days
(a)	(b)	g a.s./ha	Water (L/ha)	g.a.g./mL			2art		Buopyram as AE C656948	FEU- Benzamide as AE C656948	Fotal residues calc.	(e)
	1) 12.05.2014 3) 09.06.2014 - 16.06.2014		800 De 809 De 809 De	25 + 9 25 + 9 6 1 - 0 h	26.05.2014/0 00.0014/3	109 109 101 101		42 42 42 42 49 49 49 49 49 49 49 0 0 0	1.2 7.6 5.5 0.94 0.17	<pre>&lt;0.01 0.030 0.030 0.010 0.010 &lt;0.011</pre>	1.21 7.63 5.516 <u>0.95</u> 0.18	0* 0 3 <u>7</u> 14
Lettuce Korentina; (loose leaf variety)	1) 17.09 2010 3) 15.11 0014 ; 0012.2014		5005 3000 5 0 5 0 5 5 5 5 5 5 5 5 5 5 5		000 82014/0 00.11.2014/0 1000 0 1000 0 100000000	46 57 05 05	Arad - Did -	46 46 47 49 49	6.0 13 12 10 7.1	<0.01 0.025 0.014 0.013 <0.01	6.01 13.025 12.014 <u>10.013</u> 7.11	0* 0 3 <u>7</u> 14
vorioty: A				* /	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		head	48 48 49 49 49 49	1.1 5.7 5.4 3.9 0.85	<0.01 0.017 0.011 0.010 <0.01	1.11 5.717 5.411 <u>3.91</u> 0.86	$ \begin{array}{c} 0^*\\ 0\\ 3\\ \frac{7}{14} \end{array} $
CODEX Classifi ant	ation / Guiden J (e) (a) (c) (c) (c) (c) (c) (c) (c) (c) (c) (c	Qays after Remarks u informatic Study refe prior to la	las applicat any include: on which pecti- crener (treatment	ion (1 & Pre-h Climatic conditi abolites are inclu	arvest interval, PHI ons; Reference to an uded	, underline) nalytical metho	(h) (i) (j) (k) **	Application method information	hod (	(m) Storage ( ! based o P based o	max) n date of ana on production	
	/ Variety (a) Lettuce Parinice; oak leaf variety (loose leaf variety) Lettuce Korentina; (loose leaf variety)	Commodity / Variety1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting(a)(b)(a)(b)Lettuce Parinice; oak leaf variety (loose leaf variety)1) 12.05.2014 3) 09.06.2014 - 16.06.2014Lettuce Korentina; (loose leaf variety)1) 17.09.2014 3) 15.11 0014 ; 0012.2014 (Discut 1) 17.09.2014 (Discut 1) 11.09.2014 (Discut 1) 11.09.2014 (Discut 1) 11.09.2014 (Discut 1) 11.09.2014 (Discut 1) 11.09.2014 (Discut 1) 11.2014 (Discut 1) 11.2014 (Discut 1) 11.2014 (Discut 1) 11.2014	Commodity / Variety       1. Sowing or planting 2. Flowering 3. Harvest       Applicati         Variety       10 (b)       g a.s./ha         (a)       (b)       g a.s./ha         (a)       (b)       g a.s./ha         Lettuce Parinice; oak leaf variety (loose leaf variety)       1) 12.05.2014 - 16.06.2014       200 200         Lettuce Korentina; (loose leaf variety)       1) 17.09.2014 - 0012.2014       200 - 000         Lettuce Korentina; (loose leaf variety)       1) 17.09.2014 - 0012.2014       200 - 000         Lettuce Korentina; (loose leaf variety)       1) 11.09.2014 - 0.012.2014       200 - 0.00         Lettuce Kimpala; oakleaf       1) 11.09.2014 - 0.01.12.000       200 - 0.01.02014 - 0.01.12.000	Commodity / Variety1. Sowing or planting 2. Flowering 3. Harvest 4. TransplantingApplication rate per(a)(b)g a.s./haWater (L/ha)(a)(b)g a.s./haWater (L/ha)Lettuce Parinice; oak leaf variety (loose leaf variety)1) 12.05.2014 - 16.06.2014200 200800 800 - 16.06.2014Lettuce Korentina; (loose leaf variety)1) 17.09.200 - 10.12.0014 - 0.012.2014200 - 600 - 0.012.2014600 - 600 - 0.012.2014Lettuce Korentina; (loose leaf variety)1) 11.09.2014 - 0.012.2014 - 0.012.2014200 - 600 - 0.012.2014600 - 600 - 0.012.2014Lettuce korentina; (loose leaf variety)1) 11.09.2014 - 0.012.2014 - 0.012.2014200 - 600 - 0.012.2014Lettuce korentina; (loose leaf variety)1) 11.09.2014 - 0.012.2014 -	Commodity / Variety1. Sowing or planting 2. Flowering 3. Harvest 4. TransplantingApplication rate per treatment(a)(b)g a.s./haWater (L/ha)g a.s./haWater (L/ha)(a)(b)g a.s./haWater (L/ha)g a.s./hag a.s./haLettuce Parinice; oak leaf variety (loose leaf variety)1) 12.05.2014 - 16.06.2014200 200800 for 25 to 100025 to 1000 25 to 1000Lettuce Korentina; (loose leaf variety)1) 17.09.2014 - 16.06.2014200 - 000 - 000600 for - 00033 - 000Lettuce Korentina; (loose leaf variety)1) 17.09.2014 - 0012.2014200 - 000 - 000600 for - 00033 - 000Lettuce Korentina; (loose leaf variety)1) 11.09.2014 - 0012.2014200 - 000 - 000600 for - 00033 - 000Lettuce Kimpala; oakleaf variety1) 11.09.2014 - 000 - 0012.2014200 - 000 - 000600 - 000 - 00033 - 000	Commodity / Variety       1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting       Application rate per treatment       Dates of treatment / Application interval         (a)       (b)       g a.s./ha       Water (L/ha)       g a.s./ha       Water (L/ha)       g a.s./ha       Water (L/ha)         Lettuce Parinice; oak leaf variety (loose leaf variety)       1) 12.05.2014 3) 09.06.2014 - 16.06.2014       200 200       800 800       25       26 05.2014/0 906.2014/0 25         Lettuce korentina; (loose leaf variety)       1) 17.09.2014 3) 15.110014 coll       200       600 600       33       00 422014/0 907         Lettuce korentina; (loose leaf variety)       1) 11.09.2014 3) 20.10.2014       200       600 600       33       03 422014/0 97.11.2014/0 200         Lettuce kimpala; oakleaf       1) 11.09.2014 3) 20.10.2014       200       600 33       33       03 42.014/0 97.11.2014/0 2010	Date of I. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting       Application rate per treatment       Dates of treatment / Application integral (a)       Dates of planting         (a)       (b)       g a.s./ha       Water (L/ha)       g.s./hL       Dates of treatment / Application integral         (a)       (b)       g a.s./ha       Water (L/ha)       g.s./hL       F. C         Lettuce       1) 12.05.2014 3) 09.06.2014       200 200       800 800       25 25       26 05 2014/0 200       42         Lettuce       1) 17.09.2014 (loose leaf variety)       200 315.11.2014       200 200       600 600       33 32       04 6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/2014/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.6/0 9.	Planting Variety       planting 2. Flowering 3. Harvest 4. Transplanting       Application rate per treatment       treatment Application interval interval interval particular       treatment ast interval interval particular       freatment ast interval interval particular       freatment ast interval particular       freatment ast interval particular       freatment ast interval particular       freatment ast interval particular       freatment ast interval particular       freatment ast interval particular       freatment ast interval particular       freatment ast interval particular       freatment ast interval particular       freatment interval particular       freatment interval partic	Commodity / Variety       Date of 1. Sowing or planting 3. Harvest 4. Transplanting       Application rate per treatment       Dates of treatment Application integral       Dates of treatment Application integral       Portion Stage at analyzed       Portion stage at analyzed         (a)       (b)       g a.s./ha       Water (L/ha)       g.s./ha       Variety       Dates of treatment (L/ha)       Portion (a)       Portion (b)         Lettuce Parinice; oak leaf variety       1) 12.05.2014 (000 c) 2014       200       800 c)       25 c)       26.05.2014/0 (000 c)       Portion (c)       Portion (d)       Portion (d)         Lettuce Variety       1) 17.09.2014       200       800 c)       25 c)       26.05.2014/0 (000 c)       Portion (d)       Portion (d)       Portion (d)         Lettuce Variety       1) 17.09.2014       200       600       33       04.62.014/0 (d)       46       46         Lettuce Variety       1) 11.09.2014       200       600       33       04.62.014/0 (d)       46       46         Lettuce Variety       1) 11.09.2014       200       600       33       04.62.014/0 (d)       46       46         Lettuce Variety       1) 11.09.2014       200       600       33       03.10.2014/0 (d)       48       48         Lettuce Variety       1) 11.2014<	Commodity / Variety       Date of 1. Sowing or planting 3. Harvest 4. Transplanting       Application rate per treatment       Dates of treatment / Application integral       Optication freatment / Application integral       Portion analyzed (a)       Portion analyzed (b)       Portion analyzed (c)       Portion analyzed	Date of I. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting         Application rate per treatment         Dates of treatment / planting 3. Harvest 4. Transplanting         Portion Residues (mg/k as At Co5048         Portion analyzeit treatment / planting 3. Harvest 4. Transplanting         Application rate per treatment         Dates of treatment / planting 3. Harvest 4. Transplanting         Portion (b)         Portion as At Co5048         Portion analyzeit as At Co5048         Portion analyzeit treatment / planting         Portion analyzeit as At Co5048         Portion (d)         Portion analyzeit as At Co5048           Lettuce Korentina; (loose leaf variety)         1) 17.09.2014         200         800 ft 200         25         26.05.2014/0 40         46         6.0         -0.01           Lettuce Korentina; (loose leaf variety)         1) 17.09.2014         200         600         33         04.07.2014/0 46         46         6.0         -0.01           Lettuce Korentina; (loose leaf variety)         1) 11.09.2014         200         600         33         04.07.2014/0 47         48         -0.01           Lettuce Korentina; (loose leaf variety)         1) 11.09.20	Commodity / Variety         Date of 1. Sowing or planting 3. Harvest 4. Transplanting         Application rate per treatment (Link)         Dates of treatment (Link)         Cowth stage at analyzed integrate (1. ha)         Portion (0)         Growth analyzed as AE as AE (Link)         Provide (1. ha)         Portion (1. ha)         Fill (1. ha)         Provide (1. ha)         Portion (1. ha)



Data Point:	KCA 6.3.6/03
Report Author:	
Report Year:	2019
Report Title:	Determination of the residues of trifloxystrobin and AE 6556948 in/on fituce after spray application of AE C656948 & C6A279202 SC 500 in the greenhouse in Germany, the Netherlands and southern France
Report No:	18-2048
Document No:	<u>M-675904-01-1</u>
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parlament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guideline for the Testing of Chemicals on CropField Field Field Field (TG 509 published in September 2009) US EPA OCSPP Guidefine No 360.1560 on Crop Field Trial
Deviations from current test guideline:	
Previous evaluation:	No, not previously submatted of the second sec
GLP/Officially recognised	Yess conducted under GLP/Officially recognised testing faculties
testing facilities: Acceptability/Reliability:	Yes of the state o

#### Materials and Methods

Three supervised resolute trials on lettuce were conducted in even house (France, the Netherlands and Germany) during the 2014 season?

Two-spray applications were conducted with FLU TFS SC500, a SC (soluble concentrate) formulation containing 250 g/L of fluopyram and 250 g/L of titloxystrobin. For the purpose of this renewal, only results for fluopyram and its metabolite puopyram-benzamide will be discussed.

The applications were conducted at the BBCH of 44 As and at the application rates of 0.8 L/ha corresponding to the application 0.20 kg a S/ha. Water application rates were at 480 - 825 L/ha.

Samples were collected in a mather designed of obtain representative samples. Samples of lettuce (head) were collected at BBC1046 to 49.

Each field sample was placed in touble labeled bags and stored deep-frozen within 24 hours after sampling and until dispater. All field samples were shipped deep-frozen (at -18 °C or lower temperatures) under monitored conditions during shipment and arrived in good condition.

The field samples were stored in a freezer  $ar \leq -18$  °C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field samples were shredded and homogenized with dry ice in a cutter. Representative parts of the shredded samples were transferred into polystyrene boxes and stored at  $18^{\circ}$ C. For each field sample, one or several examination samples were prepared for analysis and one examination sample was prepared as a reserve sample.

Samples were analysed according to the analytical method 00984/M003 (**Mathematical**, 2015, <u>M-467323-03-</u> <u>1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented



within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

However, slight adaptions were made to the extraction procedure described within the analytical method modification 00984/M003 which are as follows: residues were extracted from 5% of sample interval extraction using a shaker (15 min) with a mixture of acetonitrile:water (4:1, v;v).: The filtering procedure under low vacuum was replaced by a centrifugation step. Then, 0.5 mL st internal standard solution? (1 mg/L) were added to the extract followed by 5 min certainfugation at \$750 rpm at 15⁵C and further proceeded to the HPLC-MS/MS analysis

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration cure established with at least 5 concentration levels.

The quantification was done by internal standardization using isotopically stable abelled internal standardization. The Limit of Quantification (LOQ), expressed as fluor fram, defined as the owest validated fortification level, was 0.01 mg/kg.

All final extracts were analysed within one day after extraction. Foropyram and Ouopyram-ben amide were 

In order to check the performance of the method, recovery determinations were uncluded in each set of analyses. Control samples from the study wer fortified to be used as the recovery sample. All the recovery determinations were performed concurrency to the analyses of control and treated samples from the study. The apparent residues in the control sample used for prover experiments, were below 30% of the LOQ. Recoveries were not corrected for apparent residues of the control samples used for these determinations. The mean recoveries per fortification level were within the acceptable range of 70% - 110% and with the RSDs < 20 %. The overall mean concurrent recoveries were also in the acceptable range of 70 % and 110 %,

with the RSD  $\leq 00\%$ . The storage period of the p-frozen samples intended for the analysis of fluopyram and its metabolites ranged

S. between 143 and 326 days.

The detailed results obtained for ettuces amples in greenhouse are sommarized in the Table 6.3.6-8

Ċ

### Conclusion

Four supervised residue trials of ettuce were conducted in greenhouse with the application of FLU+TFS SC500 at the required stees and according to GLP Samples of lettuce were analyzed for the residues of fluopyram and its metaboling fluopyram benzamine. The results of the trials presented above show the following residues in lettuce (head) at havest following a pre harvest interval (PHI) of 7 days.

- Euopyram residues range between 13 and 55 mg/kg
- Fluopyram henzamide range between <0.01 mg/kg
- The total residue of flug yram sum of FLU + FLU-benzamide, expressed as fluopyram) range between 1.31 and 5.51 mg/kg.

#### Assessment and conclusion by applicant;

the state of the second second



Portion	Fortification	R	ecovery (	(%)		$\sim$	ja no
analysed	level (mg/kg)	Individual recoveries	Min	Max	Mean	RSD	
Fluopyram (AI	E C656948)	iccoveries			, A		6 ⁹ 2 ⁹ 6
17 (	0.01	81; 95; 103	R R	103	Ø ⁹³	12.0	
	0.10	72; 91; 97	<u>بر</u> 72	97	87 87	150	
Lettuce / head	1.0	92; 97; 98	© 92	98	96	3.4	Q° A° K ^C
	10	69; 90; 93	69	~ 93	284 L	15.6	Ů Ů Ĺ
				10 × 1	> 90~	41/7	
Fluopyram-b	enzamide(AEF14	18815)				S.	× v
	0.01	69; 85; 496		-96	0 ⁸³	16.2	
T	0.10		69	ۍ 94 گ	83	15.6	
Lettuce / head	1.0	9 <b>Q</b> ,95; <b>2</b> 8 × ×	<u>91</u>	98 ⁰ ″	×95	\$ ^{3.7}	
		Overall recover (n= 12)	K V		ی 87 چ	12,7	
		69 58 94 Overall recovery (n= 12) uopyram and calculated a struopyra reacted as fluopyram-benzamide as the conduct of the strate 18-2048 and the			J.		



Page 423 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

otal residue calcu Trial No. / Location / EU zone / Year	lated : sum of f Commodity / Variety	luopyram+FLU-benza Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting		ion rate per	treatment	Dates of treatment / Application s interval	Growth stage at last treatment	Burtion Vanalyzed	Growth Stage at sampling	potect	FLO benzamide Coscolaria	Ferre	PHI C days
	(a)	(b)	g a.s./ha	Water (L/ha)			e rain	tor!		fluopyram (a) AE C656948	FLD benzamide as AE C656948	Total residues calc.	(e)
18-2048-01 Germany 42799 Leichlingen Europe, North G 2018	Lettuce Macai RZ; typical of region	1) 28.03.2018 3) 04.05.2018 - 15.05.2018	193 208 0670 07				D ¹ K		0 UI 47 48 UI 2 49 0 0 5	6.7 6.7	<pre>0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01</pre>	2.91 9.11 6.71 <u>5.51</u> 1.31	0* 0 3 <u>7</u> 14
18-2048-02 Netherlands 1822 AD Alkmaar Europe, North G 2018	Satine [«]	1) 65.69.2018		CON		09.10.2018/0 16.NO018/7 75		head 2	**************************************	2.2 6.6 7.6 5.0 4.6	<0.01 <0.01 <0.01 <0.01 <0.01	2.21 6.61 7.61 <u>5.01</u> 4.61	0* 0 3 <u>7</u> 14
18-2048-03 France, south B1200 Toulouse Europe, South G 2018	Lettuce Sumitie RZ; Batavia Blonde	1) 0004 2018 3) 22.05 2010 - 30.05.2018				04.05.2098/0 11.85.2018/7	46 K	head	46 46 47 49 49	0.97 5.4 2.3 1.3 0.46	<0.01 <0.01 0.010 0.011 0.014	0.98 5.41 2.31 <u>1.31</u> 0.47	0* 0 3 <u>7</u> 14
<ul><li>(a) According</li><li>(b) Only if rel</li></ul>	to CODEX Clas	sification / Guide	(e) Days a Remark	fter las Applic	ation (Libel pre	-harvest interval, PH litions; Reference to	II, underline) analytical met	(h) hod (i)	Formulation ty Application me			d validation e (max)	
<ul> <li>(c) Year must</li> <li>(d) Either gro</li> <li>G greenhous</li> </ul>	be indicated wtlotage descrip	isification / Guider b a non or BBCH cont F field Cloud With Charles With Charles	and inform (g) Study r prior to	ation which m reference astreatment	ation (1996) pre e Cumatic cond etabolites are in t	cluded		(j) (k) **	Method inform LOQ residue in cont		P based	l on date of a d on product a available	



Based on the residue definition for risk assessment, the sum of fluopyram and fluopyram-benzarade expressed as fluopyram, the total residues for lettuce (head) are summarized in the Table 6.3.6-9

Summary of fluopyram total residue data for lettuce trials to be supported Table 6.3.6- 9:

Сгор	1.08.011/11/0001	Filuopyram total residue data for lettuce Trial results relevant to the critical GAP (mg/kg)	$\sqrt[6]{(h)}$	
Lettuce / head	Greenhouse	0.24, 0.84, 0.94, 0.95, 581, 1.42, 1.61 2.11, 3.63, 3.91, 541, 5.51, 10.01	e trials to be sup SUMIR HR (e) 1.61 10	
(b) <b>STMR</b> : Superv (c) <b>HR</b> : Highest res	rised Trials Median Resid			
In four of the soyridyl-carbox	submitted greenhow cylic acid were sho	use residue trials on lettuce, cesidue of FL own to be below the LOC of 0.0 mg/kg.	9-pyridyl-acefie	i-acid and FLU
	*			
, Ø			Ş	
~				
1				
		0.24, 0.84, 0.94, 0.95, \$31, 1.42, 1.61, 2.11, 3.63, 3.91, 5.51, 10.01, ue use residue trials on lettuce, residue of FL own to be below the LOO of 0.00 mg/kg.		



#### CA 6.4 **Feeding studies**

#### **European dietary burden calculations**

Fluopyram is sought for use on cereals and apple which parts of this crops might be fed to livestoc straw and by-products of grain for barley and apple pomace).

The dietary burdens were therefore calculated for different groups of livestock as described in the OF Guidance Document on Residues in Livestock (ENV/JM/MONO(2013)8 dated of 04-Sep-2013) and as EU spreadsheet 2017 available in The Commission the Excel dated of ⊘₩el (pesticides mrl guidelines animal model 2017.xls)

Based on the proposed plant residue definition for risk assessment (sum of thuopy an and fluopy an benzamide expressed as fluopyram), input values were derived from

- the residue data from representative uses as summarized in N • 11 and Table 6.3.5-19.
- the residues data from succeeding crops sumparized

These input data are summarized Table

Table 6.4- 1:	Input residue	dat&for	livestock	dietary	burden	calculations

6			$\sim$			
Food commodity	Me	lign dietary burden	Max 🖉	aximum dietary burden		
Feed commodity	( <b>nag</b> /kg) 欲	Comment S	(mg/kg)	Comment		
Barley straw		STMR from Nt SEU	1	HR from N+SEU		
Oat straw Barley grain	0.15		0×	S HR HOIII N+SEU		
Barley grain	Ø.025	SIMR from N+SE	~0.025®	STMR from N+SEU		
Oat grain	NG4023			STMR HOILN+SEU		
Brewer's grain	O.080°	SCMRxPF (0.025 x 3.3 ª)	0.08	STMRxPF (0.025 x 3.3 ^a )		
Apple, wet pomace	0,056	STMRxPF (0.67 x 2.3®)	<b>%</b> 16	STMRxPF (0.07 x 2.3 ^a )		
Carrot C	~0.05 <u>_</u>		@ 0.06	HR rotational		
Potato, nuber	j ÓŠ°0.03 [©] S	STME rotational	0.03	HR rotational		
Rape, seed	[≫] 0.02	STMR rotational	0.02	HR rotational		
Wheat, grain	6 02	STMR rotational	0.02	HR rotational		



expresso		Dietary burden expressed in mg/kg bw/d         Above 0.004 mg         Dietary bu express in mg/kg		pressed	Highest	
Ammais	Median	Maximum	/kg bw	Median	Maximum	contributing 5 ⁷ ()
Cattle (Beef)	0.0508	0.060	Yes	2.12	2.48	Potato process waste
Cattle (Dairy)	0.0624	0.076	Yes	1.62	1.99 🔊	Potato process waste
Sheep (Ram/Ewe)	0.0717	0.094	Yes	275	2.80	
Sheep (Lamb)	0.0503	0.081	Yes	L1.18	2.80×	Potatoprocesswaste
Swine (Breeding)	0.026	0.026	Yes A	1.12	Q1.14 .	Potero process was
Swine (Finishing)	0.011	0.012	Yes	0.38	0.40	Datata drived nuln
Poultry (Broiler)	0.023	0.024	Kes	6 °0.32	0,33	Potage dried pulp
Poultry (Layer)	0.018	0.023	Yes &	0.2	\$ ^{40.34} 0	Barrey straw
Poultry (Turkey)	0.005	0.006	Yes	~0.07	Q 0.08	Carrot Olls

Livestock feeding studies were conducted on driry cow and poulto hens. Multicegion livestock diet calculations were conducted in order to conduct the studies to a manner appropriate to the entire@cope of fluopyram uses, allowing data to be generated in a fashion such that, for mimal welfare considerations, a low number of animals will be used, while yielding valid data to evaluate expected residue levels in all key animal tissues and products.

The test substance used in the feeding studies should be representative of the residue in the feedstuffs. In the case of fluopyram, by far the major part of the residue in plans is formed by parent compound Ŷ fluopyram. Ô

Based on the results of the metabolism studies several compounds were preasured in the feeding studies:

- In milk, eggs and all tissues free residues of fluopyrate (AE (656948)) and its metabolites,

Additionally, the detail residue of fluopyram (sum of BCS-AA1057 (E-isomer) and BCS-AA10650 (Z950me6)) were determined Additionally, the detail residue of fluopyram (sum of parent fluopyram + fluopyram-benzamide + dropyram-oleffes) was calculated.



Report Author:Report Year:200Report Title:Flu	CA 6.4.1/01
Report Year:20Report Title:Flu	
Report Title: Flu	
Report Title: Flu	
D	iopyram: Feeding Study Laying Hens (Gallus 🖓 lus domesticit) 🔊 🔬 🛛 🖧
Report No: MI	R-07/234 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
	<u>297674-01-1</u>
Guideline(s) followed in US	: EPA Residue Chemistry Test Guideling OPP & 860.1000 "R@kgrougd"
study: OF	PTS 860 1480 "Meal mails nonline and eggs FU 700 /VI/S lev 4 vivest Ck
fee	ding studies"; EU DRective CC 91 A44, Appendix &
OF	CD: Guidelines the losting of Chemons 50°07007-0°-08 🔦 斗 🛶
Deviations from current not	
test guideline:	
Previous evaluation: yes	s, evaluate and accepted 2. 1 to VA 3 of Dor B7 August 2012 (se Prence Srelied S) s, conducted under GDP/Officially recognised esting Occilities
	7. 1 to VAV3 of DORR B7 Avugust 2012 (reference orelied SA)
GLP/Officially recognised Ye	s, conducted upder GLP/Officially recognised esting actilities
testing facilities:	
Acceptability/Reliability: Ye	

### Materials and Methods

The purpose of his study was to determine the magnitude of the residues of fluopyram (AE C656948) and its metabolites, fluopyram-benzamide and total of fluopyram-old fins, which may be expected in meat and eggs from poultry that have been ted with feed suffs containing residues of fluopyram.

### Test system, dosing 😪

After an acclimatization phase of about 28 days, 72 laying hens (Gallus gallus domesticus) were dosed orally via commercially available ground layer hen diet ad obitum which was mixed with the test item in appropriate another corresponding to the feeding levels. Eaving hens were fed for 28 consecutive days with fluopyram at target dose rates of either:

- 0, mg/kg feed (0X, control, 1 group A of 9 heres),
- 0.05 mg/kg feed (0.1%, 3 subgroups), 12 bens),
- 🖋 0.50 mg/kg feed (14; 3 subgroups C, 12 pens),
- 1.5 mg/kg feed (3X, 3 subgroups D, 12 hens),
- 5.0 mg feed (10X subgroups  $\mathbb{E}$ , 12 hens).

These levels were based on field tesidue data and were approx. 0X (control), 0.1X, 1X, 3X and 10X the anticipated maximum dietary burden arising from the use of fluopyram in the US and EU at the time of the study conduct.

The dX group in this study is around 40% higher than the maximum calculated dietary burden for the present renewal (0024 mg/kg bw/day for Poultry/Broiler see Table 6.4- 2). As a worse case the residue results from this 1X group will be uses as input data for the risk assessment.



.use revel The actual dose levels per feed item were 0 mg fluopyram/kg feed (dose level 0X), 0.05 mg a.s./kg fæd (actual dose level 0.1X), 0.49 mg a.s./kg feed (actual dose level 1X), 1.6 mg a.s./kg feed (actual dose fevel 3X) and 4.8 mg a.s./kg feed (actual dose level 10X).

The actual dose rates per body weight (bw) were:

- $0 \ \mu g/kg \ bw/day$  (dose group A, 0X),
- $3.4 \,\mu\text{g/kg}$  bw/day (dose group B, 0.1X),
- $35 \,\mu g/kg \, bw/day$  (dose group C, 1X),
- $110 \,\mu\text{g/kg}$  bw/day (dose group D, 3X), •
- $320 \ \mu g/kg \ bw/day$  (dose group E, 10X), •
- 330 µg/kg bw/day (dose group F, 10X).

Additionally, three sub-groups of laying hens (5 hens group) were fed at the 10% feeding level for 28 consecutive days followed by untreated feed for another 8 days (dose group F1), 13 days (F2) and 21 days (F3) in order to investigate the depuration of fluopyram and its pertabolities in eggs and tissues.

	·	× •0• ·×		
		Numberoof	Dose I	levels
Dose groups	Sub-groups		🔊 Perlanimal	<b>in Geed</b>
		hens	(µg/kg bw/day)*¢	) (mg/kg DM
0X Control	, ÂQ O	\$9 Ø		
0.1X	B1, B2, B3	12	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~ 0.05
1X	£¥, C2, €3″	\$ 1 <b>0</b> *	, O [*] 35 (k	ð <u>ð</u> .49
3X	D1, D2, D3	@12 \$	110° ×	y ^> 1.6
10X	S E1, #2, E3, 9	× 12 ×	220 · · · · · · · · · · · · · · · · · ·	[*] 4.8

Table 6.4.1- 1:	Summary of	actualfi	uopyram	• <b>dose</b>	admini	stration	
-----------------	------------	----------	---------	---------------	--------	----------	--

10X depuration ( DM: dry matter

DM: dry matter *: Actual dose based on average feed consumption data confected from the stude L. Ĩ

F2, F\$

ð The hencivere fed ad libitum with a commercially avoilable ground ayer hen diet ad libitum (type: "V6220-000 ssniff Hühner-Z D Mehte.v", "ssniff Spezialdiäten GmbH, D-59494 Soest, Germany) which was mixed with the test item in appropriate amounts corresponding to the feeding levels.

4.8

The diet for the exposure period was prepared at the food peparation centre of Bayer HealthCare AG in Wuppertal, Germany under responsibility of Dr. A folkers by incorporation of technical grade fluopyram into feeding material. Content and homogeneity of the patches were also tested.

The hens were allowed ad libition access to tap water. Dose levels used in this study were based on residues found in the magnitude of the field residue trials,

Representative samples of the treated die were checked to verify the amount of technical fluopyram and to determine the stability of the test item during Obrage. A representative number of samples from each batch was analyzed before first dosing. The storage stability was verified and confirmed by reanalysis after 7 days (storage at ambient temperature) and 4 weeks (deep-freezer storage).

The actual dose dates were calculated based on the actual fluopyram concentration in feed, average body weights of hers and average feed consumption during the dosing phase.

For each individuals a weekly amount of feed was portioned and stored under deep-freezer conditions until use. Ł



Actual feed consumption was recorded once a week, individually for each hen. In case the weekly ration of feed seemed to be not sufficient, additional feed was supplied. During the dosing phase, feed hoppers were controlled daily in the morning and filled if necessary, together with morning inspection, watering and egg collection, and once per week all refused feed was emptied out, re-weighed and replaced with fresh food

The birds did not have access to other feedstuffs during the dosing period.

After the end of the dosing period (groups A, B, C, D and E) animals of the F (depuration phase) group were fed with untreated feedstuff until necropsy for approx. See (F1), two (F2) or three weeks (F3).

#### Sampling

For the purpose of this study, a Study Day period was defined from morning inspection, feeding, watering etc... to sampling of eggs on the following morning. The changeover to the following study day took place after sampling of eggs. The eggs were sampled beginning with the control A and continuing with the lowest dose group B to the highest dose groups. Clean disposable gloves were worn for egg collection and contact with surfaces that may be contaminated with feed residues was avoided. The number of eggs from each sub-group was recorded. The eggs were placed on a labelled egg tray in a refrigerator (about 4 °C) for up to 4 days and transferred then to the Test Facility for storage.

For the dose groups A, B, C, D and E eggs for analysis were collected on days \$13, -6, \$1, 0, 1, 2, 5, 7, 9, 12, 14, 16, 21, 23, 26, and 28. For the deparation group D eggs for analysis were collected on day 21, 23, 26, 28, 30, 33, 36, 37 (only F2 and F3), 40 (only F2 and F3), 41 (only F2 and F3) and for the depuration group F3 additionally on day 44, 48 and 49. A note was made if broken eggs were found D roken eggs were removed from the pen and they were not retained for analysis or part of any calculation. The eggs were pooled for each sub-group and deep-frozen on the same day.

The laying hens were withdrawn from their pens on day 28 (dose groups A (coard)), B, C, D and E), day 36 (subgroup F1), day 41 (subgroup F2), and on day 49 (subgroup F3) approximately 3 to 7 hours after the last morning inspection (with between last dosing and sacrifice). The birds were weighed, anaesthetized by a neck beat and sacrificed by immediate exsanglination by decapitation. The following tissues were collected from each bird and weighed:

• muscle, approx. equal sized pieces of leg and breast (approximately 100 g in total), trimmed of adherent connective tissue and fat,

- skin with subcutaneous fat and abdorathal fat
- liver (contine organ).

During necropsy, the cross-contamination between tissues of different dosing groups was prevented as far as possible by using tresh instruments after treating a distinct sub-group. Tissue samples were transferred as soon as possible for deep-freezing at 218 °C and sample preparation.

0

## Analysis

Egg and tissue samples were analysed for the parent compound fluopyram and its major metabolites fluopyram-benzamide, fluopyram-olefins (BCS-AA10627 (E-isomer) and BCS-AA10650 (Z-isomer)). The residues were analysed according to the malytical method 01061 (2000), 2007, M-295705-02-10 see MCA Section 41.2). Full details and acceptable validation data to support this method are presented within document M-CA which comply with the EU regulatory requirements outlined within SANCQ 3029/09 rev 4.

Briefly, the oscidues were extracted from the animal tissues and eggs by a mixture of acetonitrile/water. After filtration the extracts are cleaned-up on a Mega Bond Elut-C18 cartridges. Aliquots of the extracts are further diluted with a mixture of methanol/water (containing the corresponding internal standards). The



residues are analysed by reversed phase HPLC with electrospray and MS/MS-detection. To compensate the matrix effect, the quantification was done using external calibration with matrix matched standards.

The limit of quantitation (LOQ) was 0.01 mg/kg for fluopyram and the FLU-benzamide metabolite, expressed as parent equivalents. In case of FLU-olefins, the total residue of FLU-olefins was calculated as sum of the two individual FLU-olefin isomers, also expressed as parent equivalent. For this strictly the LOQ of the Total residue of FLU-olefins was set to 0.02 mg/kg for all matrices under actual use conditions of the study. For the total residue of fluopyram (each expressed as parent equivalents) 0.04 mg/kg was set for all investigated animal matrices.

The limit of detection (LOD) was estimated to be 0.003 mg/kg for fluepyram 0.001 mg/kg for benzamide, 0.004 mg/kg for the total residue of FLU-olefins, and 0.008 mg/kg for the total residue of fluopyram (each expressed as parent equivalents) for all investigated animal matrices.

In order to check the analytical method performance, concurrent recovery experiments, were conducted along with the analysis of samples. The concurrent recovery levels for all matrices tested (eg, liver, muscle, skin with fat) were between 0.01 mg/kg (LOQ level) and 2.0 mg/kg (200-fold LOQ level) for fluopyram and the FLU-benzamide metabolite, expressed as parent equivalents, and between 0.02 mg/kg (LOQ level) and 4.0 mg/kg (200-fold LOQ level) for the total residue of FLU-otefins, expressed as parent equivalents. All concurrent recovery values are presented in the Table 6.4.1-6

# II. Findings

#### Dose verification and storage stability

The dosing solutions for the preparation of the sortified feedstuffs of the different batches were analyzed for fluopyram in order to determine the content and homogeneity as well as the storage stability of fluopyram for the duration of use in the in-the phase of the study. The cose preparation was accurate, and the feedstuffs were shown to be stable over the course of the study.

Analysis of feed Suff

No residues of fluopyfam were detected in the untreated deedstudi.

### In-life observations

Feed consumption, body weights and egg production were not adversely affected by treatment with fluopyram. The appearance and the behavior of all birds were observed once daily throughout the study. Nothing special was observed. Stens were healthy during the whole study.

n

ð

# Analysis of eggs and Hissuer

The mean values of the concurrent recovery rates per compound, sample material, and spiking level were in the range of 70 - 110%, with relative standard deviations < 20 %. In few cases the recovery means were slightly above 110 %, or the RSD was slightly above 20 %. Nevertheless, the data demonstrate acceptable method performance during sample analysis. Details of recovery data are shown in Table 6.4.1- 6.

The tissue and egg samples in this study were analysed within 30 days after collection; therefore, freezer storage stability studies on poultry tissue and egg matrices were not required.

The control samples of oggs and tissues were analysed concurrently with the treated samples. The residues of fluopyram and its metabolites were below the relevant LOQ in all the control samples.

As an overview, the mean residue levels in eggs are presented in



Table 6.4.1-2. More details in Table 6.4.1-7.

During the course of the study, the residues of fluopyram and the total residue of the two olefin metabolites of the study in eggs remained in all dose groups below the LOO (most of the time of LOD) with in eggs remained in all dose groups below the LOQ (most of the time < LOD), with some exception for the total olefins mean in eggs on days 16, 21, 23, 26, and 28 in the group 10X in which the mean values were at the LOQ (0.02 mg/kg).

Therefore, the plateau in eggs was:

- below the LOQ (0.01 mg/kg for Fluopyram; most of the time below the LOD)
- at the LOQ (0.02 mg/kg for total residue of olefins).

During the course of the study, the residues of the EVD-benzamide metabolite in eggs in the nominal  $\frac{1}{2}$  dose group C increased from < LOD mg/kg on day. It a 0.02 dose group C increased from < LOD mg/kg on day 0 to 0.08 mg/kg on day 21, to 0.07 mg/kg on day 23 and 26, and 0.08 mg/kg on day 28. Ś 'N

Thus, the plateau of FLU-benzamide in eggs was: Ø

- 0.08 mg/kg (mean of day 21, 23, 26 and 28) for the 1X dose group

0.08 mg/kg (mean of day 21, 23, 26 and 28) for the 1X dose group (C)
0.21 mg/kg (mean of day 21, 23, 26 and 28) for the 3X tiens
0.71 mg/kg (mean of day 21, 29, 26 and 28) for the 10X hens
No residues of fluopyram or FLU-olefins above the LOD were found in any of the ess samples from the 0.1X group (with one exception & OQ for fluop fram of the day of sampling 2), whereas residues of FLUbenzamide in the eggs from the 0.1X group were always either <LOD (for the sampling days -13, -6, -1, 0,

The residues found in the individual egg samples as well as the calculated values for the total residue of

Since no residues of Tuopy am were determined in the individual egg matrices (egg yolks and egg white), the distribution could not be investigated. Nevertheless, the residues of FLU, benzamide and the total olefins

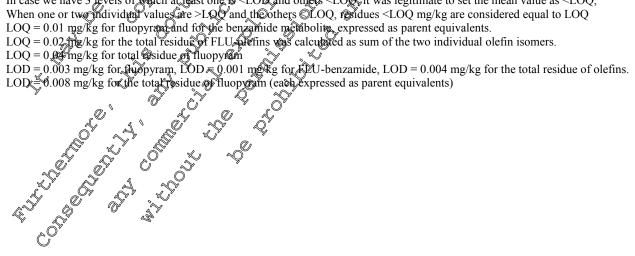
Labor of the second sec



able 6.4	able 6.4.1- 2: Residues (mg/kg) of fluopyram and its metabolites, FLU-benzamide, total of FLU-olefins and the total residue of fluopyram in eggs								° A		
		Residues (mg parent equivalents/kg) in Eggs 🖉 🖉									
Day											
Day	fluopyram	FLU-	FLU-	Total	fluopyram	FLU-	FLU-	Total 7	Ĉa		
		Benzamide	Olefins	residue	Č6	Benzamide	Olefinŝ	residue	K,		
0	<lod< td=""><td><lod< td=""><td><lod< td=""><td><lod< td=""><td><b>A</b>¢OD</td><td>&lt; IOD</td><td><lod< td=""><td>SLOD S</td><td></td></lod<></td></lod<></td></lod<></td></lod<></td></lod<>	<lod< td=""><td><lod< td=""><td><lod< td=""><td><b>A</b>¢OD</td><td>&lt; IOD</td><td><lod< td=""><td>SLOD S</td><td></td></lod<></td></lod<></td></lod<></td></lod<>	<lod< td=""><td><lod< td=""><td><b>A</b>¢OD</td><td>&lt; IOD</td><td><lod< td=""><td>SLOD S</td><td></td></lod<></td></lod<></td></lod<>	<lod< td=""><td><b>A</b>¢OD</td><td>&lt; IOD</td><td><lod< td=""><td>SLOD S</td><td></td></lod<></td></lod<>	<b>A</b> ¢OD	< IOD	<lod< td=""><td>SLOD S</td><td></td></lod<>	SLOD S			
1	<lod< td=""><td><lod< td=""><td><lod< td=""><td><lod< td=""><td>"Č, ŠLOD</td><td><b>S</b>₽OQ</td><td><lød< td=""><td>~COD S&lt;0.04 &lt;0.04</td><td>Ś</td></lød<></td></lod<></td></lod<></td></lod<></td></lod<>	<lod< td=""><td><lod< td=""><td><lod< td=""><td>"Č, ŠLOD</td><td><b>S</b>₽OQ</td><td><lød< td=""><td>~COD S&lt;0.04 &lt;0.04</td><td>Ś</td></lød<></td></lod<></td></lod<></td></lod<>	<lod< td=""><td><lod< td=""><td>"Č, ŠLOD</td><td><b>S</b>₽OQ</td><td><lød< td=""><td>~COD S&lt;0.04 &lt;0.04</td><td>Ś</td></lød<></td></lod<></td></lod<>	<lod< td=""><td>"Č, ŠLOD</td><td><b>S</b>₽OQ</td><td><lød< td=""><td>~COD S&lt;0.04 &lt;0.04</td><td>Ś</td></lød<></td></lod<>	"Č, ŠLOD	<b>S</b> ₽OQ	<lød< td=""><td>~COD S&lt;0.04 &lt;0.04</td><td>Ś</td></lød<>	~COD S<0.04 <0.04	Ś		
2	<lod< td=""><td><loq< td=""><td><lod< td=""><td><lod 4<="" td=""><td>©″ <lod< td=""><td>0.01 کې 0</td><td>ZEOD 4</td><td></td><td>×⁰</td></lod<></td></lod></td></lod<></td></loq<></td></lod<>	<loq< td=""><td><lod< td=""><td><lod 4<="" td=""><td>©″ <lod< td=""><td>0.01 کې 0</td><td>ZEOD 4</td><td></td><td>×⁰</td></lod<></td></lod></td></lod<></td></loq<>	<lod< td=""><td><lod 4<="" td=""><td>©″ <lod< td=""><td>0.01 کې 0</td><td>ZEOD 4</td><td></td><td>×⁰</td></lod<></td></lod></td></lod<>	<lod 4<="" td=""><td>©″ <lod< td=""><td>0.01 کې 0</td><td>ZEOD 4</td><td></td><td>×⁰</td></lod<></td></lod>	©″ <lod< td=""><td>0.01 کې 0</td><td>ZEOD 4</td><td></td><td>×⁰</td></lod<>	0.01 کې 0	ZEOD 4		× ⁰		
5	<lod< td=""><td><lod< td=""><td><lod< td=""><td>&lt;0.04</td><td>&gt; <lod< td=""><td>°≶ 0.04°</td><td>,≪LOD</td><td>° 0,05 "(</td><td>ŧ,×</td></lod<></td></lod<></td></lod<></td></lod<>	<lod< td=""><td><lod< td=""><td>&lt;0.04</td><td>&gt; <lod< td=""><td>°≶ 0.04°</td><td>,≪LOD</td><td>° 0,05 "(</td><td>ŧ,×</td></lod<></td></lod<></td></lod<>	<lod< td=""><td>&lt;0.04</td><td>&gt; <lod< td=""><td>°≶ 0.04°</td><td>,≪LOD</td><td>° 0,05 "(</td><td>ŧ,×</td></lod<></td></lod<>	<0.04	> <lod< td=""><td>°≶ 0.04°</td><td>,≪LOD</td><td>° 0,05 "(</td><td>ŧ,×</td></lod<>	°≶ 0.04°	,≪LOD	° 0,05 "(	ŧ,×		
7	<lod< td=""><td><lod< td=""><td><lod< td=""><td><løø< td=""><td><lod< td=""><td><i>ِ</i>رَوَرَيْ کَمَ</td><td>∛ <l@)< td=""><td>0.06</td><td></td></l@)<></td></lod<></td></løø<></td></lod<></td></lod<></td></lod<>	<lod< td=""><td><lod< td=""><td><løø< td=""><td><lod< td=""><td><i>ِ</i>رَوَرَيْ کَمَ</td><td>∛ <l@)< td=""><td>0.06</td><td></td></l@)<></td></lod<></td></løø<></td></lod<></td></lod<>	<lod< td=""><td><løø< td=""><td><lod< td=""><td><i>ِ</i>رَوَرَيْ کَمَ</td><td>∛ <l@)< td=""><td>0.06</td><td></td></l@)<></td></lod<></td></løø<></td></lod<>	<løø< td=""><td><lod< td=""><td><i>ِ</i>رَوَرَيْ کَمَ</td><td>∛ <l@)< td=""><td>0.06</td><td></td></l@)<></td></lod<></td></løø<>	<lod< td=""><td><i>ِ</i>رَوَرَيْ کَمَ</td><td>∛ <l@)< td=""><td>0.06</td><td></td></l@)<></td></lod<>	<i>ِ</i> رَوَرَيْ کَمَ	∛ <l@)< td=""><td>0.06</td><td></td></l@)<>	0.06			
9	<lod< td=""><td><lod< td=""><td><lod< td=""><td>≪<b>€</b>OD</td><td>© ~LOD</td><td>× 0.06 0</td><td>≪LØD</td><td>K) 0.0KC&gt;</td><td></td></lod<></td></lod<></td></lod<>	<lod< td=""><td><lod< td=""><td>≪<b>€</b>OD</td><td>© ~LOD</td><td>× 0.06 0</td><td>≪LØD</td><td>K) 0.0KC&gt;</td><td></td></lod<></td></lod<>	<lod< td=""><td>≪<b>€</b>OD</td><td>© ~LOD</td><td>× 0.06 0</td><td>≪LØD</td><td>K) 0.0KC&gt;</td><td></td></lod<>	≪ <b>€</b> OD	© ~LOD	× 0.06 0	≪LØD	K) 0.0KC>			
12	<loq< td=""><td><lod< td=""><td><lod< td=""><td>©0.04_0</td><td>₽° <løø< td=""><td>0.07</td><td>SLOD *</td><td>0.07</td><td></td></løø<></td></lod<></td></lod<></td></loq<>	<lod< td=""><td><lod< td=""><td>©0.04_0</td><td>₽° <løø< td=""><td>0.07</td><td>SLOD *</td><td>0.07</td><td></td></løø<></td></lod<></td></lod<>	<lod< td=""><td>©0.04_0</td><td>₽° <løø< td=""><td>0.07</td><td>SLOD *</td><td>0.07</td><td></td></løø<></td></lod<>	©0.04_0	₽° <løø< td=""><td>0.07</td><td>SLOD *</td><td>0.07</td><td></td></løø<>	0.07	SLOD *	0.07			
14	<lod< td=""><td><lod< td=""><td><lod td="" 🖉<=""><td><lop< td=""><td>stoD ℃</td><td>0.06</td><td>O<lon< td=""><td>AQ.07</td><td>&gt;</td></lon<></td></lop<></td></lod></td></lod<></td></lod<>	<lod< td=""><td><lod td="" 🖉<=""><td><lop< td=""><td>stoD ℃</td><td>0.06</td><td>O<lon< td=""><td>AQ.07</td><td>&gt;</td></lon<></td></lop<></td></lod></td></lod<>	<lod td="" 🖉<=""><td><lop< td=""><td>stoD ℃</td><td>0.06</td><td>O<lon< td=""><td>AQ.07</td><td>&gt;</td></lon<></td></lop<></td></lod>	<lop< td=""><td>stoD ℃</td><td>0.06</td><td>O<lon< td=""><td>AQ.07</td><td>&gt;</td></lon<></td></lop<>	stoD ℃	0.06	O <lon< td=""><td>AQ.07</td><td>&gt;</td></lon<>	AQ.07	>		
16	<lod< td=""><td><lod< td=""><td><lod< td=""><td>"∕~LÕØ</td><td>_∕¥ĽOD_ [×]</td><td>0.06</td><td><lod< td=""><td>0.07</td><td></td></lod<></td></lod<></td></lod<></td></lod<>	<lod< td=""><td><lod< td=""><td>"∕~LÕØ</td><td>_∕¥ĽOD_ [×]</td><td>0.06</td><td><lod< td=""><td>0.07</td><td></td></lod<></td></lod<></td></lod<>	<lod< td=""><td>"∕~LÕØ</td><td>_∕¥ĽOD_ [×]</td><td>0.06</td><td><lod< td=""><td>0.07</td><td></td></lod<></td></lod<>	"∕~LÕØ	_∕¥ĽOD_ [×]	0.06	<lod< td=""><td>0.07</td><td></td></lod<>	0.07			
21	<lod< td=""><td><lod< td=""><td><lqd< td=""><td>, ≲0.04</td><td>[™]<lqd< td=""><td>% 0.08</td><td>≪L∕OD</td><td>0.00</td><td></td></lqd<></td></lqd<></td></lod<></td></lod<>	<lod< td=""><td><lqd< td=""><td>, ≲0.04</td><td>[™]<lqd< td=""><td>% 0.08</td><td>≪L∕OD</td><td>0.00</td><td></td></lqd<></td></lqd<></td></lod<>	<lqd< td=""><td>, ≲0.04</td><td>[™]<lqd< td=""><td>% 0.08</td><td>≪L∕OD</td><td>0.00</td><td></td></lqd<></td></lqd<>	, ≲0.04	[™] <lqd< td=""><td>% 0.08</td><td>≪L∕OD</td><td>0.00</td><td></td></lqd<>	% 0.08	≪L∕OD	0.00			
23	<lod< td=""><td><lod< td=""><td><kqd< td=""><td><b>↓%</b>LOD≪</td><td>ŗ &lt;Ľ®D ∗</td><td>0.00</td><td>~LOD</td><td></td><td></td></kqd<></td></lod<></td></lod<>	<lod< td=""><td><kqd< td=""><td><b>↓%</b>LOD≪</td><td>ŗ &lt;Ľ®D ∗</td><td>0.00</td><td>~LOD</td><td></td><td></td></kqd<></td></lod<>	<kqd< td=""><td><b>↓%</b>LOD≪</td><td>ŗ &lt;Ľ®D ∗</td><td>0.00</td><td>~LOD</td><td></td><td></td></kqd<>	<b>↓%</b> LOD≪	ŗ <Ľ®D ∗	0.00	~LOD				
26	<lod< td=""><td><lod< td=""><td>LOD ?</td><td>&lt;0.04</td><td>EOD 🖓</td><td>0,<b>9</b>7 _</td><td>S <lqd< td=""><td>0.08</td><td></td></lqd<></td></lod<></td></lod<>	<lod< td=""><td>LOD ?</td><td>&lt;0.04</td><td>EOD 🖓</td><td>0,<b>9</b>7 _</td><td>S <lqd< td=""><td>0.08</td><td></td></lqd<></td></lod<>	LOD ?	<0.04	EOD 🖓	0, <b>9</b> 7 _	S <lqd< td=""><td>0.08</td><td></td></lqd<>	0.08			
28	<lod< td=""><td><lod< td=""><td>-Q<lod< td=""><td>&lt;0.04</td><td><lod,< td=""><td><b>09</b>.08</td><td><k@d< td=""><td>x 🖗 0.09</td><td></td></k@d<></td></lod,<></td></lod<></td></lod<></td></lod<>	<lod< td=""><td>-Q<lod< td=""><td>&lt;0.04</td><td><lod,< td=""><td><b>09</b>.08</td><td><k@d< td=""><td>x 🖗 0.09</td><td></td></k@d<></td></lod,<></td></lod<></td></lod<>	-Q <lod< td=""><td>&lt;0.04</td><td><lod,< td=""><td><b>09</b>.08</td><td><k@d< td=""><td>x 🖗 0.09</td><td></td></k@d<></td></lod,<></td></lod<>	<0.04	<lod,< td=""><td><b>09</b>.08</td><td><k@d< td=""><td>x 🖗 0.09</td><td></td></k@d<></td></lod,<>	<b>09</b> .08	<k@d< td=""><td>x 🖗 0.09</td><td></td></k@d<>	x 🖗 0.09			
		Dose Group	D (3X)	N° 4		Dose Gou	) E@10X) `^	Y			
Day	fluonyram	FLU	FĽU- ๙	🗼 Total 🖉	fluopyrap	Ç FLU- (	FLU	Total			
	fluopyram	Benzamide	Ølefins	residue		Benzamide	Olefins	residue			
0	<lod< td=""><td>≪LØD</td><td>∪<lqq°< td=""><td>, stop</td><td><rp>COD</rp></td><td>~~LOD~</td><td>_<b>∕\$</b>_OD</td><td><lod< td=""><td></td></lod<></td></lqq°<></td></lod<>	≪LØD	∪ <lqq°< td=""><td>, stop</td><td><rp>COD</rp></td><td>~~LOD~</td><td>_<b>∕\$</b>_OD</td><td><lod< td=""><td></td></lod<></td></lqq°<>	, stop	<rp>COD</rp>	~~LOD~	_ <b>∕\$</b> _OD	<lod< td=""><td></td></lod<>			
1	<lod< td=""><td>0.01</td><td><lod< td=""><td>£ 0.04</td><td><kod< td=""><td>[∞] 0,03× ,</td><td>LOD</td><td>0.04</td><td></td></kod<></td></lod<></td></lod<>	0.01	<lod< td=""><td>£ 0.04</td><td><kod< td=""><td>[∞] 0,03× ,</td><td>LOD</td><td>0.04</td><td></td></kod<></td></lod<>	£ 0.04	<kod< td=""><td>[∞] 0,03× ,</td><td>LOD</td><td>0.04</td><td></td></kod<>	[∞] 0,03× ,	LOD	0.04			
2	<lod< td=""><td>0.01</td><td>DOD (</td><td>0.0</td><td>Stop &amp;</td><td>0.09</td><td>S <lod< td=""><td>0.10</td><td></td></lod<></td></lod<>	0.01	DOD (	0.0	Stop &	0.09	S <lod< td=""><td>0.10</td><td></td></lod<>	0.10			
5	<lod< td=""><td>U, IU j</td><td>S~LOD</td><td>0.SM</td><td>~LOD</td><td>00.36</td><td>° <lod< td=""><td>0.37</td><td></td></lod<></td></lod<>	U, IU j	S~LOD	0.SM	~LOD	00.36	° <lod< td=""><td>0.37</td><td></td></lod<>	0.37			
7	<lod< td=""><td>. @?13 ×</td><td>୬ <løø< td=""><td>0.14 ๙</td><td>[™] <l@d< td=""><td>0.45</td><td><loq< td=""><td>0.46</td><td></td></loq<></td></l@d<></td></løø<></td></lod<>	. @?13 ×	୬ <løø< td=""><td>0.14 ๙</td><td>[™] <l@d< td=""><td>0.45</td><td><loq< td=""><td>0.46</td><td></td></loq<></td></l@d<></td></løø<>	0.14 ๙	[™] <l@d< td=""><td>0.45</td><td><loq< td=""><td>0.46</td><td></td></loq<></td></l@d<>	0.45	<loq< td=""><td>0.46</td><td></td></loq<>	0.46			
9	<loid< td=""><td><b>0.15</b> √</td><td><i>Ğ</i>LŎD ≈</td><td>×0.16×</td><td>_stod _</td><td>y Q.59</td><td><loq< td=""><td>0.51</td><td></td></loq<></td></loid<>	<b>0.15</b> √	<i>Ğ</i> LŎD ≈	×0.16×	_stod _	y Q.59	<loq< td=""><td>0.51</td><td></td></loq<>	0.51			
12	<i20q< td=""><td>0.13</td><td>∂%LOD ⊘</td><td>0.18</td><td>LOD T</td><td>×Q2359</td><td><loq< td=""><td>0.60</td><td></td></loq<></td></i20q<>	0.13	∂%LOD ⊘	0.18	LOD T	×Q2359	<loq< td=""><td>0.60</td><td></td></loq<>	0.60			
14	sLOD 0	^y 05.¥7	<lod< td=""><td><u>\$</u>\$</td><td>Co <lqb< td=""><td>0.56</td><td><loq< td=""><td>0.57</td><td></td></loq<></td></lqb<></td></lod<>	<u>\$</u> \$	Co <lqb< td=""><td>0.56</td><td><loq< td=""><td>0.57</td><td></td></loq<></td></lqb<>	0.56	<loq< td=""><td>0.57</td><td></td></loq<>	0.57			
16	<u></u> ∿_≺LOD	×0.18 ×	<lachter <="" <lachter="" <lachter<="" lachter="" td=""><td>ð.19 <i>(</i></td><td> LOQ</td><td>ک^۳ 0.62</td><td><loq< td=""><td>0.64</td><td></td></loq<></td></lachter>	ð.19 <i>(</i>	 LOQ	ک ^۳ 0.62	<loq< td=""><td>0.64</td><td></td></loq<>	0.64			
21 🌋	S ^y <lod< td=""><td>0.22</td><td>EOD</td><td>0.22</td><td>_ ∧ OD ∧</td><td>0.72</td><td><loq< td=""><td>0.73</td><td></td></loq<></td></lod<>	0.22	EOD	0.22	_ ∧ OD ∧	0.72	<loq< td=""><td>0.73</td><td></td></loq<>	0.73			
23 🔪	<pre>LOD &gt;</pre>	0:20	LOD	0.Ø	≪~LODO″	0.70	0.02	0.71			
26	<lod <lod< td=""><td><b>6</b>20</td><td></td><td>×0.22 %</td><td>, <lqd∕< td=""><td>0.70</td><td>0.02</td><td>0.71</td><td></td></lqd∕<></td></lod<></lod 	<b>6</b> 20		×0.22 %	, <lqd∕< td=""><td>0.70</td><td>0.02</td><td>0.71</td><td></td></lqd∕<>	0.70	0.02	0.71			
28	<lod< td=""><td>▲ 0.22 🖉 🕷</td><td>. ₹LØQ</td><td>@0.24 O</td><td>≲LÕD</td><td>0.72</td><td>0.02</td><td>0.73</td><td></td></lod<>	▲ 0.22 🖉 🕷	. ₹LØQ	@0.24 O	≲LÕD	0.72	0.02	0.73			

Table 6.4.1- 2:	Residues (mg/kg) of fluopyram and its metabolites, FLU-benzamide, total	of
	FLU-olefins and the total residue of fluopyram in eggs	

In case we have 3 levels of which at that one @<LOD and others <LOQ at was legitimate to set the mean value as <LOQ; When one or two ndividual values are >LQQ and the others OLOQ, residues <LOQ mg/kg are considered equal to LOQ





10X           320 μg/kg bw/day           4.8 mg/kg DM           Sub-groups: E1, E2,           E3	aole Egg 22 22 23 29 29 20 20 20 20 20 20 20 20 20 20 20 20 20	(Day)* 22 25 27 22 25 27 22 25 27 22 25 27 22 25 27 25 27 27 27 27 27 27 27 27 27 27	- - - - - - - - - - - - - - - - - - -	img/kg 0.69 0.71 0.77 0.97 0.97 0.97 0.97 0.61 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65	0.05 × 0.04 × 0.07 ×	[mg/kg]       0.71       0.73       0.80       1.03       0.80       1.04       0.67       0.68
10X           320 μg/kg bw/day           4.8 mg/kg DM           Egg           Sub-groups: E1, E2,           E3	22 22 23 29 20 20 20 20 20 20 20 20 20 20 20 20 20	27 22 25 27 22		0.77 0.970 0.094 0.094 0.97 0.01 0.01	0.03 0.08 0.04 0.07 C < LOD	0.80 0.98 0.98 0.98 0.98
320 μg/kg bw/day           4.8 mg/kg DM           Sub-groups: E1, E2,           E3	gg Yolk	22 25 27 22		0.97Q 0.04 0.97 0.61Q	0.03 0.08 0.04 0.07 C < LOD	0.80 0.98 0.98 0.98 0.98
4.8 mg/kg DM Egg <b>Sub-groups</b> : E1, E2, E3	gg Yolk 22	25 27 22		0.97Q 0.04 0.97 0.61Q	0.05 × 0.04 × 0.07 ×	0.98 0 0 1.04 ×
Sub-groups: E1, E2, E3	2	27 22	 	<u>\$97</u> ° ∧ 0.61 ∅	0.07 Q < LOD	
Ē3	2	22	 	∾ 0.61	~~~L@D	0.61
	g White	22 25 27 27 27 27 27 27 27 27 27 27 27 27 27	bayon could not bayon could not lents tite, expressed as ted as sum of the content of the conten	a in		0.67 0.68
*Overall study day *No residues of fluopyram were All metabolite residues expressed LOQ = 0.01 mg/kg for fluopyram LOQ = 0.02 mg/kg for the total re LOD = 0.003 mg/kg for the total re LOD = 0.001 mg/kg for benzamic LOD = 0.004 mg/kg for the total LOD = 0.008 mg/kg for the total As an overview, the mean r	g White 2 ere determined, ther sed in parent compo am and the benzami l residue of olefins il residue of flue yram mide 2 al residue of flue pyra residue of flue pyra residue of flue pyra a residue of flue	25 27 refore district purfer equival infer meteboli was caroulat am (each exp 5. rram(each exp 5. in tissues	biotion could not lents lite, expressed at ted to sum of the prossed as pare are presented	d in	A COOL CO	<b>9</b> .67 <b>0.68</b>
*Overall study day *No residues of fluopyram were All metabolite residues expressed LOQ = 0.01 mg/kg for fluopyram LOQ = 0.02 mg/kg for the total re LOD = 0.003 mg/kg for the total re LOD = 0.001 mg/kg for benzamic LOD = 0.004 mg/kg for the total LOD = 0.008 mg/kg for the total As an overview, the mean r	ere determined, ther sed in parent compo am and the benzami l residue of olefine l residue of flugpyra rram mide al residue of flugpyra rail residue of flugpyra p residue of flugpyra p residue of flugpyra	27 refore distributed equival intermetaboli was calculat am (each exp fram(each exp in tisspes	bation could not lents lite, expressed at ted 45 sum of the prossed as pare expressed as pare are presented	t be investigated. (sparent equivalent) te two individual o ent equivalents) (sparent e	LOD ~	**** 0.68
*Overall study day **No residues of fluopyram were All metabolite residues expressed LOQ = 0.01 mg/kg for fluopyram LOQ = 0.02 mg/kg for the total re LOD = 0.003 mg/kg for the total re LOD = 0.001 mg/kg for benzamic LOD = 0.004 mg/kg for the total LOD = 0.008 mg/kg for the total As an overview, the mean r	ere determined, ther sed in parent compo am and the benzami l residue of olefus l residue of flugpyra ram mide al residue of flugpyra al residue of flugpyra p residue of flugpyra p residue of flugpyra	refore distribute equival intermetabolit was calculat am (Each exp s. rramiteach e in tisspes	bition could not lents ted to sum oth prossed as pare supressed as pare	t be investigated. (sparent Quivalent) te two predividual o ent convalents). (cont convalents). (cont convalents). (cont convalents). (cont convalents). (convalents). (convalents). (convalents). (convalents).	in the second se	



<figure> Table 6.4.1- 4. Residues of fluopyram were always below the LOD (with one exception for the mean level of fluopyram A BA COMPANIE OF C

el of fit. e residuent and and a residuent and and a residuent and a r A consection of and the owner the consection of the owner.



1 abie 0.4.1- 4.		ts (mg/kg) of huo	pyrain and its i	netabolite in allina	
	Residu	ies (mg parent equ	ivalents/kg)		
		Dose Group B (0.	1X)		
Tissue	fluopyram	FLU-benzamide	FLU-olefins	Total residue	
Skin with Fat	< LOD	< LOQ	< LOD	<0.04	
Liver	< LOD	0.01	< LQQ	6.04	
Muscle	< LOD	< LOQ	< LOD	Q<0.04	
		Dose Group C (1	X) (V)		
Tissue	fluopyram	FLU-benzamide	DU-olefins	Total residue	
Skin with Fat	< LOD	0.04	< LOQ	°∼ 0.06 ° N	
Liver	< LOD	0.16			
Muscle	< LOD	0.03	× < LOD	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	L A .
		Dose Group D (3	X) <u> </u>		
Tissue	fluopyram	FLU-berzamide	FIQ-olefins	Total residue 🖉	×, s
Skin with Fat	< LOD	00.1	~~ 0.02×	Ø.12 Ø	
Liver	< LOD	0.41 °	°∕ <ľǿD ∖		, Q
Muscle	< LOD	a, ^v Q. <b>(p</b> ) (?			
	, second s	9.69 Dose Group E (1)	0X		ζ, [']
Tissue	fluopyram	FKU-benzâmide /	🕻 FLU-olefins 🕯 🕻		۵″
Skin with Fat	$< LOQ^{4}$				
Liver	< KOD	\$ 1.4 S	~ LOO	×1).42 ×	
Muscle	ALOD OF	0.29	¥ 9.05 O	0.32	J

#### Table 6.4.1-4: Mean residues (mg/kg) of fluopyram and its metabolite in animal tissues.

For the calculation of the mean residues, in case we have Gevels of which at least one is <LOD and others <LOQ, it was legitimate to set the mean value as <LOQ;  $\bigcirc$ 

Value as >LOQ, For the calculation of the mean residues, in case one or two matvidual values are LOQ and the others < LOQ, it was deemed appropriate to consider residues <100 mg/kg shoeing equal to LOV mg/kg) this approach represents the worst-case scenario. In tissue samples, if among the values there was at least one value LOQ, for the calculation of the mean all the other values <LOQ and <LOD was accurately a scenario of the mean all the other values <LOQ and <LOD.

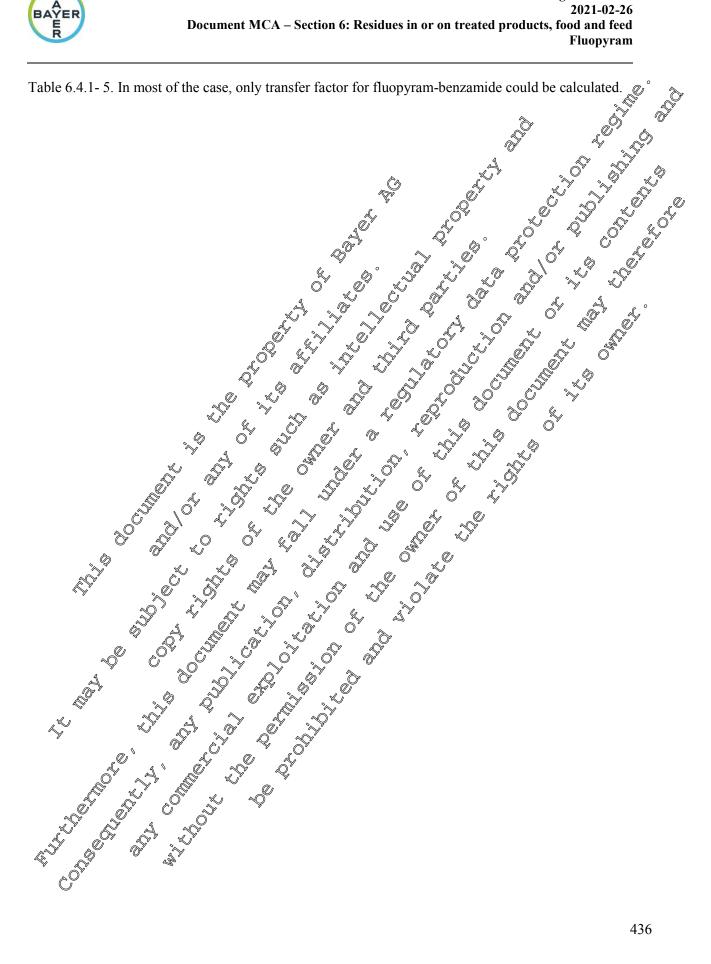
were set equal to GOQ and LOD, respectively, this approach represents the worst-case seenario,

Ċ The specimens were stored at temperatures of  $\leq 1.80^{\circ}$ C until analysis. They were stored for a maximum of 23 days between sampling and extraction Therefore, no special storage stability studies were necessary.

23 days between sampling and extraction. Therefore, no special storage stability studies were necessary. The calculated transfer factors see the factor of the factor of the tissue to the residue level in the feed, are summarized in the contract of the transfer factors of the time o

a.







able 6.4.1- 5:	Calculate	ed transfe	er factors (	IF) in po	ultry				
Feeding level	0.05 mg/ feed (0.1X		0.49 mg/ feed (1X		1.6 mg/k feed (3X §		4.8 mg/k	g dry feed ( group) 🏑	
fluopyram	- -						.1	<i>C</i>	
Commodity	mg/kg	TF	mg/kg	TF	_mg/kg	TF	^w mg/kg	, ŜŢF , ¢	
eggs	< LOD	nd	< LOD	nd	LOD	na	<loq< td=""><td>🔊 nd 🥎</td><td>- S</td></loq<>	🔊 nd 🥎	- S
Skin with Fat	< LOD	nd	< LOD	nd 🎣	< LOD	And	< LOD	nQ	×,
Liver	< LOD	nd	< LOD	nd	<lod< td=""><td>🖇 nd</td><td>&lt; LØD</td><td>-Qad</td><td>S K</td></lod<>	🖇 nd	< LØD	-Qad	S K
Muscle	< LOD	nd	< LOD	- Carlor - C	< LÔD	n độc Ngài trưởng chiến thể chiến thế	< <b>D</b> OD	🔨 nd Ö	Ű
Fluopyram-ben	zamide		1	~		~~			<u></u>
Commodity	mg/kg	TF	mg/kg 💍	TE	mg/kg	[©] TF «	mg/kg	Ŏ ŶĄĨF×	
eggs	< LOQ	nd	0.08	0.46		0.14	072	<b>0.15</b>	0
Skin with Fat	< LOQ	nd	0,64	°∽Ø.08 <u> </u> ^		9.06	0.41 (	0. <b>00</b> °	Ő
Liver	0.01	nd	Ø.16 🔊	× 0.33	Q.41	<b>∛0.26</b> ∿	°′1.4≪	.0.29	Ş
Muscle	< LOQ	nd	~~0.03 ×	0.06	× 0.09	0.06	029	~0.06 °	8
fluopyram-olefi	ins		y O'	~~~ r	V V			S S	
Commodity	mg/kg	TF [™]	mig/kg (	TF	mgAkg		0 mg/kg) QO2	, *¥ř	
eggs	< LOD		N LOD	nd	&LOD	ndÒ		0.004	
Skin with Fat	< LOD	Nnd &	< LÔQ	nd	[∞] 0.02 [∞] [∞]	0@13	0.05	[≫] 0.01	
Liver	< LOD	nd 🖓		🖉 nd 🧖	<loq td="" ĸ<=""><td></td><td>S&lt; LOQ</td><td>nd</td><td></td></loq>		S< LOQ	nd	
Muscle	< LOD	nîd A	< LOD	p.d	¢LOD ≪	nd S	0.62	0.004	

Table 6.4.1- 5:	Calculated transfer factors	(TF) in poultry
	Surveiller and an and a second	(II) m pound

### *Depuration phase:*

wêre fee at the NOX dose level for securive days, followed by untreated Three subgroups othens feeding period :

- 8 days (dose group
- 13 days (F2)
- 2Cdays (F3)

Residues were determined at sacrifice, on day 36 (P1), 41 (F2) and 49 (F3).

a

In eggs, residues of FLU-benzamide decreased from 0.83 mg/kg (day 28, mean value for eggs from group F) to 0.30 mg/kg (day 36, eggs from a) hens of group F1), @11 mg/kg (day 41, eggs from F2 and F3) and Ő 0.03 mg/kg (day 49, eggs from subgroup Fo). Ô

In tissues, fluopyram was bound to be < IOD in the three subgroups F1, F2 and F3.

Residues of FLU-benzamide were:

M In skin with at, 0.41 mg/kg on average of day 28 (dose group E) and declined to 0.12 mg/kg, 0.05 mg/kg and 0.02 mg/kg on day 36, 41 and 49 (F1, F2 and F3), respectively.

- In liver 1.4 mg/kg on average on day 28 (dose group E) and declined to 0.49 mg/kg, 0.19 mg/kg and 0.05 mg/kg on day 36, 41 and 09 (F1, F2 and F3), respectively.
- In muscle 0.29 mg/kg on average on day 28 (dose group E) and declined to 0.21 mg/kg, 0.08 mg/kg and 0.02 mg/kg on day 36, 41 and 49 (F1, F2 and F3), respectively.

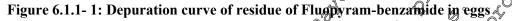
The total residues of FLU-opefins, in skin with fat, the residues were:

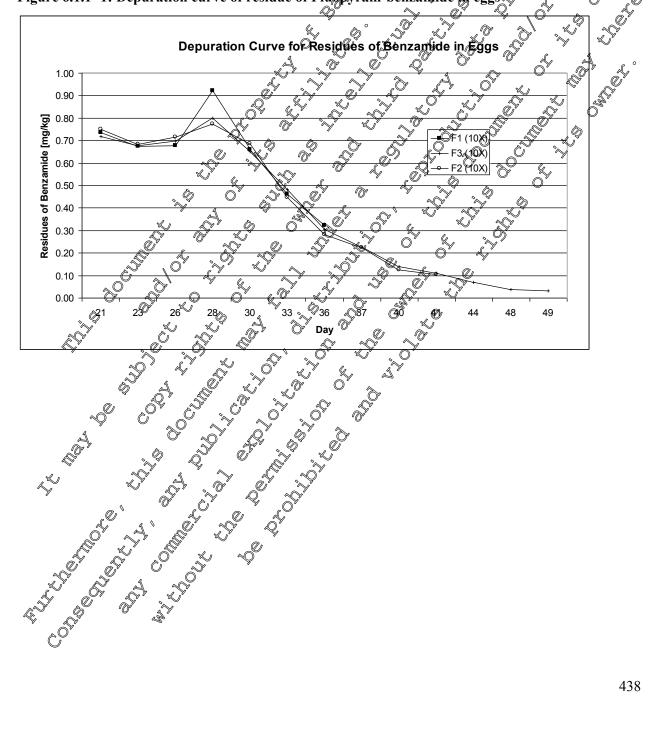
In skin with fat, 0.05 mg/kg on average on day 28 (dose group E), 0.06 mg/kg, 0.03 mg/kg and COD on day 36, 41 and 49 (F1, F2 and F3), respectively.



- In liver, 0.02 mg/kg on average on day 28 (dose group E) and declined to <0.02 mg/kg,  $<0.02^{\circ}$ • mg/kg, and <LOD on day 36, 41 and 49 (F1, F2 and F3), respectively.
- In muscle, the total residues of olefins were 0.03 mg/kg on average on day (dose group) and (dose group) and (dose group)• declined to <0.02 mg/kg, <LOD, and <LOD on day 36, 41 and 49 (F1, F2 and F3), respectively

A graphical presentation of the depuration curves for the major metabolite, fluopyratio benzamide, as presented in the Figure 6.1.1-1 and Figure 6.1.1-2. Figure 6.1.1- 1: Depuration curve of residue of Fluopyram-benzamide in eggs







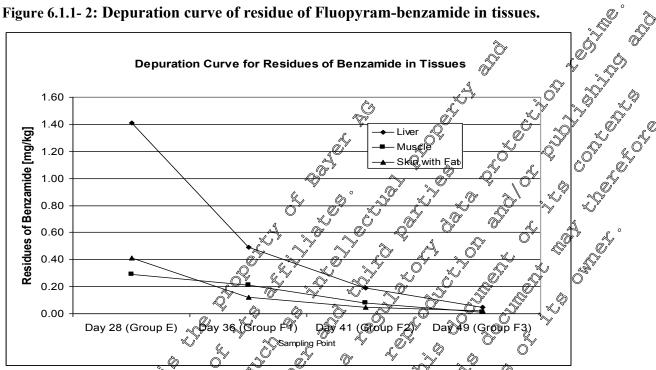


Figure 6.1.1- 2: Depuration curve of residue of Fluopyram-benzamide in tissues.

Ò According to the observed linear correlation between dose and residue levels in animal commodities after dosing, we assume that the same behavior applies during the deputation phase in the 0.1X, 1X and 3X doses.

Çoncluşions

A feeding study was conducted with fluoppram on poultry in order to elucidate the levels of relevant residues in poultry tissues and in eggs.

gs. viageed to laying hens for 28 consecutive days at the actual dose rates Fluopyrant was administered early of:

- 0 μg/kg bw. Pay (dose groop A,
- 3.4 µg/kg/w/da/ (dose group B, 0.1X),
- 35 µg/kg bw/dav (dose group)C
- 110 µg/kg bw/day @ose group D
- 320 µg/kg bw/day (dose groups F, 1025
- S30 µg/kg bw/day (dese group F, 10%)

poduction were not adversely affected by compound Feed consumption, body weights, and egg administration.

administration. sacrificed and the key edible tissues were analysed for the residues of fluopyram and its metabolites fluopyram-Denzamide, and total residues of fluopyram-olefins in all matrices. In addition, the total residues of fluopyram was determined in all animal matrices.

Overall, most of the time residues of fluopyram, and the total residues fluopyram-olefins in eggs and tissues were below the respective LOQs.



Fluoyram-benzamide was found in most of the tissue samples and this metabolite showed a clear degreesoes. During the depuration phase, the residues of fluoyyram-benzamide decreased from 0.83 ng/kg (day 28) to 0.30 mg/kg (day 36). 0.11 mg/kg (day 41) and 0.03 mg/kg (day 49). In general, the residue data provided in this study are suitable for regulatory purpose. And a stand of the second and a stand of the A consection of and the or the consection of the origination of the or



			Mean	l ô	<u>, , , , , , , , , , , , , , , , , , , </u>
Crop / Sample	FL [mg/kg]	Single values [%]	value	RSD	
material	[8]	Single values [76]	[%]	[%]	[mg/kg]
luopyram (AE	C656948) ⁽¹⁾	Č.		s de la companya de l	
	0.01	91; 96; 102; 94; 101; 97; 97;	96	4.6	
		88; 91; 97; 99	Q	1.0	o Si k
	0.10	91; 94	930 · ·	%	
Egg*	0.50	93; 97; 108; 101; 97; 99		• 5.1 <u>·</u>	λ 0.01 Č
00	1.0	94; 91; 88; 84; 100, 99; 100; 104; 98; 96; 98; 102∘	<i>~</i> 96 √	6.2	0' \$ (
	2.0	104, 98, 98, 98, 102	98		
	2.0	Overall recovery (n=32)	<b>96</b>	5.3	.r .s
	0.01	<u> </u>	96 A	 	OF OF
Liver	2.0	@91; <b>98</b> ; 102 @	97	<u>~</u> 6.2 ≪	
Enter		Qveralkrecovery (n=5)	<u></u>	4.5	
	0.01	101; <b>9</b> ; 114, <b>8</b> 0; 93	<u> </u>	128	
Muscle	2.0	104; 107; 107	N 106 O	A.6 *	
		Overall recovery (n=8)	1.0	010.3	$\sim$
	0.01	96; 95; 11 ¹ K	<b>A</b> 903	120	<pre>%</pre>
Skin with fat	2.0	\$\vee\$\vee\$\vee\$\vee\$\vee\$\vee\$\vee\$\ve	√y 96 _∿	<b>A</b> .2	© 0.01
	×,	Overall recovery (n=6)	100	×9.0 Ø	
FLU-Benzamide	(AE F148815) (24)				
	\$0.01 °	100; 98; 97; 97; 98; 90; 93; 91; 92; 99; 96 ×	° [♥] 96 ‰	3,0	
	S 0.00 .~	97:99 0 s	/ <u>98</u>	~	
	© ≈0.50 ×	© 96: 94 94: 94: 92: 95	<u> </u>	× 1.4	
Egg*	\$ 1.0¢	<b>Di</b> ; 94 <b>ci0</b> 5; 95 <b>c98</b> ; 99 <b>c1</b> 01;			0.01
Ô	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	(299; 96; 27, 96; 90)	\$ [*] 97	3.6	
	<u>\$</u> 0 %	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u>~</u>		
K V	. Ø . Ö	Overall recovery (n=32)	<b>96</b>	3.8	
		د 105; 105; 102	104	2.0	
Liver	$2.0^{\circ}$	88,91;91	° 90	1.9	0.01
		Overalk recovery (n=6)	97	8.3	
	<u>کې 0.01 کې </u>	0 106,797; 93,779; 87,57	91	9.2	
Muscle	2,00	<u>y 93; 93; 93</u>	93	0.0	0.01
		Overall recovery (n=8)	92	7.0	
	<u>\$</u> 30.01 0	© \$105;94	99		0.01
Skin with fat		<u>\$</u> 99; <b>\$</b> 99; <b>\$</b> 94	94	5.3	0.01
<u> </u>		Overall recovery (n=5)	94	8.7	
Total residues of	FLU-Oferins 🕑	× 0°		1	
Å.	A 0.02	99; 105; 112; 104; 101; 110; 107; 97; 97; 102; 99	103	5.0	
ja ka	C BO K	119; 127	123**		
a s		108; 108; 110; 112; 106; 112	123**	2.1	
, <b>Şe</b> g , S		123; 118; 112; 106; 121;	107	2.1	0.02
	S 20	122; 120; 123; 125; 122; 94;	115	10.1	
<u>Fotal residues of</u>	O S	92	110	10.1	
x Ay	4.0	79			



Crop / Sample material	FL [mg/kg]	Single values [%]	Mean value [%]	RSD [%] 10.3 5.2	LOQ [mg/kg]
		Overall recovery (n=32)	109	10.2	á ^v
	0.02	101; 106; 112	106	5.2	
Liver	4.0	84; 93; 94	90	A.1	\$02 ° a
		Overall recovery (n=6)	98	10.1	
	0.02	113; 95; 93; 72; 103 😵	95 94 5 94 5	15.9	
Muscle	4.0	92; 96; 95	94 🔗	2.2	0.92 4
		171.*	95 97	12.2 0	
	0.02	82.97.97	<u>9</u> 7 (	12.2 8.6 3.0 7.0 C	
Skin with fat	4.0	82; 97; 93 87; 82; 84	×84 ~ Ø	3.0%	$0^{\circ}$ 0 pr $a^{\circ}$
		Overall recovery $(\mathbf{x} \neq \mathbf{b})$	×84 ∘ 87√	<i>9</i> 0 °	
(2) Final determi (3) Final determi equivalents). Egg white and egg yol Egg white and egg yol	nation as: FLU-benzam nation as: FLU-olefins Both isomers were fort k are covered by egg (=	Overall recovery (n=8) 82; 97; 93 87; 82; 84 Overall recovery (n=6) rd deviation, LOQ = Practical limit of the residues calculated as: Fluopyram (E- and Z_roomer) Residues calculated a ified with a ratio of M1. whole egg without shell) 	Crotal Residue	e of metins (exp	the second as parent the second as parent the second as parent the second as parent the second as parents as a second as parents as a second as a seco
					442



Page 443 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram Ø,° 1

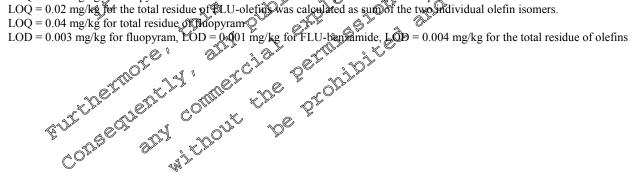
ıble 6.4.1- 7:	Residue lev	els in eggs (mea	n of 3 su			ST ^{er} vidual analyte	COPECTO S (mg/kg)	Total Resi	TEGILDO TEGILDO
Group Dose	Sampling date*	Fluopyrai	m		sup-group	Total re	values) 🖗 sidnes of 🛛 🖓 Stefins 🔬 🖉		
		Indiv.	mean	Indiv	Smean ^	Indiv.	mean		maean
	-13	3x <lod< td=""><td><lod< td=""><td>Stelop St</td><td><lod< td=""><td>3x OOD</td><td>LOD 🖗</td><td>JANLOD X</td><td>202</td></lod<></td></lod<></td></lod<>	<lod< td=""><td>Stelop St</td><td><lod< td=""><td>3x OOD</td><td>LOD 🖗</td><td>JANLOD X</td><td>202</td></lod<></td></lod<>	Stelop St	<lod< td=""><td>3x OOD</td><td>LOD 🖗</td><td>JANLOD X</td><td>202</td></lod<>	3x OOD	LOD 🖗	JANLOD X	202
	-6	3x <lod< td=""><td><lod< td=""><td>[™] 3x<lqd< td=""><td>*LOD</td><td><u>∕</u>_Ĵx<lod_∫< td=""><td>s in straight</td><td>O^Sx<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod_∫<></td></lqd<></td></lod<></td></lod<>	<lod< td=""><td>[™] 3x<lqd< td=""><td>*LOD</td><td><u>∕</u>_Ĵx<lod_∫< td=""><td>s in straight</td><td>O^Sx<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod_∫<></td></lqd<></td></lod<>	[™] 3x <lqd< td=""><td>*LOD</td><td><u>∕</u>_Ĵx<lod_∫< td=""><td>s in straight</td><td>O^Sx<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod_∫<></td></lqd<>	*LOD	<u>∕</u> _Ĵx <lod_∫< td=""><td>s in straight</td><td>O^Sx<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod_∫<>	s in straight	O ^S x <lod< td=""><td><lod< td=""></lod<></td></lod<>	<lod< td=""></lod<>
	-1	3x <lod< td=""><td><lod< td=""><td></td><td>Š (LOD *</td><td>J[™] 3x<lqd< td=""><td>K DD K</td><td>3x<lod< td=""><td>°<tod< td=""></tod<></td></lod<></td></lqd<></td></lod<></td></lod<>	<lod< td=""><td></td><td>Š (LOD *</td><td>J[™] 3x<lqd< td=""><td>K DD K</td><td>3x<lod< td=""><td>°<tod< td=""></tod<></td></lod<></td></lqd<></td></lod<>		Š (LOD *	J [™] 3x <lqd< td=""><td>K DD K</td><td>3x<lod< td=""><td>°<tod< td=""></tod<></td></lod<></td></lqd<>	K DD K	3x <lod< td=""><td>°<tod< td=""></tod<></td></lod<>	° <tod< td=""></tod<>
	0 ^b	3x <lod< td=""><td>,&lt;<b>≵</b>OD</td><td>¢ 3x<lod td="" ∞<=""><td><lqd< td=""><td></td><td>SC <lod< td=""><td>3x<lod td="" ©<=""><td><lod< td=""></lod<></td></lod></td></lod<></td></lqd<></td></lod></td></lod<>	,< <b>≵</b> OD	¢ 3x <lod td="" ∞<=""><td><lqd< td=""><td></td><td>SC <lod< td=""><td>3x<lod td="" ©<=""><td><lod< td=""></lod<></td></lod></td></lod<></td></lqd<></td></lod>	<lqd< td=""><td></td><td>SC <lod< td=""><td>3x<lod td="" ©<=""><td><lod< td=""></lod<></td></lod></td></lod<></td></lqd<>		SC <lod< td=""><td>3x<lod td="" ©<=""><td><lod< td=""></lod<></td></lod></td></lod<>	3x <lod td="" ©<=""><td><lod< td=""></lod<></td></lod>	<lod< td=""></lod<>
0.137	1	3x <lod< td=""><td>‴≫ĽOD</td><td>©[™]3x<l@d< td=""><td>_ <b>@≥ÖD</b></td><td>© x<lod O</lod </td><td>્રાજીવ</td><td>JA 3x<lqd< td=""><td><lod< td=""></lod<></td></lqd<></td></l@d<></td></lod<>	‴≫ĽOD	© [™] 3x <l@d< td=""><td>_ <b>@≥ÖD</b></td><td>© x<lod O</lod </td><td>્રાજીવ</td><td>JA 3x<lqd< td=""><td><lod< td=""></lod<></td></lqd<></td></l@d<>	_ <b>@≥ÖD</b>	© x <lod O</lod 	્રાજીવ	JA 3x <lqd< td=""><td><lod< td=""></lod<></td></lqd<>	<lod< td=""></lod<>
0.1X	2	< LOD	<lod< td=""><td><lob\$2x<loq\$< td=""><td>🖌 <loq td="" 🕉<=""><td>° 3x≤bØÐ</td><td>3 OCLOD A</td><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></loq></td></lob\$2x<loq\$<></td></lod<>	<lob\$2x<loq\$< td=""><td>🖌 <loq td="" 🕉<=""><td>° 3x≤bØÐ</td><td>3 OCLOD A</td><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></loq></td></lob\$2x<loq\$<>	🖌 <loq td="" 🕉<=""><td>° 3x≤bØÐ</td><td>3 OCLOD A</td><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></loq>	° 3x≤bØÐ	3 OCLOD A	3x <lod< td=""><td><lod< td=""></lod<></td></lod<>	<lod< td=""></lod<>
3.4 µg/kg	5	3x <lod< td=""><td>&lt; OOD</td><td>© 3x<loq< td=""><td><lod< td=""><td>X LOD</td><td>Os <lob< td=""><td>2x≪LOD; &lt;0.04</td><td>&lt; 0.04</td></lob<></td></lod<></td></loq<></td></lod<>	< OOD	© 3x <loq< td=""><td><lod< td=""><td>X LOD</td><td>Os <lob< td=""><td>2x≪LOD; &lt;0.04</td><td>&lt; 0.04</td></lob<></td></lod<></td></loq<>	<lod< td=""><td>X LOD</td><td>Os <lob< td=""><td>2x≪LOD; &lt;0.04</td><td>&lt; 0.04</td></lob<></td></lod<>	X LOD	Os <lob< td=""><td>2x≪LOD; &lt;0.04</td><td>&lt; 0.04</td></lob<>	2x≪LOD; <0.04	< 0.04
bw/day	7	36 LOD	<lodx< td=""><td>3x<loq< td=""><td>⊘,×LOD</td><td>3x<lod< td=""><td>ى D\$</td><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod<></td></loq<></td></lodx<>	3x <loq< td=""><td>⊘,×LOD</td><td>3x<lod< td=""><td>ى D\$</td><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod<></td></loq<>	⊘,×LOD	3x <lod< td=""><td>ى D\$</td><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod<>	ى D\$	3x <lod< td=""><td><lod< td=""></lod<></td></lod<>	<lod< td=""></lod<>
0.05 mg/kg	9	3x <lop< td=""><td><lod< td=""><td>AS LOQ O</td><td><lod< td=""><td>3x*ۯD</td><td>\$\$<lod o<="" td=""><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod></td></lod<></td></lod<></td></lop<>	<lod< td=""><td>AS LOQ O</td><td><lod< td=""><td>3x*ۯD</td><td>\$\$<lod o<="" td=""><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod></td></lod<></td></lod<>	AS LOQ O	<lod< td=""><td>3x*ۯD</td><td>\$\$<lod o<="" td=""><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod></td></lod<>	3x*ۯD	\$\$ <lod o<="" td=""><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod>	3x <lod< td=""><td><lod< td=""></lod<></td></lod<>	<lod< td=""></lod<>
DM	12 🔬 🖗	2x <lod loq<="" td=""><td>&lt;ĽOQ /</td><td>3x<loq< td=""><td>,≪LØD</td><td>3x<lod< td=""><td>×10\$</td><td>2x<lod; <0.04<="" td=""><td>&lt; 0.04</td></lod;></td></lod<></td></loq<></td></lod>	<ĽOQ /	3x <loq< td=""><td>,≪LØD</td><td>3x<lod< td=""><td>×10\$</td><td>2x<lod; <0.04<="" td=""><td>&lt; 0.04</td></lod;></td></lod<></td></loq<>	,≪LØD	3x <lod< td=""><td>×10\$</td><td>2x<lod; <0.04<="" td=""><td>&lt; 0.04</td></lod;></td></lod<>	×10\$	2x <lod; <0.04<="" td=""><td>&lt; 0.04</td></lod;>	< 0.04
Sub-groups:	14 mb	3x <lod< td=""><td><lod< td=""><td>× × ×</td><td>CONSTRUCTION</td><td>O 3x<lod< td=""><td>SEOD</td><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod<></td></lod<></td></lod<>	<lod< td=""><td>× × ×</td><td>CONSTRUCTION</td><td>O 3x<lod< td=""><td>SEOD</td><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod<></td></lod<>	× × ×	CONSTRUCTION	O 3x <lod< td=""><td>SEOD</td><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod<>	SEOD	3x <lod< td=""><td><lod< td=""></lod<></td></lod<>	<lod< td=""></lod<>
B1, B2, B3	16	3x <lqq< td=""><td>_&lt;¢QD</td><td>€39&lt;<loq ()<="" td="" ~=""><td><l.@d< td=""><td>3x TOD</td><td>S CLOD</td><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></l.@d<></td></loq></td></lqq<>	_<¢QD	€39< <loq ()<="" td="" ~=""><td><l.@d< td=""><td>3x TOD</td><td>S CLOD</td><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></l.@d<></td></loq>	<l.@d< td=""><td>3x TOD</td><td>S CLOD</td><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></l.@d<>	3x TOD	S CLOD	3x <lod< td=""><td><lod< td=""></lod<></td></lod<>	<lod< td=""></lod<>
	21	3x€20D _%	LOD	⊴ 3x⊲LØØ	s <lod< td=""><td>Ø, 3x<lod.< td=""><td><lod< td=""><td>3x<loq< td=""><td>&lt; 0.04</td></loq<></td></lod<></td></lod.<></td></lod<>	Ø, 3x <lod.< td=""><td><lod< td=""><td>3x<loq< td=""><td>&lt; 0.04</td></loq<></td></lod<></td></lod.<>	<lod< td=""><td>3x<loq< td=""><td>&lt; 0.04</td></loq<></td></lod<>	3x <loq< td=""><td>&lt; 0.04</td></loq<>	< 0.04
	23	, ∜Øx <lod< td=""><td><lo(< td=""><td>3. OLOQ</td><td>-<lod< td=""><td></td><td><lod< td=""><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod<></td></lod<></td></lo(<></td></lod<>	<lo(< td=""><td>3. OLOQ</td><td>-<lod< td=""><td></td><td><lod< td=""><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod<></td></lod<></td></lo(<>	3. OLOQ	- <lod< td=""><td></td><td><lod< td=""><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod<></td></lod<>		<lod< td=""><td>3x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod<>	3x <lod< td=""><td><lod< td=""></lod<></td></lod<>	<lod< td=""></lod<>
	26	© 3x <lod< td=""><td>_≪LOD</td><td>3x<loq< td=""><td><lod< td=""><td>∂x<lod< td=""><td><lod< td=""><td>2x<lod; <0.04<="" td=""><td>&lt; 0.04</td></lod;></td></lod<></td></lod<></td></lod<></td></loq<></td></lod<>	_≪LOD	3x <loq< td=""><td><lod< td=""><td>∂x<lod< td=""><td><lod< td=""><td>2x<lod; <0.04<="" td=""><td>&lt; 0.04</td></lod;></td></lod<></td></lod<></td></lod<></td></loq<>	<lod< td=""><td>∂x<lod< td=""><td><lod< td=""><td>2x<lod; <0.04<="" td=""><td>&lt; 0.04</td></lod;></td></lod<></td></lod<></td></lod<>	∂x <lod< td=""><td><lod< td=""><td>2x<lod; <0.04<="" td=""><td>&lt; 0.04</td></lod;></td></lod<></td></lod<>	<lod< td=""><td>2x<lod; <0.04<="" td=""><td>&lt; 0.04</td></lod;></td></lod<>	2x <lod; <0.04<="" td=""><td>&lt; 0.04</td></lod;>	< 0.04
		30 LOD	-			[™] 3x <lod< td=""><td><lod< td=""><td>2x<lod; <0.04<="" td=""><td>&lt; 0.04</td></lod;></td></lod<></td></lod<>	<lod< td=""><td>2x<lod; <0.04<="" td=""><td>&lt; 0.04</td></lod;></td></lod<>	2x <lod; <0.04<="" td=""><td>&lt; 0.04</td></lod;>	< 0.04

In case we have 3 levels of which at least one is <LOD and others LOQ, it was legitimate to set the mean value as <LOQ;

When one or two individual values are >LOQ and the others LOQ or LOD, residues <LOQ or LOD are considered equal to LOQ or LOD

LOQ = 0.01 mg/kg for fhiopyram and the benzamide metabolite, expressed as parent equivalents.

LOQ = 0.02 mg/kg for the total residue of ELU-olefing was calculated as sum of the two individual olefin isomers.

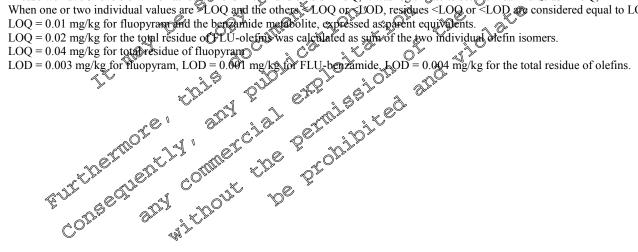




					Å	P.G	at 7 Silo	, ce	jing and
				Residue levels	of individ	lual analytes 🖗	@¥ ng/kg)		P T P F
Group Dose	Sampling date*	Fluopy	ram	FLU-benzar	nide		sidues of	Total F	pyram
		Indiv.	mean	Indiv.	mean	NO Indix, O	mean	¶¶¶¶¶¶¶¶¶	m@n
	-13	3x <lod< td=""><td><lod< td=""><td>3xKLOD 🔬 🌀</td><td></td><td>° 3x≤EQD</td><td>¥OD S</td><td>3x<lod< td=""><td>€ O[®]LOD</td></lod<></td></lod<></td></lod<>	<lod< td=""><td>3xKLOD 🔬 🌀</td><td></td><td>° 3x≤EQD</td><td>¥OD S</td><td>3x<lod< td=""><td>€ O[®]LOD</td></lod<></td></lod<>	3xKLOD 🔬 🌀		° 3x≤EQD	¥OD S	3x <lod< td=""><td>€ O[®]LOD</td></lod<>	€ O [®] LOD
	-6	3x <lod< td=""><td><lod< td=""><td>C3x<lqd< td=""><td>୍ୟୁଡ଼ିଅ</td><td>30 LOD</td><td><lod< td=""><td>3x<lod< td=""><td>≥[™] <lod< td=""></lod<></td></lod<></td></lod<></td></lqd<></td></lod<></td></lod<>	<lod< td=""><td>C3x<lqd< td=""><td>୍ୟୁଡ଼ିଅ</td><td>30 LOD</td><td><lod< td=""><td>3x<lod< td=""><td>≥[™] <lod< td=""></lod<></td></lod<></td></lod<></td></lqd<></td></lod<>	C3x <lqd< td=""><td>୍ୟୁଡ଼ିଅ</td><td>30 LOD</td><td><lod< td=""><td>3x<lod< td=""><td>≥[™] <lod< td=""></lod<></td></lod<></td></lod<></td></lqd<>	୍ୟୁଡ଼ିଅ	30 LOD	<lod< td=""><td>3x<lod< td=""><td>≥[™] <lod< td=""></lod<></td></lod<></td></lod<>	3x <lod< td=""><td>≥[™] <lod< td=""></lod<></td></lod<>	≥ [™] <lod< td=""></lod<>
	-1	3x <lod< td=""><td><lod< td=""><td>OF 3X KOB</td><td>×LOD &amp;</td><td>3x<loio< td=""><td>ACOD 3</td><td>[™]3x<lode<sup>™</lode<sup></td><td><lod< td=""></lod<></td></loio<></td></lod<></td></lod<>	<lod< td=""><td>OF 3X KOB</td><td>×LOD &amp;</td><td>3x<loio< td=""><td>ACOD 3</td><td>[™]3x<lode<sup>™</lode<sup></td><td><lod< td=""></lod<></td></loio<></td></lod<>	OF 3X KOB	×LOD &	3x <loio< td=""><td>ACOD 3</td><td>[™]3x<lode<sup>™</lode<sup></td><td><lod< td=""></lod<></td></loio<>	ACOD 3	[™] 3x <lode<sup>™</lode<sup>	<lod< td=""></lod<>
	0	3x <lod< td=""><td><lod *<="" td=""><td>Bollon O</td><td><lqb< td=""><td>3x≪∎OD</td><td><lod< td=""><td>3x≪KØĎ</td><td><lod< td=""></lod<></td></lod<></td></lqb<></td></lod></td></lod<>	<lod *<="" td=""><td>Bollon O</td><td><lqb< td=""><td>3x≪∎OD</td><td><lod< td=""><td>3x≪KØĎ</td><td><lod< td=""></lod<></td></lod<></td></lqb<></td></lod>	Bollon O	<lqb< td=""><td>3x≪∎OD</td><td><lod< td=""><td>3x≪KØĎ</td><td><lod< td=""></lod<></td></lod<></td></lqb<>	3x≪∎OD	<lod< td=""><td>3x≪KØĎ</td><td><lod< td=""></lod<></td></lod<>	3x≪KØĎ	<lod< td=""></lod<>
	1	3x <lod< td=""><td>stop</td><td>GLOD; 2x<løq< td=""><td>× ACOQ</td><td>&amp; Ox COD</td><td></td><td>≪stx<lod< td=""><td><loq< td=""></loq<></td></lod<></td></løq<></td></lod<>	stop	GLOD; 2x <løq< td=""><td>× ACOQ</td><td>&amp; Ox COD</td><td></td><td>≪stx<lod< td=""><td><loq< td=""></loq<></td></lod<></td></løq<>	× ACOQ	& Ox COD		≪stx <lod< td=""><td><loq< td=""></loq<></td></lod<>	<loq< td=""></loq<>
1X	2	3x <lod< td=""><td>K LOD</td><td>3300.001</td><td>0.01</td><td>≫ 3x<lod″< td=""><td>€OD ∢</td><td>S[©]3x<lqq°< td=""><td><loq< td=""></loq<></td></lqq°<></td></lod″<></td></lod<>	K LOD	3300.001	0.01	≫ 3x <lod″< td=""><td>€OD ∢</td><td>S[©]3x<lqq°< td=""><td><loq< td=""></loq<></td></lqq°<></td></lod″<>	€OD ∢	S [©] 3x <lqq°< td=""><td><loq< td=""></loq<></td></lqq°<>	<loq< td=""></loq<>
35 μg/kg bw/day	5	3x <lod< td=""><td>S <lous< td=""><td>2x0.04; 0.03</td><td>0.00</td><td></td><td>C <lod< td=""><td>2x0,05, 0.04</td><td>0.05</td></lod<></td></lous<></td></lod<>	S <lous< td=""><td>2x0.04; 0.03</td><td>0.00</td><td></td><td>C <lod< td=""><td>2x0,05, 0.04</td><td>0.05</td></lod<></td></lous<>	2x0.04; 0.03	0.00		C <lod< td=""><td>2x0,05, 0.04</td><td>0.05</td></lod<>	2x0,05, 0.04	0.05
0.49  mg/kg DM	7	3x <lod< td=""><td>_ ₹LÕD</td><td>∞²x0.05; 0.04</td><td>A @.05</td><td>Jac-LODer</td><td><u> A</u>ØD</td><td><b>2x</b>0.06; 0.05</td><td>0.06</td></lod<>	_ ₹LÕD	∞ ² x0.05; 0.04	A @.05	Jac-LODer	<u> A</u> ØD	<b>2x</b> 0.06; 0.05	0.06
Sub-groups:	9	3x <lod< td=""><td> ↓ LOD ♀</td><td>2x0,06; 0.05</td><td>0.06</td><td>3x&lt;€00</td><td>CVLOD &amp;</td><td>2x0.07; 0.06</td><td>0.07</td></lod<>	↓ LOD ♀	2x0,06; 0.05	0.06	3x<€00	CVLOD &	2x0.07; 0.06	0.07
C1, C2, C3	12	2x <l00; <l0q<="" td=""><td><lqq< td=""><td><b>SX</b>0.07; 0,06</td><td>0.07</td><td>、 ðax<lod td="" ∧<=""><td>O <lob< td=""><td>2x0.07; 0.08</td><td>0.07</td></lob<></td></lod></td></lqq<></td></l00;>	<lqq< td=""><td><b>SX</b>0.07; 0,06</td><td>0.07</td><td>、 ðax<lod td="" ∧<=""><td>O <lob< td=""><td>2x0.07; 0.08</td><td>0.07</td></lob<></td></lod></td></lqq<>	<b>SX</b> 0.07; 0,06	0.07	、 ðax <lod td="" ∧<=""><td>O <lob< td=""><td>2x0.07; 0.08</td><td>0.07</td></lob<></td></lod>	O <lob< td=""><td>2x0.07; 0.08</td><td>0.07</td></lob<>	2x0.07; 0.08	0.07
C1, C2, C3	14	OC3x <lodo< td=""><td>, SEOD</td><td>, 3x0,00</td><td>∞ 0.06%</td><td>3x<lqd td="" €<=""><td><b>4</b>.OD</td><td>3x0.07</td><td>0.07</td></lqd></td></lodo<>	, SEOD	, 3x0,00	∞ 0.06%	3x <lqd td="" €<=""><td><b>4</b>.OD</td><td>3x0.07</td><td>0.07</td></lqd>	<b>4</b> .OD	3x0.07	0.07
	16	0 ³ 3x≤000D	S COR S	J\$x0.06	0_06 🏷	330100D	CLOD CLOD	3x0.07	0.07
	21	3x <lod 3x<lod< td=""><td>QD</td><td>∕2x0.08; 0.09</td><td><u>()</u>.08</td><td>Š\$₹<lod_₹< td=""><td><pre>LOD</pre></td><td>2x0.09; 0.10</td><td>0.09</td></lod_₹<></td></lod<></lod 	QD	∕2x0.08; 0.09	<u>()</u> .08	Š\$₹ <lod_₹< td=""><td><pre>LOD</pre></td><td>2x0.09; 0.10</td><td>0.09</td></lod_₹<>	<pre>LOD</pre>	2x0.09; 0.10	0.09
	23	3x <lod< td=""><td>QLOD C</td><td>2x0.07; 0.08</td><td>) 0.07 🖉</td><td>&gt; 3x<l@< td=""><td><lod< td=""><td>2x0.08; 0.09</td><td>0.08</td></lod<></td></l@<></td></lod<>	QLOD C	2x0.07; 0.08	) 0.07 🖉	> 3x <l@< td=""><td><lod< td=""><td>2x0.08; 0.09</td><td>0.08</td></lod<></td></l@<>	<lod< td=""><td>2x0.08; 0.09</td><td>0.08</td></lod<>	2x0.08; 0.09	0.08
	26	3xCLOD X	S <lqd< td=""><td>¥x0.07 √</td><td>0,07</td><td>3x€LOD</td><td><lod< td=""><td>3x0.08</td><td>0.08</td></lod<></td></lqd<>	¥x0.07 √	0,07	3x€LOD	<lod< td=""><td>3x0.08</td><td>0.08</td></lod<>	3x0.08	0.08
In ango wa hava 2 lava	28	X <lod< td=""><td><b>BOD</b></td><td>2x0.08;@.09</td><td><b>6.08</b></td><td>©3x<lod< td=""><td><lod< td=""><td>2x0.09; 0.10</td><td>0.09</td></lod<></td></lod<></td></lod<>	<b>BOD</b>	2x0.08;@.09	<b>6.08</b>	©3x <lod< td=""><td><lod< td=""><td>2x0.09; 0.10</td><td>0.09</td></lod<></td></lod<>	<lod< td=""><td>2x0.09; 0.10</td><td>0.09</td></lod<>	2x0.09; 0.10	0.09

In case we have 3 levels of which at least one is <LQD and others LOQ, it was legitimate to set the mean value as <LOQ;

When one or two individual values are LOQ and the others LOQ or LOD, residues <LOQ or <LOD are considered equal to LOQ or LOD



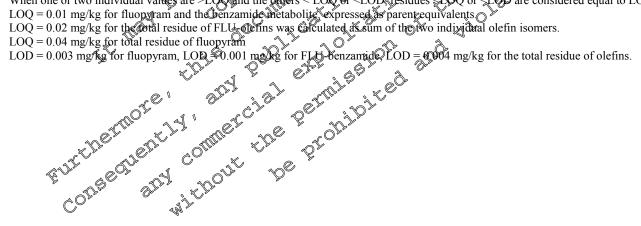


					«C.	PÇ.	£.J. 870	ye ^{oj}	209 Jug
	S					lual analytes (mg/l individuat values)	kg) **	AT A She	Ġ
Group Dose	Sampling date	Fluopy	ram	FLU-benzan	nides °	Total residu	es of 🔊	Of otal Re	yram _© ,
		Indiv.	mean	Indiv. 🔬 🔗	[∨] meap _h ∛	Indiv.	mean	Ind W. (	, 🔿 mean
	-13	<lod< td=""><td><lod< td=""><td>C CLOD</td><td>્ય છેઈ</td><td>Jo KLOD K</td><td><body></body></td><td></td><td>LOD</td></lod<></td></lod<>	<lod< td=""><td>C CLOD</td><td>્ય છેઈ</td><td>Jo KLOD K</td><td><body></body></td><td></td><td>LOD</td></lod<>	C CLOD	્ય છેઈ	Jo KLOD K	<body></body>		LOD
	-6	<lod< td=""><td><lod td="" 🖉<=""><td>ÔF 4.60</td><td>×LOD 🌫</td><td>CLOQ CO</td><td>SLOD &gt;</td><td>K <lode< td=""><td><lod< td=""></lod<></td></lode<></td></lod></td></lod<>	<lod td="" 🖉<=""><td>ÔF 4.60</td><td>×LOD 🌫</td><td>CLOQ CO</td><td>SLOD &gt;</td><td>K <lode< td=""><td><lod< td=""></lod<></td></lode<></td></lod>	ÔF 4.60	×LOD 🌫	CLOQ CO	SLOD >	K <lode< td=""><td><lod< td=""></lod<></td></lode<>	<lod< td=""></lod<>
	-1	<lod< td=""><td><lod td="" 🎾<="" 🖓=""><td>BOD N</td><td><lqbc< td=""><td>OD</td><td><lod< td=""><td>″ &lt;<b>K</b>ØĎ</td><td><lod< td=""></lod<></td></lod<></td></lqbc<></td></lod></td></lod<>	<lod td="" 🎾<="" 🖓=""><td>BOD N</td><td><lqbc< td=""><td>OD</td><td><lod< td=""><td>″ &lt;<b>K</b>ØĎ</td><td><lod< td=""></lod<></td></lod<></td></lqbc<></td></lod>	BOD N	<lqbc< td=""><td>OD</td><td><lod< td=""><td>″ &lt;<b>K</b>ØĎ</td><td><lod< td=""></lod<></td></lod<></td></lqbc<>	OD	<lod< td=""><td>″ &lt;<b>K</b>ØĎ</td><td><lod< td=""></lod<></td></lod<>	″ < <b>K</b> ØĎ	<lod< td=""></lod<>
	0	3x <lod< td=""><td>SK OD</td><td>∫ G 3x<lod< td=""><td>× SCOD</td><td>× O3x<lodo< td=""><td><løď< td=""><td>_a∯x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></løď<></td></lodo<></td></lod<></td></lod<>	SK OD	∫ G 3x <lod< td=""><td>× SCOD</td><td>× O3x<lodo< td=""><td><løď< td=""><td>_a∯x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></løď<></td></lodo<></td></lod<>	× SCOD	× O3x <lodo< td=""><td><løď< td=""><td>_a∯x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></løď<></td></lodo<>	<løď< td=""><td>_a∯x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></løď<>	_a∯x <lod< td=""><td><lod< td=""></lod<></td></lod<>	<lod< td=""></lod<>
	1	3x <lod< td=""><td>لاً ČDD</td><td>3x0.901</td><td>0.01</td><td>≫ 3x≤tQOD "</td><td>LOD «</td><td>10 3x0 02 °</td><td>&lt; 0.04</td></lod<>	لاً ČDD	3x0.901	0.01	≫ 3x≤tQOD "	LOD «	10 3x0 02 °	< 0.04
3X	2	3x <lod< td=""><td>S <lois< td=""><td>2x0.03; 0.02</td><td>0.03</td><td>A34×LOD 0</td><td><lqd< td=""><td>2x0.04; 0.03</td><td>0.04</td></lqd<></td></lois<></td></lod<>	S <lois< td=""><td>2x0.03; 0.02</td><td>0.03</td><td>A34×LOD 0</td><td><lqd< td=""><td>2x0.04; 0.03</td><td>0.04</td></lqd<></td></lois<>	2x0.03; 0.02	0.03	A34×LOD 0	<lqd< td=""><td>2x0.04; 0.03</td><td>0.04</td></lqd<>	2x0.04; 0.03	0.04
110 µg/kg	5	3x <lod< td=""><td>, ≰LOD</td><td>3x0,10</td><td>Q. 10</td><td>C 3x<lod< td=""><td><b>∂</b>¶2ÓD</td><td>3x0.11</td><td>0.11</td></lod<></td></lod<>	, ≰LOD	3x0,10	Q. 10	C 3x <lod< td=""><td><b>∂</b>¶2ÓD</td><td>3x0.11</td><td>0.11</td></lod<>	<b>∂</b> ¶2ÓD	3x0.11	0.11
bw/day	7	3x <lod< td=""><td>No LOD</td><td>200.13</td><td>0.13</td><td>3 POD</td><td>LOD&amp;</td><td>3x0.14</td><td>0.14</td></lod<>	No LOD	200.13	0.13	3 POD	LOD&	3x0.14	0.14
1.6 mg/kg DM	9	3 KLOD	<lqd< td=""><td>3x0.15</td><td>0.15</td><td>s ⊜3x<lod< td=""><td><lqd< td=""><td>3x0.16</td><td>0.16</td></lqd<></td></lod<></td></lqd<>	3x0.15	0.15	s ⊜3x <lod< td=""><td><lqd< td=""><td>3x0.16</td><td>0.16</td></lqd<></td></lod<>	<lqd< td=""><td>3x0.16</td><td>0.16</td></lqd<>	3x0.16	0.16
Sub-groups:	12	, 25 €LOD; ∢I@Q	, CLOQ	2x0.12 0.18	∞ \$0.17	S [™] 3x <lod< td=""><td>€≲LOD</td><td>2x0.17; 0.19</td><td>0.18</td></lod<>	€≲LOD	2x0.17; 0.19	0.18
D1, D2, D3	14	0 3x≲ <b>(@</b> )D	C School Contraction	3x0.17	0,17	AXXLOD	<lod< td=""><td>3x0.18</td><td>0.18</td></lod<>	3x0.18	0.18
	16	Do LOD	≪¢OD	3x0.18	6.18	x <lobc td="" ♥<=""><td><lod< td=""><td>3x0.19</td><td>0.19</td></lod<></td></lobc>	<lod< td=""><td>3x0.19</td><td>0.19</td></lod<>	3x0.19	0.19
	21 1	3x <lod< td=""><td>QLOD</td><td>0.20; 0.22; 0.23</td><td>0.22</td><td>≥ 3x&lt;000D</td><td><lod< td=""><td>0.21, 0.23, 0.24</td><td>0.23</td></lod<></td></lod<>	QLOD	0.20; 0.22; 0.23	0.22	≥ 3x<000D	<lod< td=""><td>0.21, 0.23, 0.24</td><td>0.23</td></lod<>	0.21, 0.23, 0.24	0.23
	23	3xCLOD	S <lqd< td=""><td>x 0.20; 0.24</td><td>0,20</td><td><b>≸x</b><lod< td=""><td><lod< td=""><td>2x0.21, 0.22</td><td>0.21</td></lod<></td></lod<></td></lqd<>	x 0.20; 0.24	0,20	<b>≸x</b> <lod< td=""><td><lod< td=""><td>2x0.21, 0.22</td><td>0.21</td></lod<></td></lod<>	<lod< td=""><td>2x0.21, 0.22</td><td>0.21</td></lod<>	2x0.21, 0.22	0.21
	26	X <lqd< td=""><td>SCOD ≦</td><td>≥2x0.20;@≥21</td><td>Ø.20</td><td>@x<lod; <loq<="" td=""><td><loq< td=""><td>2x0.22; 0.21</td><td>0.22</td></loq<></td></lod;></td></lqd<>	SCOD ≦	≥2x0.20;@≥21	Ø.20	@x <lod; <loq<="" td=""><td><loq< td=""><td>2x0.22; 0.21</td><td>0.22</td></loq<></td></lod;>	<loq< td=""><td>2x0.22; 0.21</td><td>0.22</td></loq<>	2x0.22; 0.21	0.22
	28	Ĵ 3x <lod< td=""><td></td><td>0.20; 22; 0.23</td><td>0.22 🏷</td><td>2x<lod; <loq<="" td=""><td><loq< td=""><td>0.22; 0.24; 0.25</td><td>0.24</td></loq<></td></lod;></td></lod<>		0.20; 22; 0.23	0.22 🏷	2x <lod; <loq<="" td=""><td><loq< td=""><td>0.22; 0.24; 0.25</td><td>0.24</td></loq<></td></lod;>	<loq< td=""><td>0.22; 0.24; 0.25</td><td>0.24</td></loq<>	0.22; 0.24; 0.25	0.24

In case we have 3 levels of which at least one is LOD and others < LOQ, It was legitimate to set the mean range alue as <LOQ;

When one or two individual values are >LOGORI the others < LOQOR <LOD vesticutes \$200 or <LOP are considered equal to LOQ or LOD

LOO = 0.01 mg/kg for fluonyram and the enzamide inetabolite expressed as parent equivalents



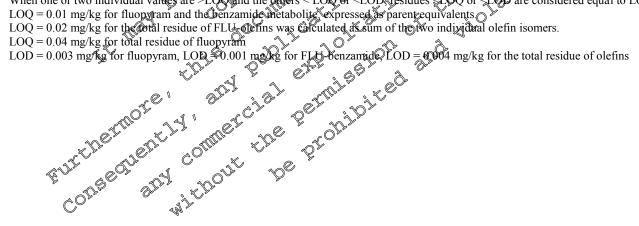


						PĜ	6.J 9.D	ye ^{oj}	209 grad
	6 P					lual analytes (mg/l individual values) Total residu ELC olefi Indiv.	kg) **	Still a jelli	¥ \$
Group Dose	Sampling date	Fluopy	ram	FLU-benz:	amide ^o °	Total residu	es of K	Of of Fluor	sidue yram⊘
		Indiv.	mean		» ^{Sy} mean ^A	Indiv.	Vmean S		) 🖉 mean
	-13	<lod< td=""><td><lod< td=""><td></td><td></td><td>O. KLOD K</td><td>&lt; OD</td><td>C</td><td>LOD</td></lod<></td></lod<>	<lod< td=""><td></td><td></td><td>O. KLOD K</td><td>&lt; OD</td><td>C</td><td>LOD</td></lod<>			O. KLOD K	< OD	C	LOD
	-6	<lod< td=""><td><lod "<="" td=""><td>OF <fod< td=""><td>ALOD &amp;</td><td><lod correction<="" td=""><td>SLOD 2</td><td>Se <lode< td=""><td><lod< td=""></lod<></td></lode<></td></lod></td></fod<></td></lod></td></lod<>	<lod "<="" td=""><td>OF <fod< td=""><td>ALOD &amp;</td><td><lod correction<="" td=""><td>SLOD 2</td><td>Se <lode< td=""><td><lod< td=""></lod<></td></lode<></td></lod></td></fod<></td></lod>	OF <fod< td=""><td>ALOD &amp;</td><td><lod correction<="" td=""><td>SLOD 2</td><td>Se <lode< td=""><td><lod< td=""></lod<></td></lode<></td></lod></td></fod<>	ALOD &	<lod correction<="" td=""><td>SLOD 2</td><td>Se <lode< td=""><td><lod< td=""></lod<></td></lode<></td></lod>	SLOD 2	Se <lode< td=""><td><lod< td=""></lod<></td></lode<>	<lod< td=""></lod<>
	-1	<lod< td=""><td><lod td="" ®<=""><td>ALOD</td><td>&lt; LOD</td><td>, ALOD</td><td><lod< td=""><td>≪KØĎ</td><td><lod< td=""></lod<></td></lod<></td></lod></td></lod<>	<lod td="" ®<=""><td>ALOD</td><td>&lt; LOD</td><td>, ALOD</td><td><lod< td=""><td>≪KØĎ</td><td><lod< td=""></lod<></td></lod<></td></lod>	ALOD	< LOD	, ALOD	<lod< td=""><td>≪KØĎ</td><td><lod< td=""></lod<></td></lod<>	≪KØĎ	<lod< td=""></lod<>
	0	3x <lod< td=""><td><u>≪L</u>@D</td><td>∫ Ĝ 3x<lod td="" ≫<=""><td>,≨1\$©D</td><td>× O3x<lodo< td=""><td><lqd< td=""><td>AL<tod< td=""><td><lod< td=""></lod<></td></tod<></td></lqd<></td></lodo<></td></lod></td></lod<>	<u>≪L</u> @D	∫ Ĝ 3x <lod td="" ≫<=""><td>,≨1\$©D</td><td>× O3x<lodo< td=""><td><lqd< td=""><td>AL<tod< td=""><td><lod< td=""></lod<></td></tod<></td></lqd<></td></lodo<></td></lod>	,≨1\$©D	× O3x <lodo< td=""><td><lqd< td=""><td>AL<tod< td=""><td><lod< td=""></lod<></td></tod<></td></lqd<></td></lodo<>	<lqd< td=""><td>AL<tod< td=""><td><lod< td=""></lod<></td></tod<></td></lqd<>	AL <tod< td=""><td><lod< td=""></lod<></td></tod<>	<lod< td=""></lod<>
	1	3x <lod< td=""><td>KLOD 3</td><td>2x0.03 9.02</td><td>0.03</td><td>≫ 3x≤tQOD _</td><td>Kelod</td><td>2x0.04;0.03</td><td>0.04</td></lod<>	KLOD 3	2x0.03 9.02	0.03	≫ 3x≤tQOD _	Kelod	2x0.04;0.03	0.04
10X	2	3x <lod< td=""><td>S <lob< td=""><td>2a0.09; 0.10 S</td><td>0.000</td><td>ANK LOD OF</td><td><lqq< td=""><td>2x0,10; 0.11</td><td>0.10</td></lqq<></td></lob<></td></lod<>	S <lob< td=""><td>2a0.09; 0.10 S</td><td>0.000</td><td>ANK LOD OF</td><td><lqq< td=""><td>2x0,10; 0.11</td><td>0.10</td></lqq<></td></lob<>	2a0.09; 0.10 S	0.000	ANK LOD OF	<lqq< td=""><td>2x0,10; 0.11</td><td>0.10</td></lqq<>	2x0,10; 0.11	0.10
320 µg/kg	5	3x <lod< td=""><td>≨LOD</td><td>2x0.35; 0.38</td><td>N &amp;36</td><td>^O 3x<lqq< td=""><td><b>∂</b>¶2ÓD</td><td><b>A</b>x0.36; 0.39</td><td>0.37</td></lqq<></td></lod<>	≨LOD	2x0.35; 0.38	N &36	^O 3x <lqq< td=""><td><b>∂</b>¶2ÓD</td><td><b>A</b>x0.36; 0.39</td><td>0.37</td></lqq<>	<b>∂</b> ¶2ÓD	<b>A</b> x0.36; 0.39	0.37
bw/day	7	3x <lod< td=""><td>Selon \$</td><td>2x0 6, 0.43</td><td>0.45</td><td>2x<loq,<lod< td=""><td>LOQG</td><td>2x0.47; 0.44</td><td>0.46</td></loq,<lod<></td></lod<>	Selon \$	2x0 6, 0.43	0.45	2x <loq,<lod< td=""><td>LOQG</td><td>2x0.47; 0.44</td><td>0.46</td></loq,<lod<>	LOQG	2x0.47; 0.44	0.46
4.8 mg/kg DM	9	3 KLOD	<lqd< td=""><td>0.50, 0.54; 0.45</td><td>0.50</td><td>s ⊜3x<loq o<="" td=""><td><l'qq< td=""><td>0.51;0.55; 0.46</td><td>0.51</td></l'qq<></td></loq></td></lqd<>	0.50, 0.54; 0.45	0.50	s ⊜3x <loq o<="" td=""><td><l'qq< td=""><td>0.51;0.55; 0.46</td><td>0.51</td></l'qq<></td></loq>	<l'qq< td=""><td>0.51;0.55; 0.46</td><td>0.51</td></l'qq<>	0.51;0.55; 0.46	0.51
Sub-groups:	12	OC3x <lodo< td=""><td>, CEOD</td><td>2x0.56,0.64</td><td>0.59</td><td>3x<loq< td=""><td>.≪sLOQ</td><td>0.57; 0.65; 0.57</td><td>0.60</td></loq<></td></lodo<>	, CEOD	2x0.56,0.64	0.59	3x <loq< td=""><td>.≪sLOQ</td><td>0.57; 0.65; 0.57</td><td>0.60</td></loq<>	.≪sLOQ	0.57; 0.65; 0.57	0.60
E1, E2, E3	14	O 3x≲tooD	Stop St	0.57, 0.62; 0.50		AXXLOQ	<loq< td=""><td>0.58; 0.63; 0.51</td><td>0.57</td></loq<>	0.58; 0.63; 0.51	0.57
	16	2x<000; <l00< td=""><td>. ≪¢QQ</td><td>0,63, 0.57, 0, 37</td><td>0.62</td><td>3x<lq@< td=""><td><loq< td=""><td>0.64; 0.68; 0.58</td><td>0.64</td></loq<></td></lq@<></td></l00<>	. ≪¢QQ	0,63, 0.57, 0, 37	0.62	3x <lq@< td=""><td><loq< td=""><td>0.64; 0.68; 0.58</td><td>0.64</td></loq<></td></lq@<>	<loq< td=""><td>0.64; 0.68; 0.58</td><td>0.64</td></loq<>	0.64; 0.68; 0.58	0.64
	21 1	3x <lod< td=""><td></td><td>0.70, 0.70, 0.71</td><td>0.72</td><td>3x&lt;0000</td><td><loq< td=""><td>0.71; 0.77; 0.72</td><td>0.73</td></loq<></td></lod<>		0.70, 0.70, 0.71	0.72	3x<0000	<loq< td=""><td>0.71; 0.77; 0.72</td><td>0.73</td></loq<>	0.71; 0.77; 0.72	0.73
	23	3xCLOD	S <lqd< td=""><td>0,76, 0.71, 0.6</td><td>0.20</td><td>0.00, 2x<loq< td=""><td>0.02</td><td>0.77; 0.72; 0.65</td><td>0.71</td></loq<></td></lqd<>	0,76, 0.71, 0.6	0.20	0.00, 2x <loq< td=""><td>0.02</td><td>0.77; 0.72; 0.65</td><td>0.71</td></loq<>	0.02	0.77; 0.72; 0.65	0.71
	26	X <lqd< td=""><td></td><td>0.69; 0.67 0.75</td><td>6.70</td><td>@0.02, 2x<loq< td=""><td>0.02</td><td>0.70; 0.68; 0.76</td><td>0.71</td></loq<></td></lqd<>		0.69; 0.67 0.75	6.70	@0.02, 2x <loq< td=""><td>0.02</td><td>0.70; 0.68; 0.76</td><td>0.71</td></loq<>	0.02	0.70; 0.68; 0.76	0.71
	28	Ĵ 3x<⊾ØĎ	C LOD	0.76; 074; 0.65	SN 0.72 K	2x0.02; LOQ	0.02	0.77; 0.75; 0.66	0.73

In case we have 3 levels of which at least one is LOD and others < LOQ, It was legitimate to set the mean range alue as <LOQ;

When one or two individual values are >LOQ and the others < LOQ of <LOD are slove side or <LOP are considered equal to LOQ or LOD

LOO = 0.01 mg/kg for fluonyram and the enzamide inetabolite expressed as parent equivalents



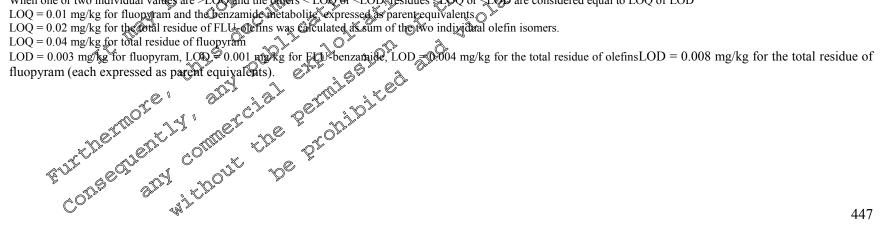


					a f	p ^G	CTI OD	~~~~	LLU OLDO
	Same lin a			Residue leve Mean of 3 s	els of individ ub groups (	lual analytes (mg individuat walues	/kg) ) **(	2 ^{t,1} 0 ¹ ,19 ¹	, Ô
Group Dose	Sampling date*	Fluopyr	am	FLU-benza		Total resid	ues of 🔊	Of otal Re	sidue
		Indiv.	mean		<b>S^Vmean</b> K	Ipdiv.	mean	Ind®.	) 🔿 mean
	-13	<lod< td=""><td><lod< td=""><td>Stop, 7</td><td></td><td></td><td></td><td>a <lod td="" 。<=""><td>LOD</td></lod></td></lod<></td></lod<>	<lod< td=""><td>Stop, 7</td><td></td><td></td><td></td><td>a <lod td="" 。<=""><td>LOD</td></lod></td></lod<>	Stop, 7				a <lod td="" 。<=""><td>LOD</td></lod>	LOD
	-6	<lod< td=""><td><lod< td=""><td>JOF <lqa< td=""><td>€ LOD ≥</td><td>S <loid< td=""><td>DD 2</td><td><lod C <lod< td=""><td><lod< td=""></lod<></td></lod<></lod </td></loid<></td></lqa<></td></lod<></td></lod<>	<lod< td=""><td>JOF <lqa< td=""><td>€ LOD ≥</td><td>S <loid< td=""><td>DD 2</td><td><lod C <lod< td=""><td><lod< td=""></lod<></td></lod<></lod </td></loid<></td></lqa<></td></lod<>	JOF <lqa< td=""><td>€ LOD ≥</td><td>S <loid< td=""><td>DD 2</td><td><lod C <lod< td=""><td><lod< td=""></lod<></td></lod<></lod </td></loid<></td></lqa<>	€ LOD ≥	S <loid< td=""><td>DD 2</td><td><lod C <lod< td=""><td><lod< td=""></lod<></td></lod<></lod </td></loid<>	DD 2	<lod C <lod< td=""><td><lod< td=""></lod<></td></lod<></lod 	<lod< td=""></lod<>
	-1	<lod< td=""><td><lod td="" 🖓<=""><td></td><td><re>LOD</re></td><td>AFOD ~</td><td>, <lod< td=""><td>AKQD Ø Ø Ø Ø</td><td><lod< td=""></lod<></td></lod<></td></lod></td></lod<>	<lod td="" 🖓<=""><td></td><td><re>LOD</re></td><td>AFOD ~</td><td>, <lod< td=""><td>AKQD Ø Ø Ø Ø</td><td><lod< td=""></lod<></td></lod<></td></lod>		<re>LOD</re>	AFOD ~	, <lod< td=""><td>AKQD Ø Ø Ø Ø</td><td><lod< td=""></lod<></td></lod<>	AKQD Ø Ø Ø Ø	<lod< td=""></lod<>
	21	2x <loq; <lod<="" td=""><td>-4.QQ</td><td>064; 0.75; 0.72</td><td>,004</td><td>20 LOQ; 0, 00 "</td><td>0.0</td><td>0.47; 0.78; 0.75</td><td>0.77</td></loq;>	-4.QQ	064; 0.75; 0.72	,004	20 LOQ; 0, 00 "	0.0	0.47; 0.78; 0.75	0.77
	23	3x <lod< td=""><td><i>₹</i>ŁÖD</td><td>2x0.68 0.67</td><td>0.68</td><td>}~ 3x&lt;⊾&amp;Q</td><td>LOQ ¢</td><td>0.69; 0.20; 0.70</td><td>0.70</td></lod<>	<i>₹</i> ŁÖD	2x0.68 0.67	0.68	}~ 3x<⊾&Q	LOQ ¢	0.69; 0.20; 0.70	0.70
<b>10X depuration</b>	26	3x <lod< td=""><td>S <lod< td=""><td>0.68, 0.72; 0.70</td><td></td><td>AN LOQ</td><td><lqc< td=""><td>0.70 0.74; 0.72</td><td>0.72</td></lqc<></td></lod<></td></lod<>	S <lod< td=""><td>0.68, 0.72; 0.70</td><td></td><td>AN LOQ</td><td><lqc< td=""><td>0.70 0.74; 0.72</td><td>0.72</td></lqc<></td></lod<>	0.68, 0.72; 0.70		AN LOQ	<lqc< td=""><td>0.70 0.74; 0.72</td><td>0.72</td></lqc<>	0.70 0.74; 0.72	0.72
330 µg/kg	28	3x <lod< td=""><td>&lt;10D</td><td>92; 0.77; 0.80</td><td>A 683</td><td>Qx0.02; 0:09</td><td>£92</td><td>695; 0.79; 0.82</td><td>0.85</td></lod<>	<10D	92; 0.77; 0.80	A 683	Qx0.02; 0:09	£92	695; 0.79; 0.82	0.85
bw/day	30	2x <lod loq<="" td=""><td>Set OQ</td><td>0.66; 0.69; 0.65</td><td>0.67</td><td>3x≹QØQ</td><td>NELOQ &amp;</td><td>2x0.68; 0.71</td><td>0.69</td></lod>	Set OQ	0.66; 0.69; 0.65	0.67	3x≹QØQ	NELOQ &	2x0.68; 0.71	0.69
4.8 mg/kg DM	33	3 KLOD	<lod></lod>	0,45, 0.45; 0,48	0.46	、 β3x <loq∧o< td=""><td><løq< td=""><td>0.48; 0.47; 0.50</td><td>0.48</td></løq<></td></loq∧o<>	<løq< td=""><td>0.48; 0.47; 0.50</td><td>0.48</td></løq<>	0.48; 0.47; 0.50	0.48
Sub-groups:	36	O ^C 3x <loqo< td=""><td><u>, 6</u>,00Q</td><td>0.32; 0.28; 0.30</td><td></td><td>3x<lqq< td=""><td><b>SLOQ</b></td><td>0.35; 0.29; 0.33</td><td>0.32</td></lqq<></td></loqo<>	<u>, 6</u> ,00Q	0.32; 0.28; 0.30		3x <lqq< td=""><td><b>SLOQ</b></td><td>0.35; 0.29; 0.33</td><td>0.32</td></lqq<>	<b>SLOQ</b>	0.35; 0.29; 0.33	0.32
F1, F2, F3	37	2x≤t@9Q	LOQ X	0,22,0.23	O [™] 0.23 [™]	2x320Q	C <loq< td=""><td>0.25; 0.26</td><td>0.25</td></loq<>	0.25; 0.26	0.25
	40	<lød; <lqq<="" td=""><td><iqq< td=""><td>0.12; 0.14</td><td>6.13</td><td>[™]2x<lqqk<sup>™</lqqk<sup></td><td><loq< td=""><td>0.14; 0.17</td><td>0.15</td></loq<></td></iqq<></td></lød;>	<iqq< td=""><td>0.12; 0.14</td><td>6.13</td><td>[™]2x<lqqk<sup>™</lqqk<sup></td><td><loq< td=""><td>0.14; 0.17</td><td>0.15</td></loq<></td></iqq<>	0.12; 0.14	6.13	[™] 2x <lqqk<sup>™</lqqk<sup>	<loq< td=""><td>0.14; 0.17</td><td>0.15</td></loq<>	0.14; 0.17	0.15
	41 1	2x <lod< td=""><td>QOD C</td><td>0.11;30,91</td><td>© 0.11</td><td>2x≤IØQ</td><td><loq< td=""><td>2x0.13</td><td>0.13</td></loq<></td></lod<>	QOD C	0.11;30,91	© 0.11	2x≤IØQ	<loq< td=""><td>2x0.13</td><td>0.13</td></loq<>	2x0.13	0.13
	44	COD .X	S <lod td="" 🏷<=""><td></td><td>0.07</td><td>~€LOQ</td><td><loq< td=""><td>0.09</td><td>0.09</td></loq<></td></lod>		0.07	~€LOQ	<loq< td=""><td>0.09</td><td>0.09</td></loq<>	0.09	0.09
	48	LOD OF	୍ବର୍ଚ୍ଚପି	0.04	0.04	C <loq< td=""><td><loq< td=""><td>0.06</td><td>0.06</td></loq<></td></loq<>	<loq< td=""><td>0.06</td><td>0.06</td></loq<>	0.06	0.06
In case we have 3 leve	49	Ju <lqd< td=""><td>LOD</td><td>033³</td><td>🔊 0.03 🖔</td><td>LOQ</td><td><loq< td=""><td>0.05</td><td>0.05</td></loq<></td></lqd<>	LOD	033 ³	🔊 0.03 🖔	LOQ	<loq< td=""><td>0.05</td><td>0.05</td></loq<>	0.05	0.05

In case we have 3 levels of which at least one is LOD and others LOQ, it was legitimate toget the mean value as LOQ;

When one or two individual values are >LOCORING the others < LOQOR <LOD vesidues \$2000 or <LOD are considered equal to LOQ or LOD

LOO = 0.01 mg/kg for fluonyram and the enzamide inetabolite expressed as parent equivalents





Page 448 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram @°

								<u> </u>
able 6.4.1	- 8: Residu	e levels in r	ooultry tissu	ies		P.C	art y and	OR TEGINE OF
Group	Dose (µg/kg	Dose (mg/kg	Sub-	Sampling Time	<u> </u>	Residue	vels (mg/kg)	O ^r V Total <b>R</b> esidue
Group	bw/day)	DM)	group	(Day)	Fluopyram	FLU-benzamide	FLASolefins	of A Hoopyrand
Skin with f	at	•	•	· · · · ·				60° 60°
0.1X	3.4	0.05	B1	28			DEOD 35	LOQ
			B2 B3	280 × 28	<pre> EDD **** ******************************</pre>		S ^D < L€D	<loq c <loq< td=""></loq<></loq 
					< LOD	0.01 × 0.01		< LOQ
			C1	<u>© Mean</u> 280	Chi < LOD			
1X	35	0.49		28	S < LODS	«Ø.04 «O	0.02	0.06
			. C3	0 ⁻¹ 28 \$	LOD	~ 0.04 O	C< 0_02_S	0.06
		_Ĉ	Jen of	Mean		0.04	Ø∽ Ø.02	0.06
		<u>}</u>		28 0	A COD . OF	×0.10 ×9	0.03	0.13
3X	110	s \$1.6	() D1	28 🗸	LOD C	0.1*	\$ 0.02	0.13
	AN AN	D.T.	D3	28	S S DOD	\$10	0.02	0.12
	• >>		AU II	🕱 Mean	SLOD S	0.10	0.02	0.12
		\$	El S	28	l ∿ © ` < 0 Al	0.33	0.08	0.41
10X	320	4.80°	52	TA 28	Contraction of the second seco	×× 0.63	< LOD	0.64
		Ģ	E3	¥ 290.V	< LOD	0.26	0.06	0.32
			<u>, 1</u>	🐒 Mean	× 0× < 0:01	0.41	0.05	0.47
10X		Č,	A P	× 36	¢ [∞] ≤LOD 、	0.12	0.06	0.18
lepuration	33602	4.8	€ F2 × C	41	O K LOD	0.05	0.03	0.08
epuration		L	F3>	~Q9	< <b>L</b> QD	0.02	< LOD	0.04
	>>		P ^{ULLE} C	<u>ÇÇ Meğn</u>	<u> <u>S</u>LOD</u>	0.06	0.03	0.10

In case we have 3 levels of which at least one is <LOD and others 2DOQ or <DOQ, it was legitimate to set the mean value as <LOQ; When one or two individual values are >LOQ and the others 2DOQ or <DOQ, residues <LOQ or <LOD are considered equal to LOQ or LOD LOQ = 0.01 mg/kg for the parameter of FCO-olefins as calculated as parent equivalents. LOQ = 0.02 mg/kg for the total residue of FCO-olefins as calculated as sum of the two individual olefin isomers.

$$LOQ = 0.04 \text{ mg/kg}$$
 for total festidue of floopyram  $\%$ 

LOD = 0.004 mg/kg for Duopyram, COD = 0.001 mg/kg for FLU-benzamide, LOD = 0.004 mg/kg for the total residue of olefinsLOD = 0.008 mg/kg for the total residue of fluopyram (each expressed as parent expressed as parent



							O.D.	a ji hu ada
						PC	~0°	Legille and
					al	R.s.	at the	
					.10 [×]	> di		LE 1 LEF
	Dose	Dose	Sub-	Sampling	- 0-7-	Residue leve	$(\log/kg) \rightarrow \sqrt{kg}$	
Group	(µg/kg	(mg/kg		Time	Fluopyram 🖉 🕺 FLU		Total residences of 🔬	S Total Residue
	bw/day)	DM)	group	(Day)*		-benzamide	🕱 ° FLU@lefins 📣	of Ruopyram
Liver					A KO'			
			B1	28	SLOD C	0.02 ≪ [∞]	× × LOOV	
0.1X	3.4	0.05	B2	28	V CLOB	0.0		0.04
			B3	28	S < KOD S C	00.01 d	گ ^ر LOD کُ	0.04
				Mean	′ &LOD\\$\\$\> \`\}		< <b>LO∕D</b>	♥ 0.04
			C1	128	$\mathcal{K} \mathcal{K} \leq \mathcal{L}(\mathcal{A})$	0816	LOD S	0.16
1X	35	0.49	C2	à 28 ¢	< COD Or Or	≫0.16 °C	2 ¹ < 0.02 ¹	0.18
			C3 🌾	28 0	CAR LOD OF	0.160		0.18
		<u> </u>	A.C.	Mean	Sa < ron J			0.18
			<b>B</b> Ì	a 50 a	LOD &			0.43
3X	110	1.6	D2 S	285	$\bigcirc$ < LOD	039 0	LOD C	0.40
		<u>2</u> 0	£G4	28 28 28	C SLOD S	0.43 🐒	© ≫ LOD	0.44
		. Ġ		🦻 Meďn	<b>₩LOD</b> × >	0.41	چ <lod< td=""><td>0.42</td></lod<>	0.42
		C.D. J.	E1 K	28	$\langle \rangle > \langle 1000 \rangle$	al 6 🔊	< 0.02	1.62
10X	320 *	4.8	¥€2	28 K		$\frac{21.0}{1.4}$	< 0.02	1.42
			$\mathbb{O}^{\mathbb{O}}_{\mathrm{E3}}$	28_1		1,3 \$	0.02	1.32
		\$ ³ \$ \$		Mean	Strain Constraints	0.49	0.02	1.42
1037		G ^{ran}	, H	36	< POD O	0.49	< 0.02	0.51
10X	330	A.8 .	j F2 j	4000	, O'' < LOB	0.19	< 0.02	0.22
depuration	. 1		F3Ulle	× 49		0.05	< LOD	0.05
		þ	30 ⁰ 30	Ô Metan	Control Contro	0.24	< 0.02	0.26
1	21 1 6 1	nich at loost and	(Papa 1)		wer logitimeto to got the mean valu	4.00		

In case we have 3 levels of which at least one is <LOD and others <DOQ, it was legitimate to set the mean value as <LOQ;

When one or two hydrvidual values are  $\ge LOQ$  and the others < LOQ or < LOQ, residues  $\ge LOQ$  or < LOD are considered equal to LOQ or LOD LOQ = 0.01 mg/kg for fluopyram and the benzamide metabolite, expressed as parent equivalents.

LOQ = 0.01 mg/kg for fluopyram and the benzamide metabolite, expressed as parent equivalents. LOQ = 0.02 mg/kg for the total residue of FLU-olefins was calculated as sum of the two individual olefin isomers. LOQ = 0.04 mg/kg for total residue of fluopyram. LOD = 0.003 mg/kg for fluopyram. LOD = 0.000 mg/kg for FLU-benzunde, LOD = 0.004 mg/kg for the total residue of olefinsLOD = 0.008 mg/kg for the total residue of fluopyram (each expressed as parent equivalents) The fluopyram (each expressed as parent equivalents)

449

Ø



							OTR -	an the de
						D ^G	et I	COTIN SIDO
						A. Er	at 1	
						~1 ⁰		Le Claible
	Dose	Dose	Sub-	Sampling		Residue le Q	is (ilig/kg) 🐃 🔬 🗸 🗸	
Group	(µg/kg	(mg/kg	group	Time	Fluopyram	FLU-benzamide	Total resideres of	> Total Residue
	bw/day)	DM)	g. oup	(Day)*			<u>5° FLU@lefins</u>	of Buopyram
Muscle					~~~. ×,			
			B1	28	JUOD N	C < 0.01 < C	× 0 × LOD	C ⊴tøĎ
0.1X	3.4	0.05	B2	28	Q ^e <lod<sup>, y</lod<sup>	<u>&gt; &lt;009</u>	DeOD S	<u>√</u> €LOD
			B3	28	S < KOD z C	@.0.01 US	ON LOD N	LOD <
				Mean	✓LOD \s \ssac	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u> </u>	[♥] <lod< td=""></lod<>
			C1	<u>,2</u> \$	S & CLOD	()) (N)) (N)	K < LOD	0.04
1X	35	0.49	C2	à 28 ¢	< 120D			0.04
			05	28 0	∕s≫≮LOD ⊘s ^{ys}	0.040		> 0.04
			A.F	Mean	<u>کې &lt; ۲۵</u> ۵			0.04
				ຼົ່ນ ເ	ŠEOD 🔗			0.09
3X	110	1.6	a∵ D2 _≪	28 V	O < LOD	0.09	See C ≥OD	0.09
		30	Ð3	<u>}</u> 28 ~	C <lod .="" s<="" td=""><td>× 9.10 \$</td><td>© ≫&lt; LOD</td><td>0.10</td></lod>	× 9.10 \$	© ≫< LOD	0.10
		A	a the	🛛 🖉 Meán 🌶	~~LOD x ∑	£ 0.09	s <lod< td=""><td>0.09</td></lod<>	0.09
			El 炎	28 © 28 &		0 12 00	<pre>LOD</pre>	0.33
10X	320 \$	<b>4.8</b>	_¥€2	<u>ک</u> 28 ک	©`≪LOD©	00.24 j	0.06	0.30
			E3 0	281			< 0.02	0.31
		<u></u>		Mean	Street - LOB	× 0×29	0.03	0.32
101		20 ^{C4.8}	14	36	_<⊈OD ⊍	~ 0.21	< 0.02	0.23
10X dopuration	330	A.8 _	j F2 €	40 ^{°°}		× 0.08	< LOD	0.08
depuration	.1	~~ ^{\$\$4.8}	F3Ulle	× 49		0.02	< LOD	0.04
		>	30 ⁰ 30	O Metur	Ver legitimete to set the p	0.10	< 0.02	0.12
1		high at least one	O-IOD and	1	were logitimeter to get the m			

In case we have 3 levels of which at least one is <LOD and others <DOQ, it was legitimate to set the mean value as <LOQ;

When one or two hydrvidual values are  $\geq LOQ$  and the others  $\leq LOQ$  or  $\leq LOQ$ , residues  $\geq LOQ$  or  $\leq LOQ$  are considered equal to LOQ or LOD LOQ = 0.01 mg/kg for fluopyram and the benzamide metabolite, expressed as parent equivalents.

LOQ = 0.01 mg/kg for fluopyram and the benzamide metabolite, expressed as parent equivalents. LOQ = 0.02 mg/kg for the total residue of FLQ-olefins was calculated as sum of the two individual olefin isomers. LOQ = 0.04 mg/kg for total residue of fluopyram. LOD = 0.003 mg/kg for the parent equivalents) LOD = 0.003 mg/kg for the total residue of olefinsLOD = 0.008 mg/kg for the total residue of fluopyram (each expressed as parent equivalents)

450

Ø



#### CA 6.4.2 Ruminants

CA 6.4.2 Rumi	nants
Data Point:	KCA 6.4.2/01
Report Author:	
Report Year:	
Report Title:	Fluopyram: Feeding study with dair wows
Report No:	MR-07/367
Document No:	<u>M-298635-01-1</u>
Guideline(s) followed in	US: EPA Residue Chemistry ast Guidelines PPTS 860.1000 "Background"
study:	US: EPA Residue Chemistry Lest Guidelines CPPTS 860.1060 "Background" OPPTS 860.1480 "Meat, mok, poultry and Egs", FC. 7031/91/95 167. 4 "Livestock" feeding studies"; EU Directive FS 91/41 Appendix G (CD: Saidelines for the
	feeding studies"; EU Directive ES 91/41 Appendix G @CD: Suidelines for no
	Testing of Chemicals, 95, 2000-01-08
Deviations from current	none A & O Q O O A A o
test guideline:	
Previous evaluation:	yes, evaluated and accepted rev. 1 to Vol S f D & MB7 August 2012 (references Filed on S Yes, conducted under GLPA fificiated recognised testing fastities
	rev. 1 to Vol S of D & B7 August 2012 (references selled on )
GLP/Officially recognised	Yes Q X Q A Q A A A A A A A A A A A A A A A
testing facilities:	
Acceptability/Reliability:	Yes Q X & X A A A A A A A A A A A A A A A A A

Materials and Methods

The purpose of the study was to determine the magnitude of the residues of fluopyram and its metabolites Fluopyram-benZamide, and total residue of Quopyram-obstines (BCS-AA10627 and BCS-AA10650) that may be expected in milk, muscle, liver, kidney and fat following oral administration of fluopyram to dairy cows.

### Test system, dosing

Fifteen clinically healthy, not-pregnant in their 1) to 4% lactation period dairy cows were selected for the study. Fourteen days before the first application (-149, the animals were taken up into the experimental housing facilities for the allocation and adaptation. The cows were divided into five experimental groups and one control animal (according to random group mapping) on the day they were introduced into the experimental stall. During the acolimatisation period the animals of the depuration group (10XE) served as reserve animals for the experimental groups 0X, 6/IX, 1X, 3X and 10X.

During the acclimatisation period (at the bay -5) Sone cow had to be excluded from the study due to the aboniasal dislocation - this cow was replaced by another one (animal number 8) and the data set were recorded only as of study day of the acclimatisation period. Further, due to the low average food intake during the dosing period, one cow (mimal@umber 12) had to be excluded from the study.

After the acclimatisation period the dair cows were dosed orally via double-coated gelatine capsules with fluopyrate for 2% consecutive days. The actual daily dose rates were 0.04 mg/kg bw/day (dose group 0.1X), 0.44 mg/kg bw/day (dose group 1X), 1.21 mg/kg bw/day (dose group 3X), 4.05 mg/kg bw/day (dose group 10X and 4.38 mg/kg by/day (dose group 10XE, during feeding phase), corresponding to actual daily residue infake in diet of 1.5 mg/kg dry feed/day (dose group 0.1X), 14.4 mg/kg dry feed/day (dose group 1X), 401 mg/kg dry feed/day (dose group 3X), 133.1 mg/kg dry feed/day (dose group 10X) and 145.9



mg/kg dry feed/day (dose group 10XE, during feeding phase), respectively. Details of the doses for corresponding groups are given in the Table 6.4.2-1.

Dose group	Number of animals	Animal number	Actual dose level (mg/kg bw/day)	Dose levels in feed (mg/kg(DM)	
0X	1	1	0 *	-QŬ	
0.1X	3	2, 3, 4	0.04	1.5	
1X	3	5, 6, 7	0,47	1404° 0	
3X	3	8, 9, 10	ر 1.21 ° °	× × 44.1	
10X	2	11, 13	O [™] 4.05 <i>©</i> [™] ×	× 133	
10XE	3	14, 15, 16	4.338	Q 149.9	of a s

Table 6.4.2- 1:	Summary of	fluopyram (	(AE C656948	) dose a	dministration	Ż

DM – feed, dry matter

bw - body weight

The doses were calculated based on the were body weight of dairy cows on average feed ratio and the worst-case residue derived from field studies and were approximately 0.1X, 3X, 3X and 40X of the anticipated maximum dietary burden arising from the use of fluopyrapon the US.

The 1X group in this study is around 4/5 times higher than the calculated maximum dietary burden for the present renewal (0.094 mg/kg bw/da% for Ram/Ewe see Table 6.442).

- In tissues, as a worse case the residue results from this 1X group will be used as input data to calculate the risk assessment.
- For milk, the dietary burden of 0.076 mg/kg bw/day in diavy cather is close to the 0.1 X dose value of 0.04 mg/kg bw/day. Values in milk from the 0.1 X dose group are considered to calculate the dietary rist assessment.

The dose capsules were prepared prior to the dosing phase by weighing the test item into capsules. Capsules were analysed for fluopyram in order to determine the content and komogeneity as well as the storage stability of Puopyram in capsules for the duration of the in-life phase of the study. A representative number of samples from dose groups OX and 10X were applysed mimediately after preparation.

The gelatine capsules with different dosages were stored separately in labelled plastic boxes at room temperature. The oral administration was performed to a bolus dispenser. After the cows swallowed the gelatine capsules, the personnel waited for possible retching reaction. In case the capsule was disgorged, the test item was registered once again.

Every day, the animal in the control group  $(0, \mathbb{X})$  received a gelatine capsule without the test item. The animals in the groups  $(0, \mathbb{X})$ , and  $(0, \mathbb{X})$  received one capsule per day and the animals in the groups 10X and 10XE two capsules per day. The capsules were administered in the order of sequence of the dosage groups 0X, 0.1X, 1X, 3X, 10X, and 10XE. The first application was performed on day 0; and for 29 consecutive days, the application was performed after the evening milking and evening feeding.

General health status of animals was observed and inspected daily by veterinarian.

The animals had ad libitum access to druking water via automatic drinking troughs providing water from the municipal druking water sopply.

The animals were fed twice daily via their throughs. The daily food consumption of the animals was recorded daily and for this purpose, the expected daily need for each cow was weighed individually. The weights of the feed leftwers were determined individually for each animal on the day after the feeding in the morning before the new morning feeding. For this purpose, the feed leftovers were taken from the



troughs and weighed. Since each cow had their individual through area, it was always possible clearly  $t^{0}$ assign the respective feed leftovers to the individual cow. The composition of the species-adequate mixed feed (with cereal-based dietary supplement improving milk yield and vitamin-mineral mixtures covering the daily requirements) is presented in the Table 6.4.2-2. 

Table 6.4.2- 2:	Feed ration	composition
-----------------	-------------	-------------

-	CA	
Ingredient	%	
Corn silage	546	
Gras silage	342	
Corn pellets	Q 4.9	$\sim$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$
Soy pellets	دي [°] 2.9 _€ °	
Rape seed pellets	$ \begin{array}{c} & 2.9 \\ \bigcirc & 4 \\ \bigcirc & 4 \\ & & \\ \end{array} $	
Feed lime	0.1	
Salt		
Molasses cutlets	× 1.0	
QS- Mineral Feed Blatin 205 ADE SM for Cattle (Percentage of ingredients: 13.1% Calcium, 6.0%)		
(Percentage of ingredients: 13.1% Calcium, 6.0%)	0.2	
Phosphorus, 10.2% Sodium, 10.0% Magnesium		
Sampling I V		

#### Sampling

- Contraction of the second se The cows were milked twice daily (in the mothing and in the evening) with mobile milking unit according to a good professional and hygienic practice common in dairy farming. Or the day of slaughtering the cows were milked in the morning. Milk yields were recorded twice daily.

On day -12 during the acclimatization period, approximately 2 kg milk were taken from animal no. 1. Until its transfer to Sample Logistics Lab this sample was deep frozen at -18°C.

For the residue analysis, deplicate milk samples of the animats of the groups 0X, 0.1X, 1X, 3X, and 10X were taken before the lor application as well as on the 1st, 2nd, 4th, 8th, 19th, 13th, 17th, 21st, 24th, 26th and 29th day after the sting. Milk samples of the three animals from the depuration group 10XE were taken accordingly from the 21st day of the experiment antil the 29th day. Additionally, milk samples were taken from the animals of the group 10XE three times per week from the 30th day of the experiment until the day of the respective diagnostic slaughtering. O

Milk samples were taken directly after witking after thorough mixing of the milk yield of one individual animal. If mastitis was diagnosed, the prilk from the affected udder quarters was not mixed into the milk for the taking *Complete*, The morning and the evening milk samples were always taken in proportion to the respective milk yields, so that the proportions of evening and morning milk in one milk sample corresponded to the respective weight proportions of the milk yield. The evening milk sample was deepfrozen ac below – 18 °C. After the morning milking, the necessary amount of morning milk was added to the frozen evening wilk. These mixed samples were deep-frozen at below -18 °C until their transfer to Sample Logistics Lab for the residue analysis.

In the evening of the 20th day of the experiment and in the morning of the 21st day of the experiment, approximate by 1 kg milk of each mimal from the group 10X was taken for analytical evaluation of the accumulation of active items in the milk fat. These milk samples were stored cooled at 4 - 8 °C, and transferred to Spriple Rogistics Lab, cooled at > 0 °C, on the 21st day of the experiment.

The boelling of the sample containers indicated study number, group membership, animal or stall position number and time of the milking (date and indication of morning or evening milking).



The deep-frozen milk samples were transferred on dry ice between facilities and upon consultation. The sample duplicates (reserve samples) remained at one facility until the second confirmed complete and intact arrival of the samples.

Skim milk and cream was prepared by centrifugation of milk taken from the dose about 10X.

#### *Terminal procedure*

The diagnostic slaughtering was performed at the slaughterhouse in compliance with requirements and controlled by a public veterinary officer.

A dissection with pathological-anatomical examination was performed. Relevant findings that decrated O from the physiological status were recorded in the dissection and sampling protocol. The diagnostic slaughtering of the animals of the study group 0.1XXX, 3X, and 19X as well as of the control animals of the 0X group took place on the day after the final dosing Every day, the dosing occurred after the evening milking. Thus, it was ensured that the time point of the dagnostic slaughtering of the mimals of the groups 0X, 0.1X, 1X, 3X and 10X was less than 24 hours after the final application The animals were staughtered diagnostically in groups, beginning with the control animal and subsequently with increasing decage groups. The animals of the group 10XE were slaughtered diagnostically 7, 14 or 21 days after the final application (36, 43, and 50 days counting from the 1st day of this experiment).

The absolute organ weights of the liver and both kidneys were determined and recorded in the dissection iken from each animal. and sampling protocol. At least the following duplicate samples were taken from each animat.

- _
- Intestinal fat (approx.  $2 \times 250^{\circ}$ ) Subcutaneous fat (approx.  $2 \times 400^{\circ}$  g)
- _
- Muscular tissue from sirloin, round muscle and skirt muscle approx 2 x 100 g each). The muscles samples were prixed into a joint musole sample.

Samples were pixed into a joint muscle sample. On the day of sampling, the organized tissue samples were cut into pieces of approx.5 cm side lengths and frozen in layers in a sampling bag. The sampling bags were labelled with the study number, the group membership, the animal or stall position number, the type of sample and the day of the sampling. The samples were stored at below -18 C until their transfer to Sample Logistics Lab.

The deep-frozen organ and tissue samples, were transferred on dry ice between facilities and upon consultation. The sample duplicates (reserve samples) remained at one facility until the second confirmed complete and intact arrival of the samples

### <u>Analysis</u>

The tissue samples except for at were chopped together with dry ice by means of a meat chopper. Two 100-seportions of each sample were transforred into labelled containers. One container was handed over to the analytical laboratory. The second population was retained and stored at -18 °C.

The fat sample were chopped together with dry ice and divided into three 100-g portions. One container was handed over to the analytical aboratory. The second portion was retained and stored at -18 °C. The third contamer was sent for to SGS for many GmbH, Laboratory Services Hamburg, Weidenbaumsweg 137, D-24035 Hamburg to determine the actual fat content.

Residue of Apopyram and its metabolites (Fluopyram-benzamide and the total residue of Fluopyramolethrs) in milk and tissues were determined using the analytical method 01061 (

2007, Mc295705-02-1; see MCA Section 4.1.2). Full details and acceptable validation data to support this



method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

The residues of fluopyram and its metabolites Fluopyram-benzamide and total residue of Fluopyramolefines were extracted from milk, fat, liver, muscle, and kidney using a mixture of acetonitrile/water (4/5)? After filtration, the extracts were cleaned-up on Mega Bond Elut-C18 cartridges. Aliquots of the extracts were diluted with a mixture of methanol/water (containing the corresponding internal standards).

The residues were determined by LC-MS/MS equipped with electrospray detection. (external calibration, matrix-matched standards + internal standards).

The limit of quantification (LOQ) is 0.01 mg/kg for all analytes (expressed as parent equivalents for all matrices. (whereas the LOQ for the total residues of elefins is 0.02 mg/kg for all matrices). Any residue measured or calculated to be less than the LOQ was reported as "LOQ"

The Limit of Detection (LOD) was set to 0.003 mg/kg for fluopyram, 0.001 mg/kg for FLU-benzamide and 0.002 mg/kg for the two FLU-olefins isomers expressed as parent equivalents each. The SOD for the total residues of olefines was set to 0.004 mg/kg. Any residue value that was below the LOD is given as "< LOD"

In order to check the performance of the analytical method concurrent recovery experiments were conducted along with the analysis of the samples.

The fortification levels for the measured matrices were between 0.01, mg/kg (LOG level) 40 mg/kg for fluopyram and FLU-benzamide (expressed as parent equivalents). The fortification levels for the measured matrices were between 0.02 mg/kg (GOQ level) and 80 mg/kg for total residues of FLU-olefins (expressed as parent equivalents). Recoveries for the total residues of olefins were measured by spiking both isomers at fortification levels of 0.01 mg/kg each, separate analyses of both isomers, subming up residues and subsequent calculation of the recovery.

Concurrent recoveries are presented in Table 6.4.2-3.

# Dose verification and storage stability

Capsules were prepared ptior to the dosing phase by weighing the test item into capsules. Upon analysis by HPLC-MS/MS, fluopyrum concentration in capsules ranged from 94 % to 110 % of nominal values (mean per level: 22.75 mg/capsule, n = 5 for dose group 0.1X; mean per level: 1145 mg/capsule, n = 5 for dose group 10X) immediately after application. After the final dosing, fluopyrum concentration in capsules ranged from 92 % to 154 % of nominal values (mean per level: 23.65 mg/capsule, n = 5 for dose group 0.1X; mean per level: 23.65 mg/capsule, n = 5 for dose group 0.1X; mean per level: 0.154 % of nominal values (mean per level: 23.65 mg/capsule, n = 5 for dose group 0.1X; mean per level: 0.154 % of nominal values (mean per level: 23.65 mg/capsule, n = 5 for dose group 0.1X; mean per level: 0.154 % of nominal values (mean per level: 23.65 mg/capsule, n = 5 for dose group 0.1X; mean per level: 0.154 % of nominal values (mean per level: 23.65 mg/capsule, n = 5 for dose group 0.1X; mean per level: 0.154 % of nominal values (mean per level: 23.65 mg/capsule, n = 5 for dose group 0.1X; mean per level: 0.154 % of nominal values (mean per level: 23.65 mg/capsule, n = 5 for dose group 0.1X; mean per level: 0.154 % of nominal values (mean per level: 23.65 mg/capsule, n = 5 for dose group 0.1X; mean per level: 0.154 % of nominal values (mean per level: 23.65 mg/capsule, n = 5 for dose group 0.1X; mean per level: 0.154 % of nominal values (mean per level) (mean per level

### In-life observations

All 15 animals of the groups 0, 0.1X, 1X, 5X, 10X and 10XE tolerated the 29-fold oral application of the test material without any chinical complications. During the dosing period and also during the depuration period, the daily clinical control of the health status of none of the animals resulted in any findings deviating from the physiological normal values that plated to the application of the test item. Further, no negative influence of the test item of food consumption was determined with the study conditions.

a.

## Analysis of milk milk products and tissues

Recoveries of fluopyram and is metabolites were measured concurrently with each set of samples to verify method performance. The concurrent recovery data are summarized in Table 6.4.2-3. The data demonstrate acceptable method performance during sample analysis.



No apparent residues of fluopyram and its metabolites above 30 % of LOQ were found in any of the control samples used for recovery experiments. Procedural recoveries from the fortified control samples were not corrected for any apparent residue in the associated unfortified control.

The tissue and milk samples in this study were analysed within 30 days of collection; therefore, freezer storage stability studies on dairy cattle tissue and milk matrices were not required.

ti	ssues		Q [×] , .		
Sample material	FL	Single values [%]	Meanyalue	<b>© RSD</b>	LÕQ
-	[mg/kg]*				
Fluopyram					
	0.01	89; 82; 112; 102; 92; 94; 109; 917;	98	13.2	
	0.10	\$7; 98; 103; 102 ×	£100 °	29	
Cattle/milk	1.0	Q 73,70;71, ~ ~	× 71×	\$2.1 Å	6.0
	5.0	143; 115; 03; 143; 111; 197		§ 4.1.OV	
	20	83:91	<b>08</b> 7 ô		N.
		Ovéráll re@very (n = 24)	<u> </u>	<b>4</b> .9	×
	0.01 🖌	95; 92 ° ~	94 · · · ·	or K	
Cattle/cream	0.10	<u>\$ 0</u> 90; 94 ~ 4	<u></u>	O`	0.01
Cattle/ cream	20		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u></u>	0.01
	×	Qverall recovery (n = 5)	~ 93, ×	2.8	
	Q.01 @	<u>* x,* 103; 106</u> * x,* x	/ 105 .	»	
Cattle/skim milk	0.10	2 100: <b>3</b> 03	0 ⁷ 02 x		0.01
	× 20 [×]	$\sim$	100		0.01
	ð'	V (Overall recovery (n = 5)	¢ [¥] 1402	2.5	
Ŭ,	\$0.01 O		83		
Cattle/muscle	0.10		<i>©</i> 88		0.01
	×20	<u> </u>	72		0.01
K, ^x	. C . Ó	Óverall recovery (n ≠ \$)	× 81	10.1	
~	$0.01^{\circ}$	× 5 64 88 × ×	76		
Cattle/kidney	0,10	57 N 88 N A	88		0.01
	<u>2</u> 0 5	× × 70 >	70		0.01
	,o× _o ~	Overall recovery (n 4)	78	16.0	
*	0.00	<u>~</u> <u>104x 91</u>	98		
Cattle/liver	0.10		80		0.01
	<u>∿</u> 40 Q		108		0.01
^~~^~~		────────────────────────────────────	96	13.3	
× *	0.01	<b>8</b> ; 93; <b>1</b> 91; 112; 94	98	9.5	
Cattle/fat	<b>9</b> .10 C	y 0 [*] 92	92		0.01
	× 10 ×	83; 79	81		0.01
		V Overall recovery (n = 8)	93	11.1	
Sample materiat	Ôĩ ×	Single values [%]	Mean value	RSD	LOQ
	[mg/kg]*	· Single values [70]	[%]	[%]	[mg/kg]*
Fluopyram-benzar	nide 🛷				
Cattle/milk	0:01	86; 87; 97; 98; 100; 97; 115; 118; 90	99	11.4	0.01
	0.10	87; 88; 99; 98	93	6.9	0.01
L-O	0.10	01,00,77,70	,,	0.7	

 Table 6.4.2- 3:
 Concurrent recovery data for fluopyram and its metabolites in milk and boyine tissues



Sampla matarial	FL	Single velves [0/]	Mean value	RSD	LOQ
Sample material	[mg/kg]*	Single values [%]	[%]	[%]	[mg/kg]
	1.0	92; 89; 92	91	≫1.9	S O
	5.0	110; 112; 108; 99; 106; 100	106	\$ 5.0	
	20	79; 86	83	Ø	
		Overall recovery (n = 24)	97	10.5	
	0.01	100; 96 🖏	98	,/	
Cattle/cream	0.10	95; 94	2 <b>S</b> U	õ	
Cattle/cream	20	95 🛒	_0 <b>9</b> 5	J.	
		Overall recovery (n = 5)	<b>96</b>	<b>Q.4</b>	Q . O .
	0.01	99; 99	× 990	a d	
Cettle / 1	0.10	90; 93	\$2	× -10	\$0.01 °
Cattle/skim milk	20	854 Q	× 95 × 0	<u>ک</u>	
		Overall recovery $(\mu = 5)$	950	<b>4.1</b>	
	0.01	79.00	R .79°	6	
	0.10		78 0		
Cattle/muscle	20	<u> </u>	0 [°] 67, [°]	~~~ ì	
		Overall secovers (n = 3)	75	8.9	řŐ
	0.01	58; 101	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	-	
	0.10		074		, w ^a
Cattle/kidney	20 *		69°	»O /	[™] 0.01
	20	© Overal recovery (n = 4)	2 76	24.2	
	0.Q1Q	○ .☆ 99; <b>0</b> 6 ♡		24.6	
	0.10			<u> </u>	
Cattle/liver	×40		104		0.01
	\$ <del>4</del> 0	$\sim$ Overall recovery (n $=$ 4)		15.9	
&	0.01	Solution (11, 10)	096	6.2	
, N		86 2	90 ·		
Cattle/fat		75: 92			0.01
Ô,		Overall recordery (n 8)	<u>91</u>	10.5	
<u> </u>	ГО- ~~ БД.*		Wean value	RSD	LOQ
Sample material		Single alues [%]	[%]	[%]	[mg/kg]*
+ x XX #				[70]	11112/ K21 ***
<i>K</i> ♥	[mg/kg]		<u> [/•]</u>		
Fotal Residue of F	litopyrain-ol		۶ ۱		
Total Residue of F	litopyrain-ol	efins** ~ 100;.12; 94;400; 96;90; 125	103	10.5	
Fotal Residue of F	litepyraia ₇ ol	efins** ~ (100;,102; 94; 400; 96; 90; 125) ~ (100; 101)	103		
Fotal Residue of F	<b>İmpyrain-o</b> 0.01	efins** 100;.1 Q; 94; 400; 96; 90; 125 2 2 2 90; 93; 101 2 90; 93; 101; 97	103	5.0	
Fotal Residue of F	1000 0.01	efins**         O         O           100; 102; 94; 100; 96; 90; 125         0           100; 1010         0           90, 93; 101; 97         0           0         97; 98, 98	103 95 97	5.0 1.6	0.02
Fotal Residue of F	10000000000000000000000000000000000000	efins** 100;.102; 94;.400; 96; 90; 125 100; 1010 90; 93; 101; 97 90; 93; 101; 97 90; 93; 101; 97 1400; 46; 139; 132;031; 133	103 95 97 135	5.0 1.6 4.7	
Total Residue of F	1000 0.01	efins** 100; 102; 94; 400; 96; 90; 125 100; 101 90; 93; 101; 97 97; 95; 98 1400; 46; 139; 132; 31; 133 97; 85	103 95 97 135 82	5.0 1.6 4.7	
Fotal Residue of F	10000000000000000000000000000000000000	efins** 100; 102; 94; 400; 96; 90; 125 100; 101 90; 93; 101; 97 97; 99; 98 1400; 46; 139; 132; 31; 133 9; 85 Overall recovery (n = 24)	103 95 97 135 82 107	5.0 1.6 4.7  17.7	
Total Residue of F	itepyrain, of 0.01 0.01 0.00 0.00 0.00 0.00 0.00 0.0	efins** 100; 102; 94; 400; 96; 90; 125 100; 101 90; 93; 101; 97 90; 93; 98 97; 95; 98 140; 46; 139; 132; 31; 133 79; 85 Overall recovery (n = 24) 97; 96	103 95 97 135 82 <b>107</b> 97	5.0 1.6 4.7  17.7 	
Total Residue of F	10000000000000000000000000000000000000	efins**       0       0         100; 102; 94; 400; 96; 90; 125       100; 101         90; 93; 101; 97       0         90; 93; 101; 97       0         90; 93; 101; 97       0         90; 93; 101; 97       0         90; 93; 101; 97       0         90; 93; 101; 97       0         90; 93; 101; 97       0         97; 95; 98       0         97; 95; 98       0         97; 95; 98       0         97; 95; 98       0         97; 95; 98       0         97; 95; 98       0         97; 95; 98       0         97; 95; 98       0         97; 95; 98       0         97; 96       0         97; 96       0         97; 95       0	103 95 97 135 82 <b>107</b> 97 98	5.0 1.6 4.7  17.7  	
Total Residue of F	10000000000000000000000000000000000000	efins** 100;.10; 94; 400; 96; 90; 125 100; 101 96; 93; 104; 97 97; 95; 98 1400; 46; 136; 132; 31; 133 97; 85 Overall recovery (n = 24) 97; 96 92 92	103           95           97           135           82           107           97           98           92	5.0 1.6 4.7  17.7   	0.02
Total Residue of F	10000000000000000000000000000000000000	efins** $0$ $0$ 100; 102; 94; 400; 96; 90; 125 $0$ 100; 101 $0$ $0$ 90; 93; 104; 97 $0$ 90; 93; 104; 97 $0$ 90; 93; 104; 97 $0$ 90; 93; 104; 97 $0$ 90; 93; 104; 97 $0$ 90; 93; 104; 97 $0$ 97; 99; 98 $0$ 97; 99; 98 $0$ 90; 95 $0$ 92 $0$ $0$ $92$ $0$ $92$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ <td>103 95 97 135 82 107 97 98 92 92 96</td> <td>5.0 1.6 4.7  17.7   3.0</td> <td>0.02</td>	103 95 97 135 82 107 97 98 92 92 96	5.0 1.6 4.7  17.7   3.0	0.02
Cattle/mok	10000000000000000000000000000000000000	efins** $0$ $0$ 100; 102; 94; 400; 96; 90; 125 $0$ 100; 101 $0$ $0$ 90; 93; 101; 97 $0$ 90; 93; 101; 97 $0$ 90; 93; 101; 97 $0$ 90; 93; 101; 97 $0$ 90; 93; 101; 97 $0$ 90; 93; 101; 97 $0$ 90; 93; 102; 93]; 133 $0$ 90; 93; 90; 95 $0$ 0 $0$ 90; 95 $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$	103           95           97           135           82           107           97           98           92           96           97	5.0 1.6 4.7  17.7   	0.02
Total Residue of F	1000 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01	efins** $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$	103           95           97           135           82           107           97           98           92           96           97           93	5.0 1.6 4.7  17.7   3.0	0.02
Total Residue of F	1000 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01 0.01	efins** $0$ $0$ 100; 102; 94; 400; 96; 90; 125 $100; 101$ 90, 93; 101; 97 $0$ 90, 93; 101; 97 $0$ 90, 93; 101; 97 $0$ 90, 93; 101; 97 $0$ 91, 95, 98 $0$ 91, 95, 98 $0$ 91, 92, 95 $0$ 92, 96 $0$ 92, 96 $0$ 92, 96 $0$ 92, 96 $92$ $0$ $92, 95$ $0$ $92, 95$ $93, 93$ $94$	103           95           97           135           82           107           97           98           92           96           97           93           94	5.0 1.6 4.7  17.7  3.0    	0.02
Total Residue of F	1000 0.01 0.01 0.01 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00	efins** $0$ 100; 102; 94; 400; 96; 90; 125         100; 101         90; 93; 101; 97         90; 93; 101; 97         90; 93; 101; 97         90; 93; 101; 97         90; 93; 101; 97         90; 93; 101; 97         90; 93; 101; 97         90; 93; 98         0verall recovery (n = 24)         90; 95         92         0verall recovery (n = 5)         93; 93         94         Overall recovery (n =5)	103           95           97           135           82           107           97           98           92           96           97           93           94           95	5.0 1.6 4.7  17.7  3.0  	0.02
Total Residue of F	10000000000000000000000000000000000000	efins** $0$ $0$ 100; 102; 94; 400; 96; 90; 125 $100; 101$ 90, 93; 101; 97 $0$ 90, 93; 101; 97 $0$ 90, 93; 101; 97 $0$ 90, 93; 101; 97 $0$ 91, 95, 98 $0$ 91, 95, 98 $0$ 91, 92, 95 $0$ 92, 96 $0$ 92, 96 $0$ 92, 96 $0$ 92, 96 $92$ $0$ $92, 95$ $0$ $92, 95$ $93, 93$ $94$	103           95           97           135           82           107           97           98           92           96           97           93           94	5.0 1.6 4.7  17.7  3.0    	0.02
Total Residue of F	1000 0.01 0.01 0.01 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00	efins** $0$ 100; 102; 94; 400; 96; 90; 125         100; 101         90; 93; 101; 97         90; 93; 101; 97         90; 93; 101; 97         90; 93; 101; 97         90; 93; 101; 97         90; 93; 101; 97         90; 93; 101; 97         90; 93; 98         0verall recovery (n = 24)         90; 95         92         0verall recovery (n = 5)         93; 93         94         Overall recovery (n =5)	103           95           97           135           82           107           97           98           92           96           97           93           94           95	5.0 1.6 4.7  17.7  3.0   2.6	0.02



Sample material	FL [mg/kg]*	Single values [%]	Mean value [%]	RSD [%]	LOQ [mg/kg]
		Overall recovery (n = 3)	87	≫1.1	S O
	0.01	72; 103	88	~~	
Cattle /laide are	0.10	108	108	Ø	
Cattle/kidney	20	81	81		
		Overall recovery (n = 4) 🖏	91	19.0	
	0.01	103, 92	28	8	
Cattle/linear	0.10	102	O02	J.	
Cattle/liver	40	99 3	<i>6</i> [√] 99	_0	
		Overall recovery (n = 4)	<u> </u>	∱∕ 5.0 <u>√</u>	
	0.01	82; 94; 87; 93; 101	\$\$H	[∞] 7.9 ⁰	× 0.02 → 0.02
Cattle/fat	0.10		×100 ×	Ì,	
Cattle/fat	10	, 81; 92 🗶 Ö	87,0	~ c	<i>▼</i> 0.02 [∞]
		Overall recover (n = 8)	<u>9</u>	8.2	

FL = Fortification level, RSD = Relative standard deviation (LOQ = Reactical funct of quantification)

* : Expressed as parent equivalents.

** : Both isomers (E- and Z-isomer) were fortified with a ratio of 1/1.

Final determination as: Fluopyram Residues calculated as: Fluopyram

Final determination as: FLU-benzamide Residues of Culated as: Fluopyram

Final determination as: FLU-olefins (E- and Z-isomer) Recidues calealated as Fotal Recidue of Orefins (expressed as parent equivalents)

No residues of fluopyram and its metabolites above the respective LOOs were detected in any of the untreated samples of milk and tissue (control samples).

Residues of fluopyram and its metabolites in bovine milk and bissues samples are subrimarized in the Table 6.4.2-4 and Table 6.4.2-6 respectively.

All residues further discussed are conculated and expressed as fluopyrar@parent/equivalents.

The mean residues of fluopyram in milk

- residues remained below the DOD in the dose group B (QCX)
- between <LOD and 0.02 mg/kg in the dose group C (1X) until residue plateau at 0.01 mg/kg.
- between 0.02 and 0.05 mg/kg gooup D (3X), until residue plateau around 0.3 mg/kg.
- between 0.08 and 0 10 mg/kg, group E (HX), (£16 mg/kg occurring on day 4). Until residue plateau around 0.16,0.12 mg/kg O

Mean residues of LU-benzamide in mulk :

- between <LQQ and 604 mg/kg group B (61X), with residue plateau at 0.02 mg/kg
- between 0.01 mg/kg and 0.25 mg/kg group C (1X), until residue plateau around 0.23-0.25 mg/kg
- between 0.03 mg/kg and 0.65 mg/kg group D2(3X), (0.65 mg/kg occurring on day 4) until residue plateau around 0.52-0.65 mg/kg
- between 0.05 mg/kg and 3.8 mg/kg group E (10X), (1.8 mg/kg occurring on day 8) until residue plateau around 12-1.4 mg/kg

The mean values of the total residues of FLS-olefins in milk:

- residues remained below the LOD in the group B (0.1X)
- between LOD and 0.02 mg/kg in the dose group C (1X) until residue plateau at 0.02 mg/kg.
- Detween <LQD and 003 mg/kg group D (3X)g until residue plateau around 0.02-0.03 mg/kg
- between < COD and 0.12 mg/kg group E (10X), (0.12 mg/kg occurring on day 26) until residue plateau around 0.1 mg/kg

The resolts are summarized in the table Table 6.4.2- 4 and detailed in the Table 6.4.2- 8.



able 6	e 6.4.2- 4: Residues (mg/kg) of AE C656948 and its metabolites in milk								
		Residues (mg parent equivalents/kg) in Milk 🔬 🕺 🔗							
Day		Dose Group	B (0.1X)			Dose Grou	C (1X)		
2.43	fluopyram	FLU- benzamide	FLU- olefins	Total residue	fluopyram	FLU- ^{(@} benzam <del>id</del> e	FLU-	Total residue	Ča
-7	<lod< td=""><td><lod< td=""><td><lod< td=""><td><lod< td=""><td>≪Ĉ∕DD</td><td><lqd< td=""><td><lqd></lqd></td><td>×COD ×</td><td>Ĵ</td></lqd<></td></lod<></td></lod<></td></lod<></td></lod<>	<lod< td=""><td><lod< td=""><td><lod< td=""><td>≪Ĉ∕DD</td><td><lqd< td=""><td><lqd></lqd></td><td>×COD ×</td><td>Ĵ</td></lqd<></td></lod<></td></lod<></td></lod<>	<lod< td=""><td><lod< td=""><td>≪Ĉ∕DD</td><td><lqd< td=""><td><lqd></lqd></td><td>×COD ×</td><td>Ĵ</td></lqd<></td></lod<></td></lod<>	<lod< td=""><td>≪Ĉ∕DD</td><td><lqd< td=""><td><lqd></lqd></td><td>×COD ×</td><td>Ĵ</td></lqd<></td></lod<>	≪Ĉ∕DD	<lqd< td=""><td><lqd></lqd></td><td>×COD ×</td><td>Ĵ</td></lqd<>	<lqd></lqd>	×COD ×	Ĵ
1	<lod< td=""><td><lod< td=""><td><lod< td=""><td>&lt; 0.04</td><td>LOQ</td><td>6.02</td><td><lõd "<="" td=""><td>S&gt;&lt;0.04€</td><td></td></lõd></td></lod<></td></lod<></td></lod<>	<lod< td=""><td><lod< td=""><td>&lt; 0.04</td><td>LOQ</td><td>6.02</td><td><lõd "<="" td=""><td>S&gt;&lt;0.04€</td><td></td></lõd></td></lod<></td></lod<>	<lod< td=""><td>&lt; 0.04</td><td>LOQ</td><td>6.02</td><td><lõd "<="" td=""><td>S&gt;&lt;0.04€</td><td></td></lõd></td></lod<>	< 0.04	LOQ	6.02	<lõd "<="" td=""><td>S&gt;&lt;0.04€</td><td></td></lõd>	S><0.04€	
2	<lod< td=""><td><lod< td=""><td><lod< td=""><td>&lt; 0.04</td><td><i>∲</i> 0.02</td><td>ŐÖ.05</td><td>LOD a</td><td>0,07</td><td></td></lod<></td></lod<></td></lod<>	<lod< td=""><td><lod< td=""><td>&lt; 0.04</td><td><i>∲</i> 0.02</td><td>ŐÖ.05</td><td>LOD a</td><td>0,07</td><td></td></lod<></td></lod<>	<lod< td=""><td>&lt; 0.04</td><td><i>∲</i> 0.02</td><td>ŐÖ.05</td><td>LOD a</td><td>0,07</td><td></td></lod<>	< 0.04	<i>∲</i> 0.02	ŐÖ.05	LOD a	0,07	
4	<lod< td=""><td>0.01</td><td><lod< td=""><td>&lt;0.04 🛋</td><td>0.01</td><td>0.12</td><td>LOQ</td><td></td><td>$\checkmark$</td></lod<></td></lod<>	0.01	<lod< td=""><td>&lt;0.04 🛋</td><td>0.01</td><td>0.12</td><td>LOQ</td><td></td><td>$\checkmark$</td></lod<>	<0.04 🛋	0.01	0.12	LOQ		$\checkmark$
8	<lod< td=""><td>0.02</td><td><lod< td=""><td>&lt;0.04</td><td>0.01 👡</td><td>× 6,19 4</td><td>0.0</td><td>0.22</td><td>ĺ</td></lod<></td></lod<>	0.02	<lod< td=""><td>&lt;0.04</td><td>0.01 👡</td><td>× 6,19 4</td><td>0.0</td><td>0.22</td><td>ĺ</td></lod<>	<0.04	0.01 👡	× 6,19 4	0.0	0.22	ĺ
10	<lod< td=""><td>0.02</td><td><lod< td=""><td>&lt;0.04</td><td>° 0.01℃</td><td>× × 0.19</td><td>ં ≼ોઁ૦૦ ≼ે</td><td>0.22</td><td></td></lod<></td></lod<>	0.02	<lod< td=""><td>&lt;0.04</td><td>° 0.01℃</td><td>× × 0.19</td><td>ં ≼ોઁ૦૦ ≼ે</td><td>0.22</td><td></td></lod<>	<0.04	° 0.01℃	× × 0.19	ં ≼ોઁ૦૦ ≼ે	0.22	
13	<lod< td=""><td>0.02</td><td><lod< td=""><td>Ø.04 (</td><td>0,00</td><td>√ 0.2 K</td><td>~~0.02 ×</td><td>Ø<u>.2</u>4</td><td></td></lod<></td></lod<>	0.02	<lod< td=""><td>Ø.04 (</td><td>0,00</td><td>√ 0.2 K</td><td>~~0.02 ×</td><td>Ø<u>.2</u>4</td><td></td></lod<>	Ø.04 (	0,00	√ 0.2 K	~~0.02 ×	Ø <u>.2</u> 4	
17	<lod< td=""><td>0.02</td><td><lod< td=""><td>&lt;0.04[∞]</td><td>0.01</td><td>002</td><td>® 0.0<b>£</b></td><td>A0.25 °</td><td></td></lod<></td></lod<>	0.02	<lod< td=""><td>&lt;0.04[∞]</td><td>0.01</td><td>002</td><td>® 0.0<b>£</b></td><td>A0.25 °</td><td></td></lod<>	<0.04 [∞]	0.01	002	® 0.0 <b>£</b>	A0.25 °	
21	<lod< td=""><td>0.04</td><td><lod< td=""><td>J ~Q.04</td><td><b>₩0.01</b></td><td>A0.24 S</td><td>0.02</td><td>0.25</td><td></td></lod<></td></lod<>	0.04	<lod< td=""><td>J ~Q.04</td><td><b>₩0.01</b></td><td>A0.24 S</td><td>0.02</td><td>0.25</td><td></td></lod<>	J ~Q.04	<b>₩0.01</b>	A0.24 S	0.02	0.25	
24	<lod< td=""><td>0.02</td><td><lod< td=""><td><b>≥</b>≪9.04</td><td>Q.60</td><td>0.25</td><td>×0.02</td><td>032</td><td></td></lod<></td></lod<>	0.02	<lod< td=""><td><b>≥</b>≪9.04</td><td>Q.60</td><td>0.25</td><td>×0.02</td><td>032</td><td></td></lod<>	<b>≥</b> ≪9.04	Q.60	0.25	×0.02	032	
26	<lod< td=""><td>0.02</td><td><l00< td=""><td>&amp;×0.04</td><td>~0.01 ×</td><td>0,23</td><td>Ø 0.0<b>2</b></td><td>0.25</td><td></td></l00<></td></lod<>	0.02	<l00< td=""><td>&amp;×0.04</td><td>~0.01 ×</td><td>0,23</td><td>Ø 0.0<b>2</b></td><td>0.25</td><td></td></l00<>	&×0.04	~0.01 ×	0,23	Ø 0.0 <b>2</b>	0.25	
29	<lod< td=""><td>0.02</td><td>Stop '</td><td>℗҉&lt;0.0¥</td><td>[∞]0.01</td><td>a9.25 a</td><td>QQ92 (</td><td>0.28</td><td></td></lod<>	0.02	Stop '	℗҉<0.0¥	[∞] 0.01	a9.25 a	QQ92 (	0.28	
		Dose Group	<b>D</b> (3X)				p <b>F</b> (10X)*~~	,	
Day	fluopyram	FLU-	FLW-	🖉 Total 🔗	fluopyram	FLQ-	^O FLU-	Total	
		benzamide	<b>felefins</b>	🔊 residue		benzamide	olŒňs	residue	
-7	<lod< td=""><td><f00< td=""><td>~rop~</td><td>, Steel Ste</td><td>^V &lt; LOD</td><td></td><td><b>S</b>LOD</td><td><lod< td=""><td></td></lod<></td></f00<></td></lod<>	<f00< td=""><td>~rop~</td><td>, Steel Ste</td><td>^V &lt; LOD</td><td></td><td><b>S</b>LOD</td><td><lod< td=""><td></td></lod<></td></f00<>	~rop~	, Steel Ste	^V < LOD		<b>S</b> LOD	<lod< td=""><td></td></lod<>	
1	0.02	×0.03	<loq< td=""><td>\$0.06 °</td><td>6009</td><td></td><td>0.02</td><td>0.18</td><td></td></loq<>	\$0.06 °	6009		0.02	0.18	
2	0.05	~~0.13 ~ ^y	_≪LOQ	0.200	× 0.13 ×	(0.34 C	0.03	0.50	
4	0.05	0.33	\$ ^{0.02}	0.367	0.16	0°0.81	0.05	1.01	
8	0.04 ب		y ° 0.02)°				0.09	1.95	
10	0.03	0.54	0.02	y 0.59	~09.09 Ø		0.08	1.61	
13	0.09	0.53	<b>Q</b> .02 <b>%</b>		0.085×	°1.6	0.09	1.76	
17		0.53	0.02			1.7	0.10	1.88	
21	0.02	0.45	0.402	[∞] 0.49		² 1.2	0.10	1.39	
24	0.05		0.03	∿ 0.60¥ ©770	× 0.120″	1.3	0.10	1.52	
26	0.03		~ 0.03O		0.4	1.3	0.12	1.47	
29	0.03	<u> </u>	0.02	<i>"0</i> "0.61 O	<b>0.10</b>	1.4	0.10	1.60	1

Table 6.4.2- 4:Residues (mg/kg) of AE C656948 and its metabolites in milk	
---------------------------------------------------------------------------	--

For the calculation of the mean asidues, in case we have 3 levels of which at least one is <LOD and others <LOQ, it was legitimate to set the mean value as <LOQ; 4  $\bigcirc$ 0 Ø

For the calculation of the mean residues, in case one of two individual values are >LOQ and the others < LOQ, it was deemed appropriate to consider residues <LOQ mg/kg as being equation LOQ mg/kg. The approach represents the worst-case scenario.

In milk samples, if among three values there was at east one value > LOP, for the calculation of the mean all the other values <LOQ and <LOD were set equal to LOQ and LOO, respectively, this approach persents the worst-case scenario. Ŝ ~Q

Ô Mean total residues of floopyrant (sum of FLC) FLU-benzamide+FLU-olefins) in milk :

between <LQQ and \$0.04 mg/kg group B (0.1X),

Ô

- bety@en <0,04 mg/kg and 0.32 mg/kg group C (1X), until residue plateau around 0.3 mg/kg
- between 0.06 mg/kg and 0.70 mg/kg group D (3X), until residue plateau around 0.6 mg/kg
- betwee 0.18 mg/kg and 1.95 mg/kg group E (10X), until residue plateau around 1.5 mg/kg

Milk takes from dose group E (10X) was separated by centrifugation into skim milk and cream. The mean residuce of fluopyram in skim milk and cream were 0.02 mg/kg and 1.3 mg/kg, respectively. The mean



residues of FLU-benzamide in skim milk and cream were 1.5 mg/kg and 0.85 mg/kg, respectively. The mean value of the total residues of olefins in skim milk and cream were below the LOD and 1.0 mg/kg respectively. All the residue values are presented in the Table 6.4.2-5.

	4//2	v
Table ( 1 ) 5.	Desidence (ma/les) of flucences and its motobalities in alring mills and	
Table 6.4.2- 5:	Residues (mg/kg) of fluopyram and its metabolites in skim milk and	скеані «

		Residue levels of individual analytes (mg/kg) in skim milk and cream					
Group Dose	Sampla	Mean of sub-groups (madividual values) * 🚿 🔗 🔬					
Group Dose	Sample	Fluopyram	FLU-benzamide	Føtal residues Ø	Total residue		
		ruopyram		S Olefins			
10X	Skim milk	0.02	1.5				
4.05 mg/kg	(milk	0.02					
bw/day	whey)	(0.02; n.a.; 0.02)	(1.5; n.a.; 1.4)	$(\sim 40D; n.a.; < LOD)$	(1.92; 1.42)		
133.1 mg/kg		(	, C V		¥ ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		
DM	Cream	13 .1	0.85		3 14		
Sub-groups:	(milk fat)	(1.1; n.a.; J.¥)	(9.98; n.d.; 0.72)	$(0.78; 4, a.; 1.3)^{\circ}$	Q (2 \$ 3 42)		
E1 E2 E2	· · · ·				(2(00, 5.42)		
* Mean of the 2 sub-o	rouns calculate	d based on the unround	ed residue results	nt equivalents			
n a not applicable	stoups calculate				$\bigcirc$		
I OO = 0.01  mg/kg fc	r fluonvram and	d the ben amide metab	olite expressed as name	nt equeryalents	Ô		
LOQ = 0.02  mg/kg fc	or the total resid	ue of olefins was calcul	bred as sum of the two	ind Widual defin isomers	«С [«]		
I OD = 0.003  mg/kg	for fluonyram				Y		
LOD = 0.001  mg/kg	for FLU-benzan			S			
LOD = 0.001  mg/kg  f LOD = 0.004  mg/kg  f	for the total resi	due of obstins	d a d				
LOD = 0.004  mg/kg							

In animal tissues, fluopytam residues showed a clear dose response and were mainly found as follows:

- in liver, mean residues were between 0.25 mg/kg t0.1X group) and 4.0 mg/kg (10X group).
- in fat between 0.09 and \$.69 mg/kg (mesenterie) fat), between 0.04 and 0.57 mg/kg (subcutaneous fat) and between 0.04 and 0.49 mg/kg (perirenal fat) residues were measured.
- in kidney values from <LOD (0.1% group) to 0.00mg/kg (10X group)
- in muscle values from <LOD (0.1X group) to 0.03 mg/kg (10% group).

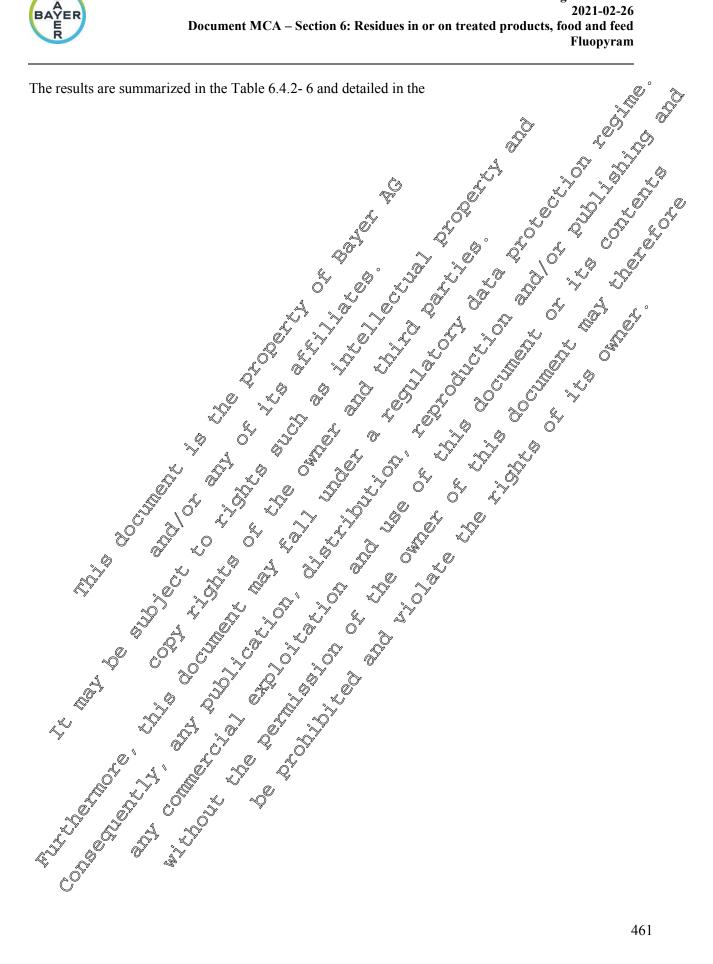
Fluopyram-benzamide residues showed a sear dose response and were mainly found as follows :

- in liver, mean residues were between 00r mg/kg (0.1X group) and 6.9 mg/kg (10X group).
- In fat between 0.01 (0.1X group) and 0.52 mg/kg (10X group) (mesenteric fat), between 0.01 (0.1X group) and 1, 9 mg/kg (10X group) (subcutations fat) and between 0.18 (1X group) and 0.85 mg/kg (10X group) (permenal fat) were measured.
- Widney between 0.03 (0.1 Xeroup) and 1.6 mg/kg (10X group).
- In muscle between 0.02 (0.1X group) and 4 mg/kg (10X group). The FLU-benzamide

Fluopyram-oletan's residues showed aclear dose response and were mainly found as follows

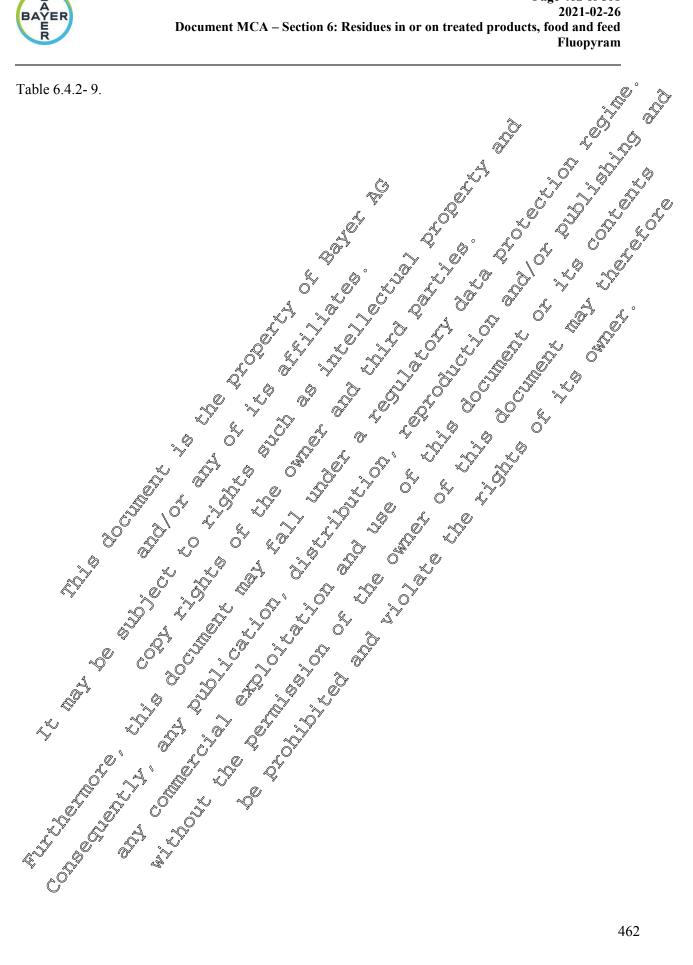
- in litter ranging from 0.04 to 0.50 mg/kg
- in(fat, residues boweer(0.09 (1) group) and 0.85 mg/kg (10X group) (perirenal fat), between \$07 (10 group) and \$90 mg/kg (10X group) (mesenteric fat) and between 0.06 (1X group) and 0.55 mg/kg 10X group) (subcutaneous fat) were measured.
- in addney alues from <LOD (0.1X group) to 0.13 mg/kg (10X group)
- muscle values from <LOD (0.1 X group) to 0.04 mg/kg (10X group)













Sable 6.4.2- 6: Residu	ies (mg/kg) o	of Fluopyram and	its metabolites i	n animætissue	
	Residues (n	ng parent equivaler	nts/kg)	Ĩ.	
		e Group B (0.1X)	<i>C)</i>	A	ô ^r ô ^r ô
Tissue	fluopyram	FLU-benzamide	DU-olefins	(Total residue)	
Perirenal Fat	< LOQ	< LOQ	<loq q<="" td=""><td>&lt;0.04</td><td></td></loq>	<0.04	
Mesenteric Fat	< LOQ	<loq< td=""><td>✓ <loq< td=""><td>&lt;0.04</td><td></td></loq<></td></loq<>	✓ <loq< td=""><td>&lt;0.04</td><td></td></loq<>	<0.04	
Subcutaneous Fat	< LOQ	0.01	$< LOQ^{*}$	° 0.04	
Liver	0.25	0.10	< ĽØD 0	<b>1 1 1 1 1 1 1 1 1 1</b>	
Muscle	< LOD	0.02	° seod x	<i>∞</i> <0.0 <b>4</b>	× ~
Kidney	< LOD	0.03 2	LOD	~ 0, <b>0</b> 4	
•	Do	se Group C.(IX)			à L°
Tissue	fluopyram	FL U-benzamide	FLOolefing	Total residue	
Perirenal Fat	0.04	Q 648 X	0.09	× 039	
Mesenteric Fat	0.03	0.16 × ×	J 2.00 ~	Q.26	
Subcutaneous Fat	0.04	õ_0.18 ́ ≫	0-06	0.28	
Liver	0. ZU .	<u>v</u> 102 s	0.04	» [©] 1.8 [©]	SY [™]
Muscle	≪Ì∕OQ	× ~ 0.29	$\sqrt{2} < LOOP$	<b>0</b> 32 🖇	
Kidney	©< LOQ	0.28	~ <1>OQ ~	<u>\$0.31</u>	
		se Group D (3X)			
Tissue 🔬	fluopyram	FLU-benzaiorde	Quildefins	Total residue	
Perirenal Fat	0.25	0.25	Ų″ 0 ⁰ .28 ⊖ [™]	×0.80	
Mesenteric Fat	° [∞] 0,25	Q.26 N	©0.29	0.80	
Subcutaneous Fat	0.24 K	<b>2</b> 9.37	~~ 0.1 <b>8</b> ~	0.79	
Liver Or S	∠© 2.1 °°	<u>لارم</u> 2.8 ک	<b>G1</b> 2	5.02	
Muscle 🖉	0.02	1 25	00.02 C	0.64	
Kidney C	6,03	<u>) 9.72</u>		0.79	
	Dos Dos	se Group E (DOX)	Q =	l	
Tissue	fluopyram	<u>FUU-benzamide</u>	FLU-olefins	Total residue	
Perirenal Fat	Q ⁴⁹	× 9.85	0.85	2.19	
Mesenteric Fat	<u></u> 0.69	0.72	0.9	2.31	
	0.57		0.55	2.12	
Milk Fat (Cream)	33	, [™] , Ø.85 0	1.0		
Milk Whey (Skim Milk)	Q0.02	×***1.45	< LOD		
Liver S	4.0		0.5	11.4	
Muscle	0.03	Q4	0.04	1.47	
Kidney	<b>9.07</b>	1.6	0.13	1.80	

In case we have Stevels of which a least one is <LOQ and others <LOQ, it was legitimate to set the mean value as <LOQ; When one or two individual values are >LOQ and the others < LOQ or <LOD, residues <LOQ or <LOD are considered equal to LOQ or LOQLOQ or LOQ = 0.00 mg/kg for fluory tam and the benzamide metabolite, expressed as parent equivalents.

LOQ = 0.02 mg/kg for the total residue of FLU-olefins was calculated as sum of the two individual olefin isomers. LOQ = 0.02 mg/kg for the total residue of FLU-olefins was calculated as sum of the parent + FLU-benzamide + the two olefin isomers LQQ = 0.002 mg/kg for the total residue of Fluopyram calculated as sum of the parent + FLU-benzamide + the two olefin isomers LQQ = 0.002 mg/kg for fluopyram, LOD = 0.001 mg/kg for FLU-benzamide, LOD = 0.004 mg/kg for the total residue of olefins.



Mean total residues of fluopyram (sum of FLU+FLU-benzamide+FLU-olefins) in tissues :

- in liver, mean residues were between 0.35 mg/kg (0.1X group) and 11.4 mg/kg (10X group) •
- In fat between <0. 04 (0.1X group) and 2.31 mg/kg (10X group) (mesenteric fat), between 0.04 • (0.1X group) and 2.12 mg/kg (10X group) (subcutaneous fat) and between 0.04 (0.1X group) and 2.19 mg/kg (10X group) (perirenal fat) were measured.
- In kidney between 0.03 (0.1X group) and 1.6 mg/kg (40X group). •
- In muscle between 0.02 (0.1X group) and 1.4 mg/kg/10X group) The FLU-benzamid •

Ś tissue to the Pesidue level of the The calculated transfer factors, i.e. the ratio of residue tevel in milk and feed, are summarised in the Table 6.4.2-7.

			91	<i></i>		(( )) ²		a 1	
Feeding level	1.5 mg/l		14.4 mg/	kg DM	<b>44.1</b> m	g∕kig DM∂ [©]	145.9 mg	kg DM	
8	feed (0.1X group)		_©feed_(1X	feed (1X group)		feed (3% group)		feed (19X group)	
Fluopyram		Ő						Õ	
Commodity	mg/kg	TQ		[™] T,F [™]	mg/kg	°∂°TF ∧	mg/kg	, 🖗 TF	
Milk	< LOD	nd	0.01°	0.0007	0.05	0.00	<u>رُ</u> نَّةً (0.12 مُ		
Perirenal Fat	<loq< td=""><td>🖇 nd 🐧</td><td>Q.Q4</td><td>Ø.003 🗸</td><td>0.25</td><td>0.006</td><td>0.49</td><td>0.003</td></loq<>	🖇 nd 🐧	Q.Q4	Ø.003 🗸	0.25	0.006	0.49	0.003	
Mesenteric Fat	<loq< td=""><td>nď√</td><td><b>0</b>.04</td><td>× 0.003</td><td>0.25</td><td>مري <b>9.006</b></td><td>0.69</td><td>0.005</td></loq<>	nď√	<b>0</b> .04	× 0.003	0.25	مري <b>9.006</b>	0.69	0.005	
Subcutaneous Fat	< LØØ	nd nd	\$0.04	0,003	0.25 ्र्	0.006	<b>9</b> .57	0.004	
Liver	.Q.25	<b>0.167</b>	0.7	<b>@</b> .05	\$2.1	<b>6.05</b>	× 4	0.03	
Muscle	SLOD 0	, nd	<loq "<="" td=""><td>🖉 nd 🏷</td><td>0,82</td><td><u>k</u>0.0005_</td><td>0.03</td><td>0.0002</td></loq>	🖉 nd 🏷	0,82	<u>k</u> 0.0005_	0.03	0.0002	
Kidney	S <lod< td=""><td>, ôð</td><td>~ LOQ</td><td>nd nd</td><td>0.03</td><td><b>Ů0.000∜∕</b></td><td>0.07</td><td>0.0005</td></lod<>	, ôð	~ LOQ	nd nd	0.03	<b>Ů0.000∜∕</b>	0.07	0.0005	
Fluopyram-benzan	nide \								
Commodio	∭mg/kg⊖	TF	ymg∕kg ⊲	Tf,	mg∕kg	ŴŤF	mg/kg	Tf	
Milk 👸	0.04	<b>B</b> ,03	0.25	0.02	0.65 (	v 0.01	1.7	0.01	
Perirenal	< KOQ	1.5 . 4		0.01	0.27	0.006	0.85	0.006	
Mesenteric Fat	. &LOQ∂	nd nd	0,16	\$`0.0 <u>1</u> ^\$	0,26	0.006	0.72	0.005	
Subcutaneous Fat ๙	LOO	<b>NA</b>	ð0.18 sy	0.01	20 <i>4</i> 37	0.008	1	0.007	
Liver	Q.1	Ø.07 Ž	y 1.2	6.08	2.8	0.06	6.9	0.05	
Muscle	@.02	0.01°	sØ.29	<b>0.02</b>	¥ 0.6	0.01	1.4	0.01	
Kidney 🔊	° ⁰ 0.030	6.02	<u>00.28</u>		0.72	0.02	1.6	0.01	
Fluopyram-olefins	ð,		Q ^Y _Q ^Y	ð					
Commodity	ू @ng/kg_⌒	TFO	mg/kg s	<b>⊘</b> TF	mg/kg	Tf	mg/kg	TF	
Milk «	× LOD	∽nd	LOQ	nd	0.03	0.0007	0.12	0.0008	
Perirenal Fat	< <b>L</b> QQ	, nd	0.08	0.006	0.28	0.006	0.85	0.006	
Mesenteric Fat	< LOQ	ັ nd ີ	007	0.005	0.29	0.007	0.9	0.006	
Subcutaneous Fat	$\mathbb{K} \times \mathrm{LO}^{\mathcal{O}}$	્યાલ	Q0.06	0.004	0.18	0.004	0.55	0.004	
Liver	[≫] < L@D	<b>n</b> d (	×0.04	0.003	0.12	0.003	0.5	0.003	
Muscle	≲©ÖD ू	∲ nd ~ 🎗	< LOQ	nd	0.02	0.0005	0.04	0.0003	
Kidney √	< LOD	nd	< LOQ	nd	0.04	0.0009	0.13	0.0009	
puration phase									

Table 6.4.2-7: Calculated transfer factors in cattle



For the depuration phase of the study, an additional dosing group of three animals were fed at the 10X dose level simultaneously with the animals from dose group E (10X) followed by untreated feeding for another 7 days (animal No. 16), 14 days (animal No. 15) and 21 days (animal No. 14).

Milk was collected from the additional dosing group on day 21 to 36 after the fast dosing and from the remaining cows additionally on 38 to 50. Residues in tissues were determined at sacrifice on Day 36 (animal No. 16), 43 (animal No. 15) and 50 (animal No. 14).

During the depuration phase (study conducted for the dose group 10XE), the mean residues of fluopyraph in milk was 0.11 mg/kg at the end of the dosing period (day 29) for the three animals. The mean residues of fluopyram decreased to mean values below the LOQ for all animals on day 31 and afterwards remained below the LOD until the end of the study.

The mean residue of FLU-benzamide in milk was 2.7 mg/kg at the end of the dosing period day 29 for the three animals and decreased to mean values (0.02 mg/kg) and  $(0.02 \text{ mg/$ 

The mean value of the total residues of ole tins in milk was 0.13 mg/kg at the end of the dosing period/day 29) for the three animals and decreased to values between 0.04 mg/kg and 0.02/from tay 36/till 45, and for one animal (cow no. 14) values below the LOQ were measured from Day 40 until the end of the study.

In tissues, residues of fluopyram were below the LOD with the exception of the liver sample taken from animal No. 16 (day 36), where 0.06 mg/kg of Auopyram were measured.

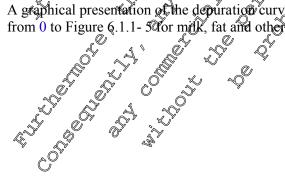
Residues of FLU-benzamide

- in liver decreased from 2.8 mg/kg (animal Nov 16, day 36) to 0.42 mg/kg measured on day 50 (animal No. 14)
- in muscle decreased from 0.77 mg/kg (animal Nov 16, day 36) to 0.15 mg/kg (animal No. 15, day 43) and 0.19 mg/kg (animal Nov 14, day 50)
- in perirenal, mesenteric and subcutance us fat on day 36 (artimal No. 16) ranged between 0.45 and 0.58 mg/kg and decreased to values below the LQQ or LQD on day 43 and 50.

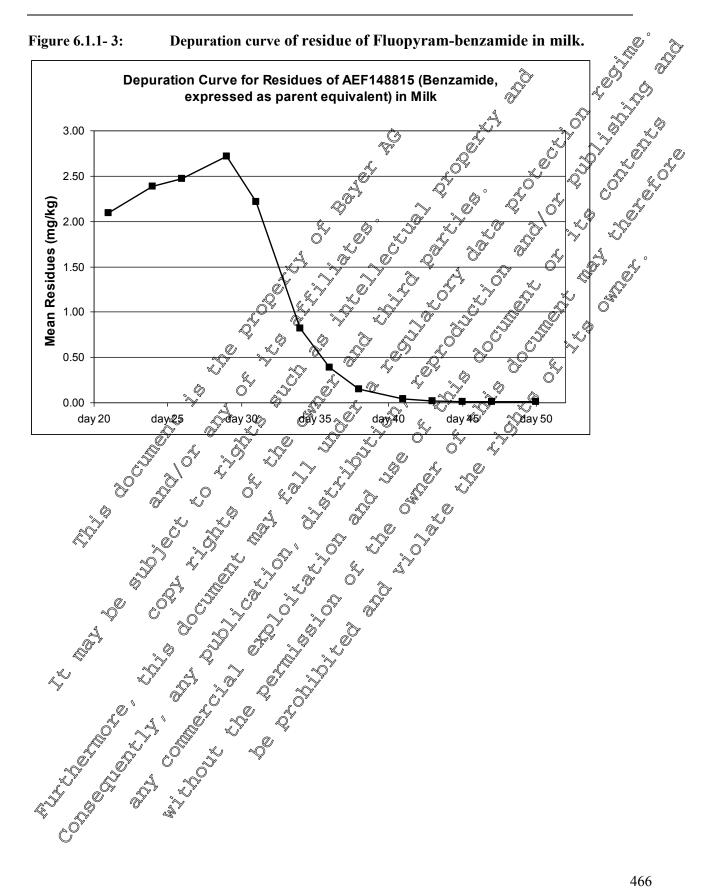
The total residues of FLU-olefins?

- An liver decreased from 0.08 mg/kg (on day \$6, animal No. 16) to 0.04 mg/kg on day 50 (animal No. 14)
- in subcutaneous fat increased from 0.04 mg/kg tanimat No. 16, day 36) to 0.28 mg/kg (animal No. 14, day 50).
- in perfernal and mesenteric fat (©12 and 0.13 mg/kg, respectively) (animal No. 16, day 36) increased to 0.21 and 0.26 mg/kg on day 43 (animal No. 15) and reached a total residue level of 0.71 mg/kg on day 50 (animal No. 14)
- m muscle were below the LOQ.

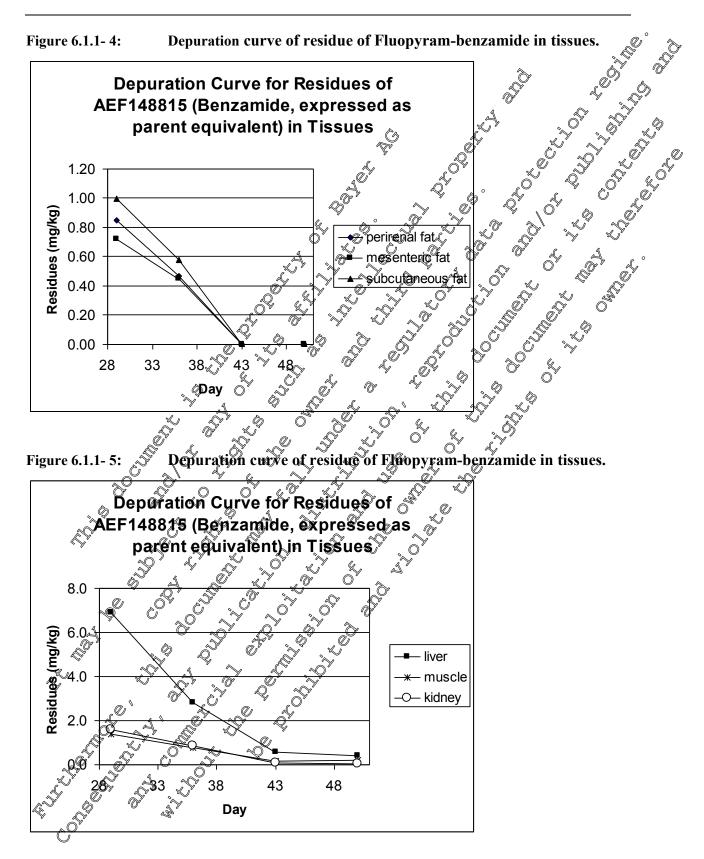
A graphical presentation of the depuration curves for the major metabolite, FLU-benzamide, is presented from 0 to Figure 6.1.1- 50 or milk, fat and other tissues, respectively.













According to the observed linear correlation between dose and residue levels in animal commodities after dosing, we assume that the same behaviour applies during the depuration phase in the 0.1X, 1X and 3Xdoses.

#### III. Conclusions

A feeding study was conducted with fluopyram on dairy coves in order to etucidate the levels of rel residues in cow tissues and in milk.

Fluopyram was administered orally via double-coated golatine capsules to dairy cows for 29 consecutive of days at the actual dose rates of 0.04 mg/kg bw/day (0.4X), 0.44 mg/kg bw/day (1X), 1.21 mg/kg bw/day (3X), 4.05 mg/kg bw/day (10X), and 4.38 mg/kg bw/day (10XE feeding + depuration phase). Feed consumption, body weights, and milk production were not adversely affected by compound administration.

ind intrives. / tainedsfrom th tes (FUF-bendamic articoseresponder there articoseresponder Prior to sacrifice, residues in milk were measured atvarious intervals. After the final dosethe animals were sacrificed and the key edible tissues were analyzed for the residues of fluopyram and its metabolites fluopyram-benzamide, and total residue of fluopyram-olefins in all matrices. Additionally, the residues were determined in skim milk and cream produced from the milk obtained from the dose group E (10X).

Overall, most of the time residues of fluopsram, and its metabolites (FLU-benzamide and total residues of FLU-olefins) were found in milk and tissues and showed a clear dose response; therefore, the residue data

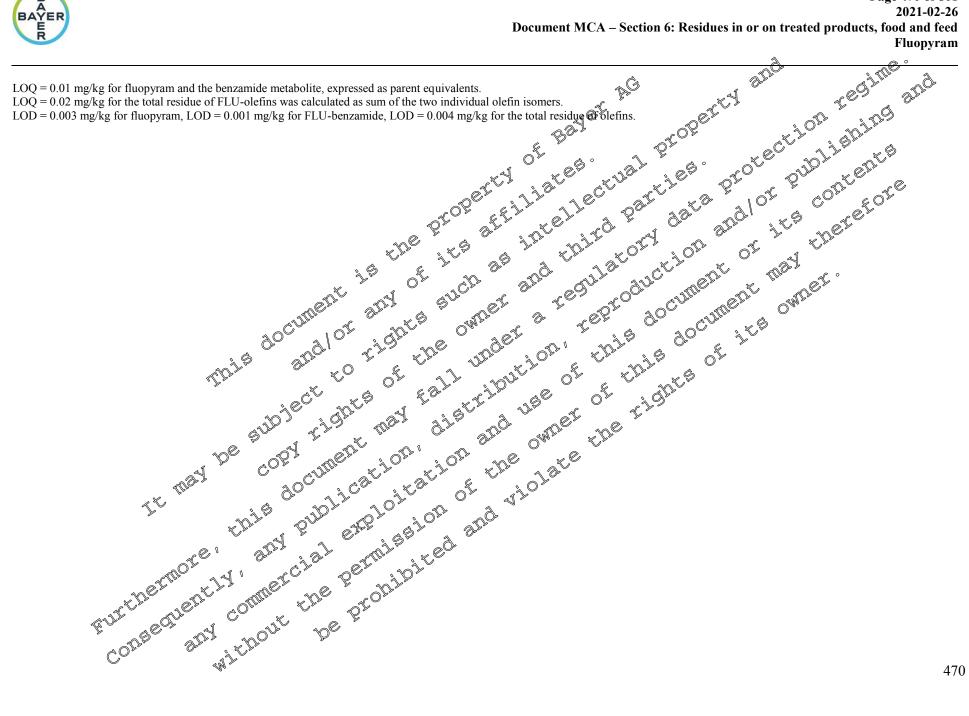


Page 469 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram

		y of residues of fluopyram and its metabolites in bovine milk, skimmed milk and cream (mg/kg) Residue levels of individual analyses (mg/kg)								
Group Dose	Sampling date*	fluopyrai	n	FLU-benza	mide	Total residue of K	of FLU [®]	I Utal Le		
		Indiv.	mean	Indiv.	mean (	<b>L</b> ndív.	mean	>° Indiy.	<b>N</b> nean	
	Pre-dosing - 7	3x <lod< td=""><td><lod< td=""><td>Â</td><td></td><td></td><td>FLOD</td><td>3×LOD</td><td>sidue</td><td>e o^{te}</td></lod<></td></lod<>	<lod< td=""><td>Â</td><td></td><td></td><td>FLOD</td><td>3×LOD</td><td>sidue</td><td>e o^{te}</td></lod<>	Â			FLOD	3×LOD	sidue	e o ^{te}
	1	3x <lod< td=""><td><lod< td=""><td>3x<loq_< td=""><td></td><td>Jys<lod td="" v<=""><td>- <loq< td=""><td>° 3x≪6004</td><td>§ &lt;0.04 °C</td><td>,L</td></loq<></td></lod></td></loq_<></td></lod<></td></lod<>	<lod< td=""><td>3x<loq_< td=""><td></td><td>Jys<lod td="" v<=""><td>- <loq< td=""><td>° 3x≪6004</td><td>§ &lt;0.04 °C</td><td>,L</td></loq<></td></lod></td></loq_<></td></lod<>	3x <loq_< td=""><td></td><td>Jys<lod td="" v<=""><td>- <loq< td=""><td>° 3x≪6004</td><td>§ &lt;0.04 °C</td><td>,L</td></loq<></td></lod></td></loq_<>		Jys <lod td="" v<=""><td>- <loq< td=""><td>° 3x≪6004</td><td>§ &lt;0.04 °C</td><td>,L</td></loq<></td></lod>	- <loq< td=""><td>° 3x≪6004</td><td>§ &lt;0.04 °C</td><td>,L</td></loq<>	° 3x≪6004	§ <0.04 °C	,L
0.1X	2	3x <lod< td=""><td><lod< td=""><td>3x<loq< td=""><td>ØPOD</td><td>3x<lqeo< td=""><td>LOD</td><td>Ø.04 €</td><td></td><td></td></lqeo<></td></loq<></td></lod<></td></lod<>	<lod< td=""><td>3x<loq< td=""><td>ØPOD</td><td>3x<lqeo< td=""><td>LOD</td><td>Ø.04 €</td><td></td><td></td></lqeo<></td></loq<></td></lod<>	3x <loq< td=""><td>ØPOD</td><td>3x<lqeo< td=""><td>LOD</td><td>Ø.04 €</td><td></td><td></td></lqeo<></td></loq<>	ØPOD	3x <lqeo< td=""><td>LOD</td><td>Ø.04 €</td><td></td><td></td></lqeo<>	LOD	Ø.04 €		
0.04 mg/kg	4	3x <lod< td=""><td><lod< td=""><td><loq 0.01;="" 0.02="" td="" ç<=""><td></td><td></td><td>)°</td><td>S≫ 3x&lt;0.04</td><td>\$0:04</td><td></td></loq></td></lod<></td></lod<>	<lod< td=""><td><loq 0.01;="" 0.02="" td="" ç<=""><td></td><td></td><td>)°</td><td>S≫ 3x&lt;0.04</td><td>\$0:04</td><td></td></loq></td></lod<>	<loq 0.01;="" 0.02="" td="" ç<=""><td></td><td></td><td>)°</td><td>S≫ 3x&lt;0.04</td><td>\$0:04</td><td></td></loq>			)°	S≫ 3x<0.04	\$0:04	
bw/day	8	3x <lod< td=""><td><lod< td=""><td>0.02; 0.02; 0.02</td><td>2,62</td><td>3x<lod< td=""><td><lod< td=""><td>3x&lt;0.04</td><td>&lt;0.04</td><td></td></lod<></td></lod<></td></lod<></td></lod<>	<lod< td=""><td>0.02; 0.02; 0.02</td><td>2,62</td><td>3x<lod< td=""><td><lod< td=""><td>3x&lt;0.04</td><td>&lt;0.04</td><td></td></lod<></td></lod<></td></lod<>	0.02; 0.02; 0.02	2,62	3x <lod< td=""><td><lod< td=""><td>3x&lt;0.04</td><td>&lt;0.04</td><td></td></lod<></td></lod<>	<lod< td=""><td>3x&lt;0.04</td><td>&lt;0.04</td><td></td></lod<>	3x<0.04	<0.04	
1.5 mg/kg	10	3x <lod< td=""><td><lod< td=""><td>0.01; 0.01, 0.02</td><td>0.02</td><td>SSS 3x≤LQD</td><td>, S€OD</td><td>€\$\$3x&lt;0.04 \$</td><td></td><td></td></lod<></td></lod<>	<lod< td=""><td>0.01; 0.01, 0.02</td><td>0.02</td><td>SSS 3x≤LQD</td><td>, S€OD</td><td>€\$\$3x&lt;0.04 \$</td><td></td><td></td></lod<>	0.01; 0.01, 0.02	0.02	SSS 3x≤LQD	, S€OD	€\$\$3x<0.04 \$		
DM	13	3x <lod< td=""><td><lqd< td=""><td>0.01; 0.02; 0.02</td><td>0.02</td><td>B 20D</td><td><lod %<="" td=""><td></td><td>0.04</td><td></td></lod></td></lqd<></td></lod<>	<lqd< td=""><td>0.01; 0.02; 0.02</td><td>0.02</td><td>B 20D</td><td><lod %<="" td=""><td></td><td>0.04</td><td></td></lod></td></lqd<>	0.01; 0.02; 0.02	0.02	B 20D	<lod %<="" td=""><td></td><td>0.04</td><td></td></lod>		0.04	
	17	3x <lod< td=""><td><b>D</b>COD</td><td>0.02; 0.02; 0.02</td><td>£02</td><td>3x<lqd< td=""><td>S BB</td><td>0.04 C</td><td>&lt;0.04</td><td></td></lqd<></td></lod<>	<b>D</b> COD	0.02; 0.02; 0.02	£02	3x <lqd< td=""><td>S BB</td><td>0.04 C</td><td>&lt;0.04</td><td></td></lqd<>	S BB	0.04 C	<0.04	
	21	3x <lod< td=""><td>Jon-Code</td><td>0.09: 0.02; 0.02</td><td>1.04 C</td><td>3x≪COD</td><td>CLOD</td><td>C2x&lt;0.04;0995</td><td>&lt; 0.04</td><td></td></lod<>	Jon-Code	0.09: 0.02; 0.02	1.04 C	3x≪COD	CLOD	C2x<0.04;0995	< 0.04	
	24	3x <lod< td=""><td>a ód</td><td>Q.Q. 0.02; 0.02</td><td>BOE -</td><td>3x<lod< td=""><td></td><td>_3x&lt;0.04</td><td>&lt; 0.04</td><td></td></lod<></td></lod<>	a ód	Q.Q. 0.02; 0.02	BOE -	3x <lod< td=""><td></td><td>_3x&lt;0.04</td><td>&lt; 0.04</td><td></td></lod<>		_3x<0.04	< 0.04	
	26	3x<160D	LOD	0.02; 0.07; 0.02	JD0.02	Obr 3x <lod< td=""><td><u>}</u>€OD</td><td>©[®]x&lt;0.04</td><td>&lt; 0.04</td><td></td></lod<>	<u>}</u> €OD	© [®] x<0.04	< 0.04	
	29	LOD "	- <lod< td=""><td>0.02 0.01; 0.02</td><td>0.02</td><td>JALOD K</td><td>LOD G</td><td>3x&lt;0.04</td><td>&lt; 0.04</td><td></td></lod<>	0.02 0.01; 0.02	0.02	JALOD K	LOD G	3x<0.04	< 0.04	
	Pre-dosing - 7	3x <lod< td=""><td>CLOD</td><td>S 3x<lod< td=""><td>, 2 ≹OD</td><td></td><td>, OOD</td><td>3x<lod< td=""><td><lod< td=""><td></td></lod<></td></lod<></td></lod<></td></lod<>	CLOD	S 3x <lod< td=""><td>, 2 ≹OD</td><td></td><td>, OOD</td><td>3x<lod< td=""><td><lod< td=""><td></td></lod<></td></lod<></td></lod<>	, 2 ≹OD		, OOD	3x <lod< td=""><td><lod< td=""><td></td></lod<></td></lod<>	<lod< td=""><td></td></lod<>	
	1	2x <loq; )<="" 0.00="" td=""><td>&lt; EOO</td><td>0,00,0.02; 0,02</td><td>0.63</td><td>SX LOD</td><td><pre>LOD</pre></td><td>3x&lt;0.04</td><td>&lt; 0.04</td><td></td></loq;>	< EOO	0,00,0.02; 0,02	0.63	SX LOD	<pre>LOD</pre>	3x<0.04	< 0.04	
1X	2	<loq; 0.02,="" 0.02<="" td=""><td>. \$0.02</td><td>0.05; 0.06; 0.04</td><td>Ø.05</td><td>W 3x<lpd< td=""><td><lod< td=""><td>0.06; 0.08; 0.08</td><td>0.07</td><td></td></lod<></td></lpd<></td></loq;>	. \$0.02	0.05; 0.06; 0.04	Ø.05	W 3x <lpd< td=""><td><lod< td=""><td>0.06; 0.08; 0.08</td><td>0.07</td><td></td></lod<></td></lpd<>	<lod< td=""><td>0.06; 0.08; 0.08</td><td>0.07</td><td></td></lod<>	0.06; 0.08; 0.08	0.07	
0.44 mg/kg	4	<lqg, 0.01;="" 0.02<="" td=""><td>0.01 D</td><td>0,12;0,12;0.12</td><td></td><td><lod 2x<loq<="" td=""><td>&lt; LOQ</td><td>0.13; 0.15; 0.16</td><td>0.15</td><td></td></lod></td></lqg,>	0.01 D	0,12;0,12;0.12		<lod 2x<loq<="" td=""><td>&lt; LOQ</td><td>0.13; 0.15; 0.16</td><td>0.15</td><td></td></lod>	< LOQ	0.13; 0.15; 0.16	0.15	
bw/day	8	LOQ; 0.01 (0.02	0.01	0,17; 0.18; 0.22	Q.Q.	2 LOQ; 0.02	0.02	0.20; 0.21; 0.24	0.22	
14.4 mg/kg	10 🔊	C < LOQ; 0.01; 0.02		@ 0.20; @1@; 0.19	0.19	∋ [≫] 3x <loq< td=""><td>&lt; LOQ</td><td>0.23; 0.20; 0.23</td><td>0.22</td><td></td></loq<>	< LOQ	0.23; 0.20; 0.23	0.22	
DM	13	<loq; 0.01;="" 0.02<="" td=""><td>0.01</td><td>0.23; 0.21; 0.19</td><td>0.21</td><td>2x<loq; 0.02<="" td=""><td>0.02</td><td>0.26; 0.24; 0.23</td><td>0.24</td><td></td></loq;></td></loq;>	0.01	0.23; 0.21; 0.19	0.21	2x <loq; 0.02<="" td=""><td>0.02</td><td>0.26; 0.24; 0.23</td><td>0.24</td><td></td></loq;>	0.02	0.26; 0.24; 0.23	0.24	
Sub-groups:	1 /	2x <lqq, 9.01<="" td=""><td>0.01</td><td>0.20; 0.20; 0.25</td><td><b>0</b>:22</td><td>2x<loq; 0.02<="" td=""><td>0.02</td><td>0.23; 0.23; 0.28</td><td>0.25</td><td></td></loq;></td></lqq,>	0.01	0.20; 0.20; 0.25	<b>0</b> :22	2x <loq; 0.02<="" td=""><td>0.02</td><td>0.23; 0.23; 0.28</td><td>0.25</td><td></td></loq;>	0.02	0.23; 0.23; 0.28	0.25	
C1, C2, C3	21	<loq, 0.01;="" 0.01<="" td=""><td>¥ 0.01 €</td><td>0.18:026; 0.27</td><td>0.24</td><td>2x<loq; 0.02<="" td=""><td>0.02</td><td>0.21; 0.31; 0.30</td><td>0.27</td><td></td></loq;></td></loq,>	¥ 0.01 €	0.18:026; 0.27	0.24	2x <loq; 0.02<="" td=""><td>0.02</td><td>0.21; 0.31; 0.30</td><td>0.27</td><td></td></loq;>	0.02	0.21; 0.31; 0.30	0.27	
	24	LOQ; 0.01; 001	0.01	0.26; 03P	0.25	2x <loq; 0.02<="" td=""><td>0.02</td><td>0.30; 0.32; 0.33</td><td>0.32</td><td></td></loq;>	0.02	0.30; 0.32; 0.33	0.32	
	26	LOQ; 0.01; 0.01	\$ 0.01	0.15; 0.22; 0.31	0.23	2x <loq; 0.02<="" td=""><td>0.02</td><td>0.15; 0.25; 0.34</td><td>0.25</td><td></td></loq;>	0.02	0.15; 0.25; 0.34	0.25	

* overall study day, n.a. not applicable, In case we have 3 levels of which the satisfies one io LOD and others <LOO, it was legitimate to set the mean value as <LOQ; When one or two individual values are >LOQ and the others <LOO or <LOD, residues <LOQ or <LOD are considered equal to LOQ or LOD

Page 470 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram



BAYER



Page 471 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram

		mary of residues of fluopyram and its metabolites in bovine milk, skipuned milk and cream (mg/kg) Residue levels of individual aparties (mg/kg) fluopyram FLU-benzamide Indiv. mean Indiv. mean In										
Group Dose	Sampling date*	fluopyra	m	FLU-benza	mide	Total resid	due of OF efins O ^T	Totalres	sidue			
		Indiv.	mean	Indiv.	mean	<b>Int</b> rv.	means	° Indiv.	♀″mean			
	Pre-dosing - 7	3x <lod< td=""><td><lod< td=""><td>3x<lod< td=""><td>CACOD.</td><td>3x<lop< td=""><td>TOD</td><td>S 3x<lolo <sup="">™</lolo></td><td></td></lop<></td></lod<></td></lod<></td></lod<>	<lod< td=""><td>3x<lod< td=""><td>CACOD.</td><td>3x<lop< td=""><td>TOD</td><td>S 3x<lolo <sup="">™</lolo></td><td></td></lop<></td></lod<></td></lod<>	3x <lod< td=""><td>CACOD.</td><td>3x<lop< td=""><td>TOD</td><td>S 3x<lolo <sup="">™</lolo></td><td></td></lop<></td></lod<>	CACOD.	3x <lop< td=""><td>TOD</td><td>S 3x<lolo <sup="">™</lolo></td><td></td></lop<>	TOD	S 3x <lolo <sup="">™</lolo>				
	1	0.03; 0.02; 0.02	0.02	0.03; 0.02; 0.03		2x <lqd; <<="" <lqq="" td=""><td></td><td>0.06006; 0.05</td><td>0.06</td></lqd;>		0.06006; 0.05	0.06			
3X	2	0.06; 0.03; 0.06	0.05	0.12; 0.13; 0.1	013	<i>x</i> ≤LOQ O	LOQ	<b>2</b> 0; 0.18; <b>0</b> ,23	0.20			
1.21 mg/kg	4	0.06; 0.03; 0.07	0.05	0.26; 0.29, 0.44	\$ 0.33 [*]	2x <lqq, 0.02<="" td=""><td>0.02</td><td>0.34; 0.84; 0.43</td><td><b>6</b> 0.37</td></lqq,>	0.02	0.34; 0.84; 0.43	<b>6</b> 0.37			
bw/day	8	0.04; 0.03; 0.04	0.04	0,63; 0.50; 0.53	0.55	0.02; 0.03; 0.03		0.69;0.56; 0.59	061			
44.1 mg/kg	10	0.04; 0.02; 0.02	0.03	9.44; 0.44 <del>;</del> 0.75	0.54	3x 0.02	200.02	0.50; 0.48; 0.79	°0.59			
DM	13	0.04; 0.02; 0.02	0.03		0.53	<loq@0.02; 0.02<="" td=""><td>0.02 200</td><td>0.72; 0.46; 0.55</td><td>0.58</td></loq@0.02;>	0.02 200	0.72; 0.46; 0.55	0.58			
Sub-groups:	17	3x 0.02	A B	055, 0.54; 0.50	A.83	3x 0.02	<u></u> 692~	e09; 0.58; 004	0.57			
D1, D2, D3	21	3x 0.02	∿ ⁰ .02	0.47; 0.48; 0.40	0 ⁴⁹ 0.45	3x 002	0.02	0.51; 0.59; 0.44	0.49			
	24	0.09; 0.03; 0.03	0.05	0.66,9.50; 0.41	0.580	0.05;0.02;0.02	0.03	0.80, 0.55; 0.45	0.60			
	26	0.03; 0.02; n.a	0:03	9.77; 0.52 n.a	J.65	@.03; 0.03, <b>u</b> .a	\$ 6.03	0.83; 0.57; -	0.70			
	29	0.04,02; 0.02	0.03 %	0.72; 0,53; 0.43	0.65		0.02 5	0.78; 0.57; 0.47	0.61			
	Pre-dosing -7	2x <lod; n.a<="" td=""><td>&lt; <b>L</b>OD</td><td>2x COD; p.a.</td><td>&lt; 1,0P</td><td>2x<lod; n.a<="" td=""><td>&lt; 600</td><td>2x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod;></td></lod;>	< <b>L</b> OD	2x COD; p.a.	< 1,0P	2x <lod; n.a<="" td=""><td>&lt; 600</td><td>2x<lod< td=""><td><lod< td=""></lod<></td></lod<></td></lod;>	< 600	2x <lod< td=""><td><lod< td=""></lod<></td></lod<>	<lod< td=""></lod<>			
	1	0.06; n.a.; 0.11	Ø.09	0.07; n.a.; 0.08	× \$0.08	LOQ; n.a., 0.02	0.02	0.15; 0.21	0.18			
10X	2	0.11; n.a.; 0.14		0.33 0.35 0.35	0.34 0.84	0.03 n.a.; 0.03	0.03	0.47; 0.52	0.50			
4.05 mg/kg	4 8	0.14; n.a.; 0,17 0.11; p.a.; 0.11	0016 1 0.11	0.80; n.a.; 0.80 1.7; n.a.; 1.8	1.8	0.11; n.a.; 0.07	0.05 0.09	0.98; 1.03	1.01 1.95			
bw/day	10	0.08 n.a.; 0.00	0.09			0.07, n.a.; 0.08	0.09	1.25; 1.97	1.95			
133.1 mg/kg	13	0.07; n.a.; 0.08	Ø,98	3; n.a.; 1, 0	Ke ^{bb}	0,07; n.a.; 0.10	0.09	1.44; 2.08	1.76			
DM	17 🔊	0.07; n.a.; 0.09		C 1.7; n. a. 1.7	5 1.7 Å	© 0.08; n.a.; 0.12	0.10	1.85; 1.91	1.88			
Sub-groups:	24	0.08; n.a.; 0.14	0.10 >	1.3On.a.; 1.1	1,2 4	0.08; n.a.; 0.11	0.10	1.46; 1.32	1.39			
E1, E2, E3	24	0.10; n.a. 0.13	0U+2	Q1.3; n.a.; 1.0 ²⁴	- Ops	0.09; n.a.; 0.11	0.10	1.49; 1.54	1.52			
	26	0.06; n.a; 0.15		ØF.2; n.a.: 19	Out 1.3	0.09; n.a.; 0.14	0.12	1.35; 1.59	1.47			
	29 y, n.a. not applica	08; n.a.; 0, t	0.10	00, it was beltimate t or <loq <lo<="" residues="" td=""><td></td><td>0.09; n.a.; 0.11</td><td>0.10</td><td>1.57; 1.62</td><td>1.60</td></loq>		0.09; n.a.; 0.11	0.10	1.57; 1.62	1.60			

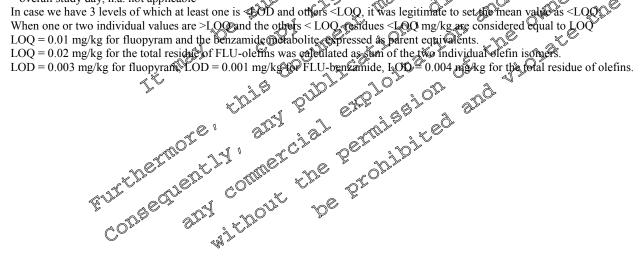


Page 472 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram

	Sampling date*	Residue levels of individual analytes (mg/kg)										
Group Dose		fluopyram		FLU-benzamide		<b>FLU-olefins</b>		Total residue				
		Indiv.	mean	Indiv.	mean [©]	Judiv.	mean °	Mindiv. N	mean			
	Pre-dosing - 7	2x <lod; <loq<="" td=""><td><lod< td=""><td>3x<lod< td=""><td>C'ELOD 1</td><td>3x<lod< td=""><td>L'ELOD</td><td></td><td>St -LODCE</td></lod<></td></lod<></td></lod<></td></lod;>	<lod< td=""><td>3x<lod< td=""><td>C'ELOD 1</td><td>3x<lod< td=""><td>L'ELOD</td><td></td><td>St -LODCE</td></lod<></td></lod<></td></lod<>	3x <lod< td=""><td>C'ELOD 1</td><td>3x<lod< td=""><td>L'ELOD</td><td></td><td>St -LODCE</td></lod<></td></lod<>	C'ELOD 1	3x <lod< td=""><td>L'ELOD</td><td></td><td>St -LODCE</td></lod<>	L'ELOD		St -LODCE			
	21	0.08; 0.06; 0.03	0.06	3.6; 0.94; 1.8	2.	0,10; 0.09; 0.00	6.00	£ <b>3</b> 8; 1.09; £9	Q.26			
	24	0.10; 0.09; 0.11	0.10	3.4; 0.98, 2.7	02.4	Ø.09; Q.08, Ø.22	0.13	∂-3.59; 1.1Z, 3.03 √	2.60			
10XE	26	0.12; 0.08; 0.16	0.12	3:20 P.1; 3.1		0.08 0.11; 0.30	0.18	3.44 (1.29; 3.52)	2.75			
4.38 mg/kg	29	0.09; 0.13; 0.12	0.11	3.1; 1,1; 4.9	Z,P	0.09; 0.10; 0.29	×0,¥3	3.28; 1.33; 4.32	2.98			
bw/day	31	<lod; 2x<loq<="" td=""><td><loq \$<="" td=""><td>2.1; 0, 94; 3.6</td><td></td><td>0.06; 0.07, 0.08</td><td>0.07</td><td>2.16; 0.99; 3.69</td><td>° 2.28</td></loq></td></lod;>	<loq \$<="" td=""><td>2.1; 0, 94; 3.6</td><td></td><td>0.06; 0.07, 0.08</td><td>0.07</td><td>2.16; 0.99; 3.69</td><td>° 2.28</td></loq>	2.1; 0, 94; 3.6		0.06; 0.07, 0.08	0.07	2.16; 0.99; 3.69	° 2.28			
145.9 mg/kg	34	3x <lod< td=""><td>≲LOD</td><td>Q184; 0.28; 13</td><td>0.81</td><td>ØX 0.05</td><td>0,050</td><td>0,89, 0.33; 1,20</td><td>0.86</td></lod<>	≲LOD	Q184; 0.28; 13	0.81	ØX 0.05	0,050	0,89, 0.33; 1,20	0.86			
DM	36	3x <lod< td=""><td>LOD 9</td><td>0.37; 0.11; 0.69</td><td>639</td><td>3x 0.0€</td><td>09.04</td><td>0.41; 0.1500.73</td><td>0.43</td></lod<>	LOD 9	0.37; 0.11; 0.69	639	3x 0.0€	09.04	0.41; 0.1500.73	0.43			
Sub-groups:	38	2x <lod; n.a.<="" td=""><td><loo< td=""><td>0.22, 0.07; n.a.</td><td>0.15</td><td>0.03; 0.04; n.a.</td><td>0.04 0</td><td>0.25, 0.11</td><td>0.18</td></loo<></td></lod;>	<loo< td=""><td>0.22, 0.07; n.a.</td><td>0.15</td><td>0.03; 0.04; n.a.</td><td>0.04 0</td><td>0.25, 0.11</td><td>0.18</td></loo<>	0.22, 0.07; n.a.	0.15	0.03; 0.04; n.a.	0.04 0	0.25, 0.11	0.18			
F1, F2, F3	41	2x <lod;< td=""><td>A 4LOD</td><td><b>0.06</b>; 0.02; <b>@</b>,a.</td><td>0<u>40</u></td><td>Q.Q3; 0.02: n.a</td><td>003</td><td>\$0.09; 0.04</td><td>0.07</td></lod;<>	A 4LOD	<b>0.06</b> ; 0.02; <b>@</b> ,a.	0 <u>40</u>	Q.Q3; 0.02: n.a	003	\$0.09; 0.04	0.07			
	43	2x ≤LØD; n.a.	S <lod< td=""><td>0.02; 001, n.a.</td><td>JD0.02 }</td><td>0 0.02; 0.08; n.a.</td><td>\$ \$ 0.03</td><td>0.04; 0.04</td><td>0.04</td></lod<>	0.02; 001, n.a.	JD0.02 }	0 0.02; 0.08; n.a.	\$ \$ 0.03	0.04; 0.04	0.04			
	45	QOD; 2x n.a	< <b>FOB</b>	0.01; 2x n.a.	0.01	0,02, n.a.; n.a.	0.025	0.03	< 0.04			
	47	LOD; 2x n.a	K-CLOD	<loq:28 n.a<="" td=""><td>_×L)9Q</td><td><loq; 2x="" n.a<="" td=""><td>JOL DQ</td><td>&lt; 0.04</td><td>&lt; 0.04</td></loq;></td></loq:28>	_×L)9Q	<loq; 2x="" n.a<="" td=""><td>JOL DQ</td><td>&lt; 0.04</td><td>&lt; 0.04</td></loq;>	JOL DQ	< 0.04	< 0.04			
	50	<lod; 2x="" n.as<="" td=""><td><lqqc *<="" td=""><td><loq; 2x="" n.a<="" td=""><td>LOQ</td><td></td><td>LOQ</td><td>&lt; 0.04</td><td>&lt; 0.04</td></loq;></td></lqqc></td></lod;>	<lqqc *<="" td=""><td><loq; 2x="" n.a<="" td=""><td>LOQ</td><td></td><td>LOQ</td><td>&lt; 0.04</td><td>&lt; 0.04</td></loq;></td></lqqc>	<loq; 2x="" n.a<="" td=""><td>LOQ</td><td></td><td>LOQ</td><td>&lt; 0.04</td><td>&lt; 0.04</td></loq;>	LOQ		LOQ	< 0.04	< 0.04			

* overall study day, n.a. not applicable

In case we have 3 levels of which at least one is GOD and others <LOQ, it was legitimate to set the mean value as <LOQ





Page 473 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram

	Dose	Dose	Sub-	Sampling		Residue levels (mg/kg)
Group	(mg/kg bw/day)	(mg/kg DM)	group	Time (Day)*	fluopyram	
Perirenal fa	at	· · · · ·				The second of th
			B1	30	< LOQ	$\frac{1}{2} = \frac{1}{2} = \frac{1}$
0.1X	0.04	1.5	B2	30	< LOQ	$\frac{1}{\sqrt{2}} \frac{1}{\sqrt{2}} \frac{1}{\sqrt{2}$
			B3	30	< LOQ	$\frac{1}{\sqrt{2}} < \overline{100} $
				Mean	<loq <sup="">5</loq>	
			C1	30	×0.96 s	
1X	0.44	14.4	C2	30 5	\$ 0.01 £	
			C3	30	0.0	
	I			Mean	0.04	0.18 C 0.09 C UT 0.38 C WILE
			D1	21130	0.2,2%	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
3X	1.21	44.1	D2	3005	0018	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$
			D305	30	0.23 0.25	
	1			O ^b Mean	0,25	0.27 0.28 0.80
1037	4.05	1001	E1	30	09.37	0.27 0.28 0.80 1.99
10X	4.05	133.1	E2	<u>Č³⁰</u>	\$ n.a. \$	- ma. sor -
			E3	30	0.60	S 0.05 2.57
			F3	Mean		
10XE	4.20	145.0 🕅		36	<pre>C &lt; LQD C &lt; D </pre>	<u>0.47</u> 0 0 0.12 0.59
depuration	4.38	145.9	F2 5 F1	42 C 30	QÓD	$0^{1}$ < LQQ $0.21$ 0.22
-		TROSY			SS < LOD SS	
	21 1 1		·	Me`an	<u>&lt;1,00</u>	0.15 0.31

In case we have 3 levels of which at least one is < LOD and others LOQ, it was legitimente to set the mean value as <LOQ;

When one or two individual values are >LOQ and the others LOQ or COD, residues <LOQ or LOQ are considered equal to LOQ or LOD LOQ = 0.01 mg/kg for fluopyram and the benzamide metabolite, expressed as parent equivalents.

LOQ = 0.01 mg/kg for thuopyram and the benzamide metabolite, expressed as parent equivalents. LOQ = 0.02 mg/kg for the total residue of FLU-oleffice was calculated as sum of the two individual olefin isomers. LOQ=0.04 mg/kg for the total residue of Fluopyram calculated as sum of the parent PLU-benzamide + the two olefin isomers LOD = 0.003 mg/kg for fluopyram, LOD = 0.001 mg/kg for FLU-benzamide, LOD = 0.004 mg/kg for the total residue of olefins.



Page 474 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram

~

C	Dose	Dose	Sub-	Sampling		tabolites in bovine tissues (mg/kg) Residue levels (mg/kg) FLU- benzamide ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU- ELU-
Group	(mg/kg bw/day)	(mg/kg DM)	group	Time (Day)*	fluopyram	FLU- benzamide FLU-olefins
Mesenteric	fat					KA KE JON KE KON OUN KER
			B1	30	< LOQ	$\frac{1}{2} = \frac{1}{2} = \frac{1}$
0.1X	0.04	1.5	B2	30	< LOQ	$\frac{1}{2} \leq LQQ > \frac{1}{2} \leq LOQ \otimes 2 $
			B3	30	< LOQ	$\leq \mathbf{E} \mathbf{O} \mathbf{O}$ $\mathbf{O} \neq \langle \mathbf{I} \mathbf{Q} \mathbf{O} \neq \mathbf{O} \rangle$
			1	Mean	< <b>L</b> QQ	LOQ
			C1	30	× 0.07 × ×	
1X	0.44	14.4	C2	30 🦻	0.04	
			C3	30	0.002	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
	· · · · ·		1	Mean	S 0.03 S	0.16 <u>~ 0.07</u> <u>UR1 0.26</u> L
			D1	30	0.33	
3X	1.21	44.1	D20 ^C	1.50%	9.16	$\bigcirc 0.27 \\ \bigcirc 0.26 \\ \bigcirc 0.26 \\ \bigcirc 0.69 \\ \bigcirc 0.75 \\ \bigcirc 0.69 \\ 0.69 \\ \bigcirc 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ 0.69 \\ $
			<u></u>	30 x	> 0.27 C	$1  \alpha \geq 0  $
	<u>,                                    </u>		j d			$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
		L. P.	E1	30	0 0.67	
10X	4.05	133.1	E2	C ^{~ 30} \$		$\sim \sqrt{n.a.} \qquad 0 \qquad 0 \qquad -$
			E3		0.71	0.80 0.94 2.45
	<u>,                                    </u>		GULD	_ √ [≫] Mean	0.69 d. l	
10XE			F3 4	36	< LOD	0.45 0 9.13 0.58
depuration	4.38	145.9 🎾	FOS	TUP B	NOTION C	0.26 0.27
asp and thom		TRAZ.	F1	C ^{UL®} 50	< LQB	€ ŠĽŐD 0.11 0.12
		<i>n</i>	9r	Mean	_ × ĽOD	0.15 0.15 0.17 0.22

In case we have 3 levels of which at least one is < LOD and others LOQ, it was legitimere to set the mean value as <LOQ;

When one or two individual values are >LOQ and the others LOQ or COD, residues <LOQ or LOD are considered equal to LOQ or LOD

When one or two individual values are >LOQ and the others LOQ or LOD, residues <LOQ of LOD are considered equal to LO LOQ = 0.01 mg/kg for fluopyram and the benzamide metabolite, expressed as parent equivalents. LOQ = 0.02 mg/kg for the total residue of FLU-olefter was calculated as sum of the two individual olefin isomers. LOD = 0.003 mg/kg for fluopyram foD = 0.001 mg/kg for FLU-benzamide, LOD = 0.004 mg/kg for the total residue of olefins.

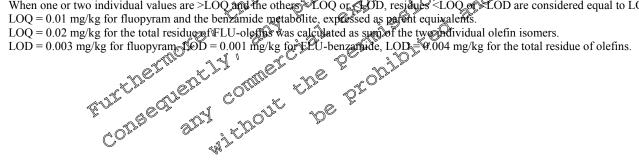


Page 475 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram

	Dose	Dose	Sub-	Sampling			levels (mg/kg)	C.C.L.	i OR injar
Group	(mg/kg bw/day)	(mg/kg DM)	group	Time (Day)*	fluopyram	FLU-	Potal residue of FLU-olefins	<b>Potal residue</b>	a ction regime. publiching and contents contents therefore
Subcutane	ous fat					~~~ x			all the second
			B1	30	< LOQ	×0.01	QQ%	0.04	
0.1X	0.04	1.5	B2	30	< LOQ	Q [©] < LOQ [°]	LOQ OF	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
			B3	30	< LOQ		≥ ^b < LQQ ^b	0.04 ⁰	t the state
				Mean	< 100	0.01	<u> </u>	0.04	L'E
			C1	30	× 0.07 × ×	0,09	* ¹ 0.06 0 ¹	≥ O ^b 0.22 O ^b	_~~
1X	0.44	14.4	C2	30 . (		<b>W</b> .13	0,04 c ²	<u> </u>	Nort .
			C3	30	Q03	5 Lb 0.31 OLb	J 0.08 JU	CO.42	Č.
			1	<u> </u>	<u>o</u> l 0.04 g ^v			0.42 C ^{ULD} 0.28 000	OWLET .
			D1	30	0.33	v 0.45 ⊘	G.¥8 D.C		
3X	1.21	44.1	D20 ^C	305	0.13	0.44	0.14 6	30 ⁰ 0.71 3 5	
			D9	<u>3.30</u>	» 0.27 0.27	0.22	× 1 0.28	0.92	
			j -	<u>Megn</u>	<u>6</u> 0.24	[~]	<u> 6.18 </u>	0.79	
		L. P.	E1	30/	0.65	. Q.93		2.10	
10X	4.05	133.1	E2	C ^{~ 30}	n.a	n.a.		-	
			E3	300	<u>10.48</u>		\$ 0.57 \$ ^y	2.15	
	1		O Uhar	<i>_</i> € [≫] Mean	10 0.57 d	09.0	0.55	2.12	
10XE			6 F3	36	< LOD	0.58 0	9.04	0.62	
depuration	4.38	145.9 🎾	F209		X Q LOD O		0.13	0.14	
r		TROS I	M	C ³⁰⁵⁰	<lqd< td=""><td>© ^{≪LOQ}</td><td>0.28</td><td>0.29</td><td></td></lqd<>	© ^{≪LOQ}	0.28	0.29	
	2 1			Mean	KEOD (	0.20	0.15	0.35	

In case we have 3 levels of which at least one is < LOD, and others ×LOD, it was legitimete to set the mean value as <LOD;

When one or two individual values are >LOQ and the others LOQ or COD, residues <LOQ or COD are considered equal to LOQ or LOD

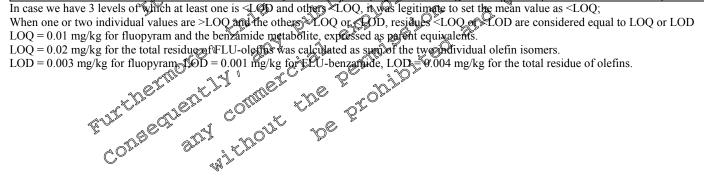




Page 476 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram

	Dose	Dose	Sub-	Sampling		Residue lexels (mg/kg)
Group	(mg/kg bw/day)	(mg/kg DM)	group	Time (Day)*	fluopyram	$\begin{array}{c c c c c c c c c c c c c c c c c c c $
Liver						Verified to the second of the second
			B1	30	0.26	0.3
0.1X	0.04	1.5	B2	30	0.24	010 $010$ $00$ $00$ $00$ $00$ $00$ $00$
			B3	30	0.24	$0.330^{\circ}$
				Mean	€25 [™]	
			C1	30	× 0.98 × ×	0.84 * **** 0.03* 0** * 0** 1.85 0*
1X	0.44	14.4	C2	30 🔬 🧔		$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
			C3	3.0	Ø.35	C. 1.90 als 6, 0.06 als 6, 2.31 at a cert
				<u>Mean</u>	్లే 0.71 ల్రీ 🖓	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
			D1	30 0	195	
3X	1.21	44.1	D20 ^{CC}	130 1	JD-1.8 (	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
					2.80	Q2.5 0 1 0 0 5 43
	1		j? (	/ inform	2.1	
		L.L.	E1	30	0 4.0 2	6 ² 0 ² 041 ² 11.11
10X	4.05	133.1	E2	C ^{~ 30} S	n.s.	7.0 0.58 5 11.48
			E3 je		3.9	<u>70</u> <u>0.58</u> <u>11.48</u>
			CA ®	- √ [≫] Mean	4.0	
10XE			F3	36	0.06	<u>2.8</u> <u>9.08</u> <u>2.94</u>
depuration	4.38	145.9 🎾	ED		LOO O	
		<u>trail</u>	M	C ^{05 50}		0.42 0.04 0.46
	21.1.1.0	a *		Mean	9.02	

In case we have 3 levels of which at least one is < LOD, and others ×LOD, it was legitimete to set the mean value as <LOD;

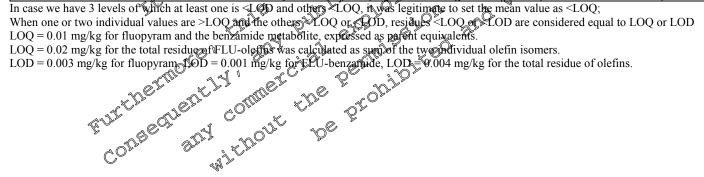




Page 477 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram

	Dose	Dose	Sub-	Sampling			e levels (mg/kg)		i OR nites
Group	(mg/kg bw/day)	(mg/kg DM)	group	Time (Day)*	fluopyram	FLU- benzami <b>đe</b>	Potal residue of FLU-olefins	<b>CPotal residue</b>	a ction regime and ction shing and ctics contents contents therefore
Muscle		· · ·			•			Les de	OUD. FEIL
			B1	30	< LOD	0.02	<u>» &lt;&amp;@D</u> *		
0.1X	0.04	1.5	B2	30	< LOD	0.02	LOD OF	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
			B3	30	< LOD	Q.02 ,	C < LQD >	0.04 ⁰	
				Mean	< FOD	<u>0.02 x x x x x x x x x x x x x x x x x x x</u>	<u> </u>	<0.04	L H DE
			C1	30	K LOQ K		K K L COQ O'	\$_O [™] 0.25 O [™]	-4
1X	0.44	14.4	C2	30 🧯	$< LOD^{39}$	0.22	<u> </u>	0,24	NOT -TO .
			C3	30	<®ØQ	0.44 8	JYLOQ JY	0.47 K	
	· · · · · · · · · · · · · · · · · · ·		51	Mean			<u> </u>	0.3201	OWLEE .
	1.01		D1	10 ¹⁰ 30 0	0.04	0.79	Ø.93 3.	0.65 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	0
3X	1.21	44.1	D20C	30%	<u>A</u> LOQ (	0.625	LOQG		
			D93	· · · · · · · · · · · · · · · · · · ·	0.00		Ch 1 0.01		
		I D		³⁴ <u>Mean</u> 30	0.02	0.00		<b>9.64</b>	
10X	4.05	133.1	E1 E2	A.A.	~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	, ~ <i>n.a.</i>	<u> </u>	1.37	
10A	4.03	155.1				<u>n.a.</u> 1,5 V		1.56	
			E3 je	A Mean	0.03			1.30	
			F3 al	36 V	LOD	0.77 0	<u>An an /u>	0.79	
10XE	4.38	145.9 🎾					<u><qloq< u=""> &lt;&lt; LOQ</qloq<></u>	0.17	
depuration	4.50	143.7 8	n M	CVI 50			Contraction of the second seco	0.21	
		<u>Tags</u>		Mean	K LOD	0.37	< <u>LOQ</u>	0.39	

In case we have 3 levels of which at least one is < LOD and others LOQ, it was legitimete to set the mean value as <LOQ;

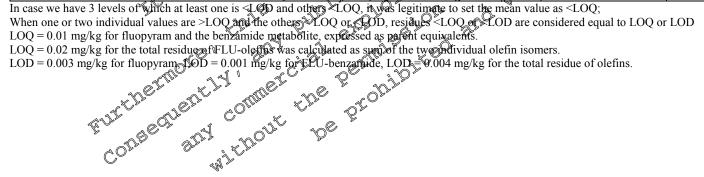




Page 478 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram

	Dose	Dose	Sub-	Sampling		Residue levels (mg/kg)
Group	(mg/kg bw/day)	(mg/kg DM)	group	Time (Day)*	fluopyram	
Kidney	• /					
*			B1	30	< LOD	$\begin{array}{c c} & & & & \\ \hline \\ \hline$
0.1X	0.04	1.5	B2	30	< LOD	0.02 $100$ $0.04$ $0$
			B3	30	< LOD	$\begin{array}{c} 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.04 \\ 0.$
				Mean	< FOD	
			C1	30	K LOQ K	$0.20 \times 10^{-1}
1X	0.44	14.4	C2	30 🦻	≥ <lqd< td=""><td>$\begin{array}{c c c c c c c c c c c c c c c c c c c$</td></lqd<>	$\begin{array}{c c c c c c c c c c c c c c c c c c c $
			C3	30	<@0Q	
	1		1	<u> </u>	S < LOQS	$\frac{9.28}{1000} + \frac{1000}{1000} + \frac{1000}{1000$
			D1	<u>30</u> 30	0.65	
3X	1.21	44.1	D20 ^C	30	0.02	
						0.61
				<u>Mean</u>	<u> </u>	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
		T.T.		30	0 0.05	
10X	4.05	133.1	E2	<u>C^V 30 5</u>	n.a.	<u>M.a.</u> <u>M.a.</u> <u>M</u>
			E3 je		J0.08 . @	<i>n.a. 0.a. - - - - - - - - - -</i>
			(cà °	<u> </u>	1 0.07 d	
10XE	4.00		F3 (	36	< LOD	0.86 0 0.03 0.89
depuration	4.38	145.9 🎾	E20		LOD O	
		TRAN	M	C ²⁰⁶⁵⁰	<lqd< td=""><td></td></lqd<>	
	21			Mean	_≪¥OD (	0.03 0.36

In case we have 3 levels of which at least one is < LOD, and others ×LOD, it was legitimete to set the mean value as <LOD;





#### CA 6.4.3 Pigs

The maximum dietary burden for pigs remains <0.004 mg/kg bw/day. Besides, the metabolic pathways do not differ significantly in the rat as compared to ruminants (cf CA 6.2.4). Therefore, a feeding study in pigs is not required.

#### CA 6.4.4 Fish

No residue study in fish was conducted. Currently no test method or Gaidance document is available for conducting such study. In these cases, waiving of this particular data requirement is considered acceptable according to the "Guidance document for applicants on preparing dossers for the approval of a chemical new active substance and the reneval of approval of the chemical active substance according to Regulation (EU) No. 283/2013 and Regulation (EU) No. 284/2013" (SANCO/10081/2013rev.2 of 2-May-2013).

#### CA 6.5 Effects of processing

Parent fluopyram and the metabolites fluopyram-Thydroxy, fluopyram-benzamide and fluopyrampyridyl-carboxylic acid (PCA) were proved to be stable under the test conditions representative for pasteurization, baking, brewing, boiling and sterilization. However, Guopyram-pyridyl-acetic acid can be transformed to fluopyram-picoline.

Processing studies for grape fractions have been previously deviewed at the EU level (DAR and adendum). Additional processing studies on grape are submitted to calculate processing factors in grape fractions. The results of the study indicate that residues of thuopyram remain to a large extent in wet pomace after pressing with processing factor at 3.2 Residues of thuopyram (mean processing factor = 0.4) are very low in wine (see Table 6.5.3 42).

Processing studies on apple are submitted to calculate processing factors in apple fractions. The results of the study indicate that residues of floopyram remain to a large extent in peel and pomace after pressing but residues of fluopyram are very low in fuice (mean processing factor = 0.2) (see Table 6.5.3-54).

## CA 6.5.1 Nature of the residue

Data to address this point were presented in the dossier submitted for first inclusion in Annex and were deemed acceptable following evaluation and peer review at EU level (2013).

For details of data submitted previously please refer also to the Baseline dossier CA 6.2. For completeness, a summar of these previously submitted studies are included below.

Data already evaluated during the first EU review process for inclusion on Annex I.(no new studies)

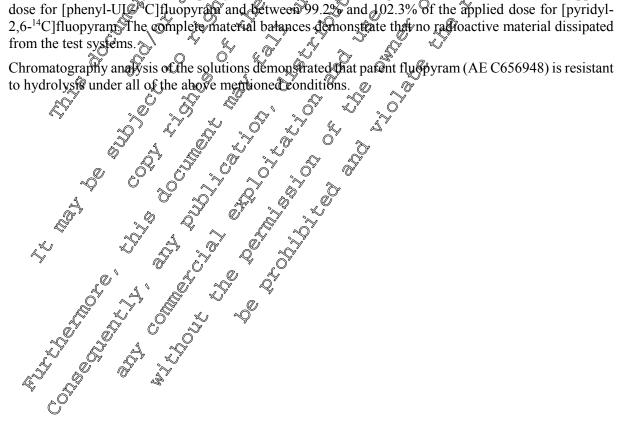
High temperature hydrolysis of parent compound



Data Point:	KCA 6.5.1/01	
Report Author:		
Report Year:	2006	Õ
Report Title:	[Phenyl-UL-14C]AE C656948 and [pyridyl-2,6-14C]AE C656948: Aqueous hydrolyses under conditions of processing studies	ŗ
Report No:	MEF-06/170	
Document No:	<u>M-278527-01-1</u>	
Guideline(s) followed in	EU: 91/414/EEC amended by 96/68/EC Section 6.5, Subsection 6.5 . Guideline	)
study:	7035/VI/95 Revision 5, Appendix (3) (July 1997)	a
Deviations from current test guideline:	None V V V V	
Previous evaluation:	rev. 1 to Vol.3 of DAR B7 august 2012 (reference relied on)	
GLP/Officially	Yes, conducted under GBP/Officially recegnised testing facilities	
recognised testing facilities:	Yes, conducted under GBP/Officially recognised testing facility s	
Acceptability/Reliability:	Yes A m Q Q A O D' A	

The degradation behaviour of [phenyl-UE¹⁴C] phopyram and [pyridyl-26¹⁴C] thuopyram was investigated in buffered local of inking water, at a projected dose of 1.0 mg/L. The hydrolysis conditions are mimicking pasteurization (90 °C at nH 4 for 20 min behing between be are mimicking pasteurization (90 at pH 4 for 20 min), baking, brewing, boiling (200 °C at pH 5 for 60 min) and sterilization (\$20 °C at pH @ for 20 min)

The material balances in the samples after incubation ranged between 100.4% and 102.2% of the applied dose for [phenyl-UI@4C]fluopyrand and between 99.2% and 102.3% of the applied dose for [pyridyl-2,6-14C]fluopyram The complete material balances demonstrate that no radioactive material dissipated





#### I. Materials and Methods

A. Materials					
1. Test Material	:			*	N O
Chemical structure					
	*positions of radiolabel	# positions of radiolabel	R		
Compound	AE C656948	JO ^O			
IUPAC name	N-{2-[3-chloro-5-(trifluoromet	thy pyridin-2-yl]eth	yl}-2-(frifluor	romethy) Benz	unade 🖉
CAS name	Benzamide, <i>N</i> -[2-[3-chlor (9Cl)	6-5-(trifuoromethy	l)-2-pyridinyl	]ethy Q-2-(trifle	ioromethyl)-
CAS no.	658066-35-4		× A	Ĵ ^{\$} 4	E G
Radiolabel position	S S	Pyridy 12,6-14C	Å Å	nlabelied	
Batch no.	BECH 1910	BECH 1905	K N	FJC633-6	KJ [®]
Specific radioactivity	3.85 MBq/mg (104.15, MCi/mg	231213900 dpm/m	g) A g g g g g g g g g g g g g g g g g g		7
Radiochemical Purity	> 99% (HPÉČ anđ TLC)	> 98% (HPLČ), 4 99% (TLC)			
Chemical Purity	> 98% (HPLC), 6	\$ 99% (HPL6)	\$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	).885 ³	
8				V	

2. Water: Aqueous buffer solutions prepared from tap water from the local provider "Verbandswaßerwerk Langenfeld-Monheum"

#### B. Study Design

#### 1. Experimental conditions:

Solutions of fluopyram AE C636948 in buffered minking water were subjected to three different pH / temperature scenarios, to munic pasteurization, baking/brewing/boiling and sterilization, respectively: pH 4/90 °C, pH 5/100 °C in a water bach) and pH 6 20 °C (in an autoclave). The durations of the treatments were 20, 60 and 20 minutes for the three scenarios, respectively. Closed 10-mL crimp-cap glass vials were used as test vessels, which contained 5 mL of test solution each.

A generic target application rate for floopyrate (AE C656948) of 1.0 mg/L buffered drinking water containing 1% acetonitrile was selected for this test.

For preparation of the stock solutions the total amounts of the radiolabelled test items were dissolved in 2 mL acetoprtrile. The content of radioactive residues was determined by LSC, and resulted in 3.8 MBq/mL, corresponding to 0.99 mg/mL, for the phenyl-label and 4.1 MBq/mL, corresponding to 1.06 mg/mL, for the pyridyl-habel.

The application solutions were prepared by diluting 500 µL of the respective stock solution with 4500 µL acetonitrile, and aliquots were used for the determination of the homogeneity and the radioactivity content by LSC and an aliquot was used for HPLC-MS/MS confirmation of the identity of the test item.



Dosing was carried out by pipetting aliquots of 50  $\mu$ L of the application solutions into two vials (each containing 4950 µL of the respective buffer solution) per scenario each.

Two vials per scenario (i.e. one per radiolabel) were incubated, another two vials per scenario served as time-zero samples and were not incubated. Additionally, control vessels containing 5 mL of the corresponding blank buffers were also subjected to incubation for monitoring the actual incubation temperature and the pH value.

#### 2. Sampling

Before opening the radioactive test vessels, 2 mL of acetonitrile were added to each sample osin syringe, and the vessels were shaken for homogeneity.

both for the time zero samples LSC. The radioactive residue content of each vessel was determined by and for the incubated solutions directly after termination of the test

#### **C. Analytical Procedures**

Aliquots of each sample were analysed by HPVC within a day. Samples from the pH 6/100 °C test series were used for exemplary confirmative TL@analysis and co-elution checks with mixtures of unlabelled reference compounds.

The radioactive residues of liquid samples were determined by liquid scintillation counting (LSC) using the scintillator Quicksafe Containing 9% of water.

II, Results and Discussion

The degradation behaviour of [phenyMUL-MC]fluopyram and pyridyl-2,6-14C]fluopyram was investigated in buffered local dynking water at a projected dose of 1.0 mg a.s./L. The hydrolysis conditions were chosen to mixic pasteurization (90°C at 9H 4 for 20 min), baking, brewing, boiling (100 °C at pH 5 for 60 min) and sterilization (120 °C at pH 6 for 20 min).

The applied dose was defined as the amount of radioactive residues measured in the samples at zero time. The total amount of applied active substance was 1.0 mg/L for [phenyl-UL-14C]fluopyram and 1.1 mg/L for [pyridyl-2,6^CC]fh@pyram Based on the results of LSC measurements immediately after test termination, a balance of adioactive residues was established for each experiment. The material balances ranged between 100.4% and 1022% of the applied dose for [phenyl-UL-14C]fluopyram and between 99.2% and 102.3% of the applied dose for [pyridyl-2,6-14C]fluopyram (Table 6.5.1-1).

The complete material balances demonstrate that no radioactive material dissipated from the test systems.

alances de



Table 6.5.1-1:	TRR values in water samples after application of [phenyl-UL-14C]fluopyram and	1
	[pyridyl-2,6-14C]fluopyram	0

Conditions	Conditions of hydrolysis	% of applied dose after incubation*	mg a.s./L
	[Phenyl-UL-	¹⁴ C]	
Pasteurization	pH=4, 90 °C, 20 min	100.4	
Baking, brewing, boiling	pH=5, 100 °C, 60 min	100.4 5 V	1.1 2 2 6
Sterilization	pH=6, 120 °C, 60 min	102.2	
	[Pyridy]	¹⁴ C] $Q$ $Q$	
Pasteurization	pH=4, 90 °C, 20 min		
Baking, brewing, boiling	pH=5, 100 °C, 60 min	9903 4	
Sterilization	pH=6, 120 °C, 60 min	Q02.3 Q	1.1 0 2 2
The corresponding zero-incu	bation control was set as 100%		

Quantitative analysis of all test samples was performed by reversed phase HOLC with radio-detection. Confirmative TLC analysis was performed exemplarity for the pH \$120 & test sories Ø

Ŋ

O

Ø In all processing scenarios the parent active substance represented the only residue and no degradation products were detected. The peak of fluopyram represented 100% of the injected adioactive dose in the samples. Thus, no degradation of the active substance occurred in the processing scenarios.

Conclusions

.0. * 0. * 0. In all processing scenarios (pasteurization, baking, brewing boiling and sterilization) the parent active substance fluopyram (AE CO6948) represented the only residue, and no degradation products were witch of the other detected. Š

No.



#### High temperature hydrolysis of fluopyram-benzamide

Data Point:	KCA 6 5 1/02
Report Author:	
Report Year:	
Report Title:	[Phenyl-UL-14C]AE C656948-benzamide: Aqueov hydrolysis under concernors of processing studies
-	of processing studies
Report No:	of processing studies
Document No:	
Guideline(s) followed in	EU: 91/414/EEC amended by 96/68/EC Section 6.5, Subsection 6.5.1, Guldeline 7035/VI/95 Revision 5, Agrendix E (July 1997)
study:	7035/VI/95 Revision 5, Afgrendix E (July 1997) $\mathcal{O}$ $\mathcal{O}$ $\mathcal{O}$
Deviations from current	
test guideline:	None
Previous evaluation:	yes, evaluated and accepted 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	None yes, evaluated and accepted rev. 1 to Vol.3 of DAR B August 2012 (references relies on) Yes, conducted under GVP/Officially (Cognical descine facilities
GLP/Officially	Yes, conducted under GLP/Off vially (2012 (Intercaces tend off))
recognised testing	
facilities:	
Acceptability/Reliability:	Yes, conducted under GP/Offmally Cognited testing facilities Yes
	Executive Summary
< 1	Executive Summary

The degradation behaviour of the petabolite [phenyl-UD-14C] fluopyram-benzamide was investigated in buffered local drinking water, at a projected dose of 19 mg/10 The hydrolysts conditions are mimicking pasteurization (90 °C at pH 4 for 20 min), paking, brewing, boiting (100 °C at pH 5 for 60 min) and sterilization (DO °C ar pH 6 Por 20 min). Õ

 $\bigcirc$ 

The material balances on the samples after incubation ranged between 97.3% and 107.8% of the applied dose. The complete material balances demonstrate that no radioactive material dissipated from the test systems.

Chromatography analysis of the folutions demonstrated that [phenyl-UL-¹⁴C]fluopyram-benzamide is resistant to hydrolysis under all of the above mentioned conditions.

 $\square$ 



#### I. Materials and Methods

A. Materials	CF ₃ O
1 Test Material:	
Chemical structure	CF ₃ O
	$H_2$
	* C S S S S S S S S S S S S S S S S S S
Compound	AE C656948-benzamide
IUPAC Name	2-(trifluoromethyl) benzamide
CAS Name	Pagamide (triffuoronative)
CAS Number	Calif NQ
Empirical formula	$\begin{array}{c c} C_{a}fi_{b}F_{3}NQ & \begin{array}{c} & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$
Molar mass	189 14 2 mol 2 0 . 5 . 5 . 6
Position of radiolabel	$[Phe fig] - U^{-1}O$
Batch number	
Specific radioactivity	$\mathcal{A}.07 \mathrm{MB}\mathrm{q/mg}^{\odot}$
Radiochemical purity	> 99% (HPFC and TLC)
Chemical purity	~ 99% (PPLC) ~ ~ ~ ~

2. Water: Aqueous buffer solutions prepared from the local provider "Verbandswasserwerk Langenfeld-Monheum"

#### 1. Experimental conditions:

Solutions of fluopyrangbenzapide in buffered drigking water were subjected to three different pH / temperature scenarios to munic pasteurization, baking/brewing/boiling and sterilization, respectively: pH 4/90 °C, pH 5/100 °C n a water bach) and pH 6 20 °C (in an autoclave). The durations of the treatments were 20, 60 and 20 minutes for the three scenarios, respectively. Closed 10-mL crimp-cap glass vials were used as test vessels, which contained approximately 5 mL of test solution each.

A generic target application rate for duopycam-benzamide of 1.0 mg/L buffered drinking water containing 1% acetonitrile was selected for this test.

For preparation of the stock solutions the total amounts of the radiolabelled test item were dissolved in ~O 2 mL acetoperile.

The appleation solutions were prepared by diluting 500 µL of the respective stock solution with 4500 pt aceptitrile and arquots were used for the determination of the homogeneity and the radioactivit, contear by LSC and resulted in 0.26 MBq/mL, corresponding to 0.10 mg/mL. An aliquot was used for HPLC-MS/MS confirmation of the identity of the test item.

Dosing was carried out by pipetting aliquots of 50  $\mu$ L of the application solutions into four vials (each containing 4950  $\mu$ L of the respective buffer solution) per scenario each.



Two vials per scenario (i.e. one per radiolabel) were incubated, another two vials per scenario served as time-zero samples and were not incubated. Additionally, control vessels containing 5 mL of the corresponding blank buffers were also subjected to incubation for monitoring the actual incubation temperature and the pH value.

#### 2. Sampling

Before sampling, 2 mL of acetonitrile were added to each sample and the vessels were shaken for homogeneity.

The radioactive residue content of each vessel was determined by LSC, both for the time ero samples and for the incubated solutions directly after termination of the test.

#### **C. Analytical Procedures**

Aliquots of each sample were analysed by HPLC. Samples from the pH 6/120°C test series were used for exemplary confirmative TLC analysis and co-elution checks with mixtures of phlabelled reference compounds.

The radioactive residues of liquid samples were determined by liquid scint ation counting (LSC) using the scintillator Quicksafe A containing 5% of water.

Respires and Discussion

The degradation behaviour of [phenyl-tel-¹⁴C]tluopytom-benzamide was investigated in buffered local drinking water, at a projected dose of 1.0 ms/a.s./k. The hydrolysis conditions were chosen to mimic pasteurization 90 °C at pH Ø for 20 mink baking, brewing, beiling (100 °C at pH 5 for 60 min) and sterilization (120 °C at pH 6 for 29 min).

The applied dose was defined as the amount of radioactive residues measured in the samples at zero time. The total amount of applied active substance was 1.07 mg/L to 1.10 mg/L. Based on the results of LSC measurements immediately after est termination, a batance of radioactive residues was established for each experiment. The material balances ranged between 97.3% and 107.8% of the applied dose (Table 6.5.1-2).

The complete material balances demonstrate that no radioactive material dissipated from the test systems.

Table 6.5.1-2: 🖑	TRR values	in wa	ter samples	after applic	ation of [phenyl-U]	L- ¹⁴ C fluopyram-
_O'	henzamate	Ŵ		11		J 17
	W ALLANDER	\$1	$\sim$			

	Conditions of hydrolysis	% of applied dose after incubation*	mg a.s./L
Pasteurization	pH=4, 90 °C, 20 min	99.8	1.09
Baking, Prewing, boiling	pH=5, 100 °C, 60 min	97.3	1.08
Sterilization	pH=6, 120 °C, 60 min	107.8	1.15

 $\ast$  The corresponding zero-incubation control was set as 100%



Quantitative analysis of all test samples was performed by reversed phase HPLC with radio-detection. Confirmative TLC analysis was performed exemplarily for the pH 6/120 °C test series. In all processing scenarios the parent active substance ([phenyl-UL-¹⁴C]fluopyram-benzamide) represented the only residue, and no degradation products were detected. represented the only residue, and no degradation products were detected. The peak of fluoryram

III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions III. Conclusions IIII. Conclusions III. In all processing scenarios (pasteurization, baking, brewing Stolling, and Sterling, but set item/metabolite fluopyram-benzamide represented the outy residie, and no degradation products see detected. Therefore, the tested processing conditions or not affect the nature of fluopyram-benzamide in raw agricultural commodities. representation of the second s



#### High temperature hydrolysis of fluopyram-7-hydroxy

Data Point:	KCA 6.5.1/03
Report Author:	
Report Year:	2006
Report Title:	[Pyridine-2,6-14C]AE C656948-7-hydroxy: Aqueory hydrolysis under conditions
Report No:	MEF-06/349
Document No:	<u>M-278554-01-1</u>
Guideline(s) followed in	EU: 91/414/EEC amended by 96/68/EC Section 6.5, Subsection 6.5.1, Guideline 7035/VI/95 Revision 5, Agrendix E (July 1997)
study:	7035/VI/95 Revision 5, Afgrendix E (July 1997)
Deviations from current	
test guideline:	
Previous evaluation:	
	rev. 1 to Vol.3 of DAR B August 2012 (references reliction)
GLP/Officially	Yes, conducted under SLP/Officially recognised testing facilities
recognised testing	Yes, conducted under GP/Off yrally Cognifed testing facilities
facilities:	
Acceptability/Reliability:	Yes of the second secon
0	Executive Summary 25 57 5
	Precutive Summary D D D

The degradation behaviour of the metabolite/test item [pyridyl-2,0-14C]fluopyram-7-hydroxy was investigated in buffered local drinking water, at a projected dose of 10 mg.C. The hydrolysis conditions are mimicking pasteurization (90 °C at pH 4 for 20 min), baking brewing, boiling (100 °C at pH 5 for 60 min) and scrilization (120 °C at PH 6 for 20 min). L L Õ

Ø

 $\bigcirc$ 

Ø

The material balances on the samples after incubation ranged between 100.7% and 102.1% of the applied dose. The complete material balances deponstrate that no radioactive material dissipated from the test systems.

Chromatography analysis of the folutions demonstrated that [pyridyl-2,6-¹⁴C]fluopyram-7-hydroxy is resistant to hydrolysis under all of the above mentioned conditions.

Ø1



#### I. Materials and Methods

A. Materials	
1 Test Material:	
Chemical structure	$\begin{array}{c c} CF_{3} \\ H \\ H \\ T
Compound	fluopyran-7-hydroxy
IUPAC Name	N-{2-[3-chloro-5-(triffuoromethyl)p@idine@-yl]-2
CAS Name	
CAS Number	
Empirical formula	C H11CHEN20
Molar mass	412.72 g/mol
Position of radiolabel	[Pyffdyl-2, 2 ⁴ C] 0 0 0 0 0
Batch number	BECH 1980 (radiolaberted)
Specific radioactivity	$3.16 \text{@HBq/mg} = 85.43 \mu\text{Ci/mg}$
Radiochemical purity	$>98\%$ (ftPLC) $\sim 0^{\circ}$ $\sim 4^{\circ}$ $\sim 5^{\circ}$
Chemical purity	>99% (HPLO)
n.a. not yet available	

2. Water: Aqueous buffer solutions prepared from tap water from the local provider "Verbands wasserwerk Eangenfeld-Monheim" B. Study Design

#### 1. Experimental conditions:

Solutions of fluopyram-70 ydrosy in byfered drinking water were subjected to three different pH / temperature scenarios, to mimic pasterization, baking/brewing/boiling and sterilization, respectively: pH 4/90°C, pH 5/100°C (in a water bath) and of 6/120 °C (in an autoclave). The durations of the treatments were 20, 60 and 20 minutes for the three scenarios, respectively. Closed 10-mL crimp-cap glass vials were used as tost vessels, which contained approximately 5 mL of test solution each.

A generic target application rate for flugpyram-7-hydroxy of 1.0 mg/L buffered drinking water containing less than 1% acconitrile was selected for this test.

For preparation of the sock solutions, the total amounts of the radiolabelled test item were dissolved in 2 mL acetonitrile.

The application solutions were prepared by diluting 500 µL of the respective stock solution with 4500 µL acetonitrile, and aliquots were used for the determination of the homogeneity and the radioactivity content by LSC and resulted in 0.43 MBq/mL, corresponding to 0.14 mg/mL. An aliquot was used for HPLC-MS/MS confirmation of the identity of the test item.



Dosing was carried out by pipetting aliquots of 38  $\mu$ L of the application solutions into four vials (each containing 4960 µL of the respective buffer solution) per scenario each.

Two vials per scenario (i.e. one per radiolabel) were incubated, another two vials per scenario served as time-zero samples and were not incubated. Additionally, control vessels containing 5 mL of the corresponding blank buffers were also subjected to incubation for monitoring the actual incubation temperature and the pH value.

#### 2. Sampling

Before sampling, 2 mL of acetonitrile were added to each sample and the vessels homogeneity.

both for the time zero samples The radioactive residue content of each vessel was determined by and for the incubated solutions directly after termination of the tes

#### **C. Analytical Procedures**

Aliquots of each sample were analysed by LPLC. Samples from the pH & test series were used for exemplary confirmative TLC analysis and co-Mution checks with th mixtures of unabelled reference compounds.

The radioactive residues of liquid samples were determined by liquid scintillation coonting (LSC) using the scintillator Quicksafe A containing 9% of water

#### Results and Discussion

The degradation behaviour of [phenyl-UL14C] Maopyram waoinvestigated in buffered local drinking water, at a projected dose of 1.0 me a.s./ The hydrolysis conditions were chosen to mimic pasteurization (90 °C acpH 4 for 20 min), baking prewing, boiling (100 °C at pH 5 for 60 min) and sterilization (120 °C at pH 6 for 20 min).

The applied dose was defined as the amount of radioactive residues measured in the samples at zero time. The total amount of applied active substance was 1.0 mg/L to 1.1 mg/L. Based on the results of LSC measurements immediately after test termination a balance of radioactive residues was established for each experiment. The material balances ranged between 100.7% and 102.1% of the applied dose (Table 6.5.1-3).

The complete material balance's demonstrate that no radioactive material dissipated from the test systems.

	xy is		
Condicions	Conditions of hydrolysis	% of applied dose after incubation*	mg a.s./L
Pasterization	pH=4, 90 °C, 20 min	100.7	1.1
Baking Frewing, boiling	pH=5, 100 °C, 60 min	102.0	1.1
Sterilization	pH=6, 120 °C, 60 min	102.1	1.1

#### TRR miues in water mappies after application of [Pyridyl-2,6-14C]fluopyram-7-**Table 6.5.1**

* The corresponding zero-incubation control was set as 100%

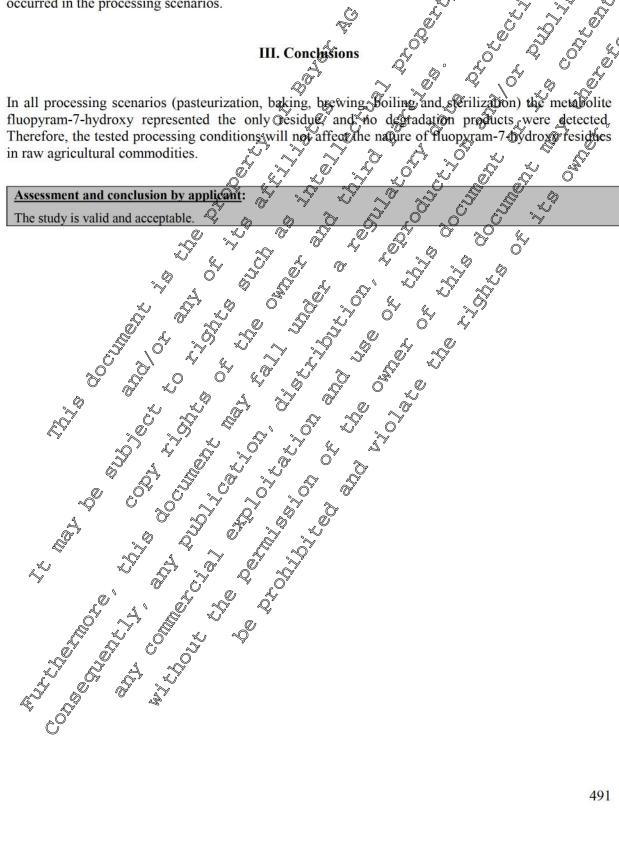


Quantitative analysis of all test samples was performed by reversed phase HPLC with radio-detection. Confirmative TLC analysis was performed exemplarily for the pH 6/120 °C test series.

In all processing scenarios the parent metabolite ([pyridyl-2,6-14C]fluopyram, Dhydroxy) represented the only residue, and no degradation products were detected. The peak of fluopyram-7-hydroxy represented 100% of the injected radioactive dose in the samples. Thus, no degradation of the test item occurred in the processing scenarios.



In all processing scenarios (pasteurization, baking, brewing Boiling and Serilization) the metabolite fluonyram-7-hydroxy represented the arth official with the series of In all processing scenarios (pasteurization, baking, bewing boiling and sering activity) of the fluopyram-7-hydroxy represented the only desidue and no degradation products were detected. Therefore, the tested processing conditions will not affect the nature of fluopyram-7 bydroxy residues in raw agricultural commodities.





ingli temperature nyur			
	KCA 6.5.1/04		
Data Point:	KCA 6.5.1/04		
Report Author:			
Report Year:			
Report Title:	[Pyridyl-2,6-14C]AE C656948-pygdyl-carboxyle acid: Aqueous Hydrofysis ung		
*	conditions of processing studies		
Report No:	KCA 6.5.1/04 2006 [Pyridyl-2,6-14C]AE C656948-py-dlyl-carboxylic acid: Aqueou Hydroty is unfor conditions of processing studies MEF-06/358 M-278803-02-1		
Document No:			
Guideline(s) followed in	<u>M-278803-02-1</u> EU: 91/414/EEC amenda Gy 96/68/EC Section 03, Subsection 05.1, Gidelin 7035/VL/95 Revision 5, Superdix E (100-1997)		
study:	EU: 91/414/EEC amend, By 96/68/EC Section 03, Subsection 05.1, Guidelin 7035/VI/95 Revision 5, Appendix E (J.O. 1997)		
Deviations from current	None A A A A A		
test guideline:			
Previous evaluation:	Providence       Providence         7035/VI/95 Revision 5, Appendix E (J.00, 199)       Providence         None       Providence         yes, evaluated and accepted       Providence         rev. 1 to Vol.3 & DAIC 7 August 2010 (references reped on providence)       Providence         Yes, conduct 9 und % GLP/Q) ficially, recogn sed testing fagorities       Providence		
	rev. 1 to Vol.3 of DAR 77 August 2019 (references relied on V		
GLP/Officially	Yes, conductor under GLP/Q)ficially tecogn sed testing families of O		
recognised testing			
facilities:			
Acceptability/Reliability:			
Freeutive Summary			
, C	Frecutive Summary		

#### High temperature hydrolysis of fluopyram-Pyridyl-Carboxylic Acid

The degradation behadiour of [pyridy1-2,60°C]fluopyram-pyridy1-carboxylic acid was investigated in buffered local drinking water, at a projected dose of 1.0 mg/L. The hydrolysis conditions are mimicking pasteurization (90 °C at pH 4 for 20 min), bacing, brewing boiling (100 °C at pH 5 for 60 min) and sterilization (120 °C at pH 6 for 20 mm). J. 0

The material balances ranged between 93.1% and 106.1% of the applied dose (AR). The complete material balances demonstrate that no radioactive material dissipated from the test systems. e de la construcción de la const

Q.

Ś

Ô

Chromatography analysis of the solutions demonstrated that [pyridyl-2,6-14C]fluopyram-pyridyl-carboxylic acid is resistant to hydrotysis under all of the above mentioned conditions.



#### I. Materials and Methods

A	Materials	
1	. Test Material:	
	Chemical structure	CI CF ₃ CF
		HU * N * ¹⁴ Cradiolaber
		$HO \xrightarrow{K} N \xrightarrow{K} N \xrightarrow{K} V \xrightarrow{K}$
	Compound	fluonyram Bridyl carboyada acid
	IUPAC Name	3-chlog S-(trifluoromethyl)py@dine-2-carbox fic acit
	CAS Name	2-Pýcidinecárboxylicacid, 3-chloro -(trifhoromethyl)- (9Cl)
	CAS Number	80194-68-9 C C C C C C C C C C C C C C C C C C C
	Empirical formula	$C_7H_4CIF_3NO_2$
	Molar mass	22\$\$,26 g/mol 37 2 2 2 2 2 2 2
	Position of radiolabel	Pyridy 2,6-14 C 2 5 5 5 2
	Batch number	BE64 1972 Jabelet AE \$6571 \$600 1897 0001 (unlabeled)
	Specific radioactivity	AC33 MBq/mg
	Radiochemical purity	
	Chemical purity	$\geq 8\% (HPUC) 0^{9} \times 0^{9} \times 0^{9}$
2	. Water: Aqueous Ouffer Solution	s prepared from tap water from the local provider
"	Verbandswasserwerk angenfeld-Mønh	
B	. Study Design	
1	. Study Design	s prepared from tap water from the local provider

#### 2. Water: solutions prepared Aquieous Guffer enfeld-Mønheim[»] "Verbandswasser

#### B. Study Design

#### 1. Experimental conditions:

Solutions of fluopyram_pyridy Carboxylic acid in buffered drinking water were subjected to three different pH / temperature sceparios, fo minic pasteurization, baking/brewing/boiling and sterilization, respectively: pH 4/90 °C, pH 5/100 °C (in a water bath) and pH 6/120 °C (in an autoclave). The durations of the treatments were 20, 60 and 20 trinutes for the three scenarios, respectively. Closed 10mL crimperap glass vials were used as lest versels, which contained 5 mL of test solution each.

Citrate buffers (20 10M) prepared from prinking water were used as test matrices. A generic target application rate for fluop am-pyridyl-acetic and of 1.0 mg/L buffered drinking water containing 1% acetonitrile was selected for this test.

For preparation of the stock solutions the total amount of the radiolabelled test item was dissolved in 2 mL acetomtrile.

The application solutions were prepared by diluting 500 µL of the respective stock solution with  $4500 \,\mu^2$  ace main integration of the homogeneity and the radioactivity content by LSC and an aliquot was used for HPLC-MS/MS confirmation of the identity of the test frem. The content of radioactive residues was determined by LSC, and resulted in 0.469 MBq/mL, corresponding to 0.11 mg/mL. Before and after treatment of all test systems, the radiochemical purity of the ¹⁴C-labeled test item within its application solution was determined by HPLC, and found to be 99.9% and 99.8%, respectively.



Dosing was carried out by pipetting aliquots of 50  $\mu$ L of the application solutions into two vials (each containing 4950  $\mu$ L of the respective citrate buffer solution) per scenario each.

Two vials per scenario were incubated and another two vials per scenario served as time-zero samples, and were not incubated. Additionally, control vessels containing 5 mL of the corresponding blank buffers were also subjected to incubation for monitoring the actual incubation the provide the provide to actual incubation for monitoring the second sec

#### 2. Sampling

After processing and cooling to room temperature, 2 mL of acetonitile were added to each test essel the vials were shaken for homogeneity and aliquots were taken for LSC and HPLC analysis.

The radioactive residue content of each vessel was determined by LSS, both for the time zero samples and for the incubated solutions directly after termination of the test.

#### **C. Analytical Procedures**

Aliquots of each sample were analysed by HPLC. Samples from the pH 6/120 C test series were used for exemplary confirmative TLC analysis. Co-elution checks with mixtures of unlabeled reference item and samples from one of the test series were conducted in both chromatography systems.

The radioactive residues of liquid simples were optermined by liquid contillation counting (LSC) using the scintillator Quicksafe a containing 5% of water.

S II Results and Discussion

The degradation behaviour of [pyridyl-2,6^{14}C] fluopyram-pyridyl-carboxylic acid was investigated in buffered local drinking water, at a projected close of 1.0 mg a.s./p. The hydrolysis conditions were chosen to mimic pasteurization (90 °C at pH 4 for 20 min), baking brewing, boiling (100 °C at pH 5 for 60 min) and sterilization (120 °C at pH 6 for 20 min).

The applied dose was befined as the amount of radioactive residues measured in the samples at zero time. The total amount of applied active substance was 1.06 mg/L–1.19 mg/L. Based on the results of LSC measurements immediately after test termination a balance of radioactive residues was established for each experiment. The material balances ranged between 93.1% and 106.1% of the AR (Table 6.5.1-4).

The complete material balances demonstrate that no radioactive material dissipated from the test systems.

## Table 6.5.1.4. TRR vatures in water samples after application of [pyridyl-2,6-14C] fluopyram- pyridyl-

Concisions		% of applied dose after incubation*	mg a.s./L
Pasteurization	pH=4, 90 °C, 20 min	93.1	1.11
Baking, brewing, boiling	pH=5, 100 °C, 60 min	106.1	1.12
Sterilization	pH=6, 120 °C, 60 min	99.5	1.07

* The corresponding zero-incubation control was set as 100%

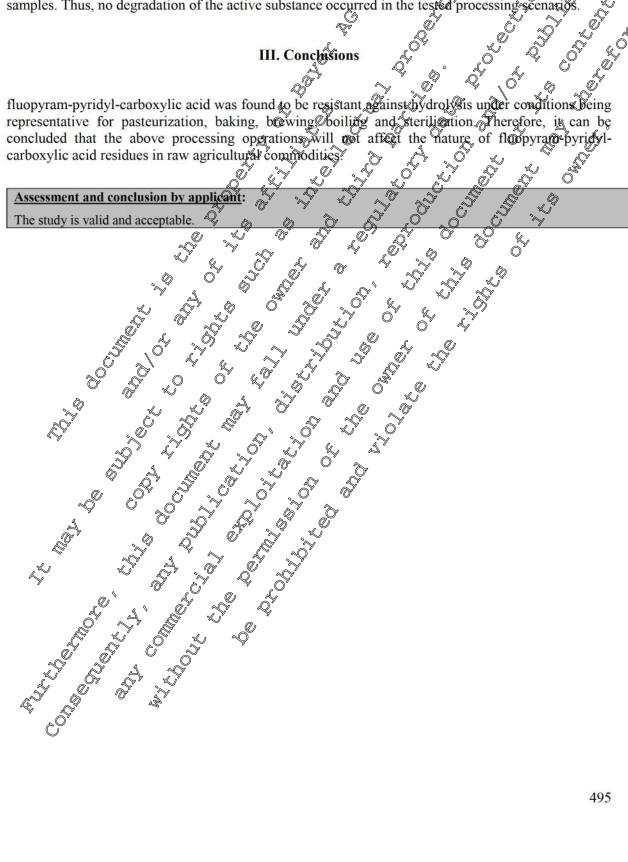


Quantitative analysis of all test samples was performed by reversed phase HPLC with radio-detection. Confirmative TLC analysis was performed exemplarily for the pH 6/120 °C test series.

di di In all processing scenarios, fluopyram-pyridyl-carboxylic acid represented the only residue and oo degradation products were detected. The peak of fluopyram-pyridyl-carboxybe acid represented 9988 99.9% of the applied radioactivity in the time zero samples, and 93.0-106.0% of the AR in the processed samples. Thus, no degradation of the active substance occurred in the tested processing scenarios. 



fluopyram-pyridyl-carboxylic acid was found to be resistant against hydrolysis under conditions being representative for pasteurization, baking, bewing/boiling and sterilination. Therefore, it can be concluded that the above processing operations will not affect the nature of floopyrate pyricyl-carboxylic acid residues in raw agricultural commodities.





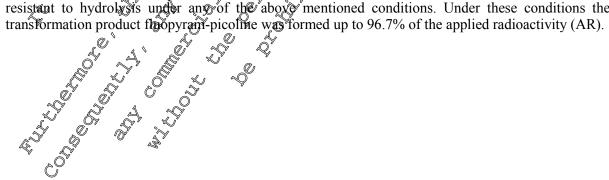
### High temperature hydrolysis of fluopyram-pyridyl-acetic acid

Data Point:	KCA 6.5.1/05
Report Author:	
Report Year:	
Report Title:	[Pyridine-2,6-14C]AE C656948-p idyl-acetic and Aqueous hypolysis under conditions of processing studies
	[Pyridine-2,6-14C]AE C656948 Pridyl-acetic and Aqueous hypolysis under of conditions of processing studies
Report No:	MEF-06/354
Document No:	<u>M-278760-01-1</u> A Q A A
Guideline(s) followed in	EU: 91/414/EEC amender By 96/68/EC Section 03, Subsection 05.1, Opidelin 7035/VI/95 Revision 5, Appendix E (J.O. 1997)
study:	7035/VI/95 Revision 5 Abpendix E (J/00 1997)
Deviations from current	None
test guideline:	
Previous evaluation:	yes, evaluated and accepted rev. 1 to Vol.3 & DAR 97 August 2010 (references refed on the second of
	rev. 1 to Vol.3 of DAR 77 August 2019 (references refred on V
GLP/Officially	Yes, conductor under GLP/Officially, ecognised testing families of O
recognised testing	rev. 1 to Vol.3 & DAIK 97 August 2010 (references reped on V Yes, conductor under GLP/Officially, recognized testing facilities of O
facilities:	
Acceptability/Reliability:	
	Y A Exception Commence
	Exceptive Sammary
i Si	

The degradation behaviour of the metabolite pyrich-2,6⁴⁴C]fluepyram-pyridyl-acetic was investigated in buffered local drinking water at a projected dose of 1.0 mg/L. The hydrolysis conditions are mimicking pasterfization (90 °C at pH4 for 20 min baking, brewing, boiling (100 °C at pH 5 for 60 min) and sterilization (120 °C at pH4 for 20 min).

The material balances ranged between 902% and 93.1% of the applied dose for the unshaken samples and between 95.2% and 97.1% of the applied dose for the shaken samples. The complete material balances demonstrate that no radio of the material dissipated from the test systems, and that small amounts of the test substance were present as volatiles in the gaseous phase of the samples.

Chromatography analysis of the solutions demonstrated that fluopyram-pyridyl-acetic acid is not resistant to hydrolysis under ano of the above mentioned conditions. Under these conditions the transformation product floopyram-picoline was formed up to 96.7% of the applied radioactivity (AR).





#### I. Materials and Methods

A. Materials	
1. Test Material:	
Chemical structure	
	HO * N * Positient of the HO * N * * * Positient of the 14C radiolable *
Compound	AE C656948-pyridyl-acetic acyd
IUPAC Name	[3-chloro-1-(trifluoromethol)pyridine-2-x0-acetic acid C
CAS Name	
CAS Number	
Empirical formula	General CIENTON CONTRACTOR OF CONTRACTOR
Molar mass	239.58 g/mot viree a 90);
Position of radiolabel	[Pyridine-2,6- ¹⁴ C]
Batch number	BEOH 1986 (labelor), BCS AA10089-PL@1 (uplabeled)
Batch number	A 68 MBg/mg (126.42 (Ci/mg))
Radiochemical purity	> 98% (HPLC)
Chemical purity	$>08\%$ (HELC), $O^{2}$ & $O^{2}$

# 2. Water: Aqueous ouffer, solutions prepared, from tap water from the local provider "Verbandswasserwerk cangenfeld-Monheim"

A R

#### B. Study Design

#### 1. Experimental conditions

Solutions of fluopyram-pyridyl acetic acid in buffered drintong water were subjected to three different pH / temperature scharios to minic pasteus zation baking/brewing/boiling and sterilization, respectively pH 4/90 °C, pH 5/100 °C (in a water bath) and pH 6/120 °C (in an autoclave). The durations of the treatment@were@0, 60 and 20 minut@ for the three scenarios, respectively. Closed 10mL crimpecap glass vials were used a test vessels, which contained 5 mL of test solution each.

Citrate buffers (20 mM) prepared from frinking water were used as test matrices. A generic target application rate for fluopypam-pyridyl-agetic ard of 1.0 mg /L buffered drinking water, containing less than 1% acetonin the, was selected for this test.

For preparation of the stock solutions the total amount of the radiolabelled test item was dissolved in 1.9 mL water and 100 µL 0.4 Meaqueons sodium hydroxide.

The appreciation solutions were prepared by diluting 500 µL of the respective stock solution with 4400 nL pure water and 100 µL 0.4 M aqueous sodium hydroxide, and aliquots thereof were used for the determination of the bomogeneity, the radioactivity content by LSC and the confirmation of the identity of the test item by HPLC-MS/MS. The content of radioactive residues accounted for 0.586 MBq/mL, corresponding to 0.125 mg/mL.

For each of the three test scenarios, dosing was carried out by pipetting aliquots of 42  $\mu$ L of the application solutions into six vials, each containing 4960  $\mu$ L of the respective citrate buffer solution.



Four vials per scenario were incubated and another two vials per scenario served as time-zero samples and were not incubated. Additionally, control vessels containing 5 mL of the corresponding blank buffers were also subjected to incubation for monitoring the actual incubation temperature and the pH value.

#### 2. Sampling

After processing and cooling to room temperature, 5 mb of acetonitrile were pipeted into the test solutions, the solutions were shaken gently and aliquots were taken for LSC and HPLC analysis. Two vials per scenario were further processed in order to dissolve possible volatiles into the organic phase (denoted as shaken samples): After incubation and cooling to room temperature 5 mL of acetonitrice were injected through the septa into the test solutions. The vials were chaken vigorously for approximately 2 minutes prior to LSC and HPLC analysis.

The radioactive residue content of each vessed was determined by SC, both for the time zero samples and for the incubated solutions directly after termination of the test.

#### **C. Analytical Procedures**

Aliquots of each sample were analysed by HPLC. Samples from the H 4/90 °C test series were used for exemplary confirmative HPLC-MS/MS analysis and co-plation checks with maxtures of unlabelled and labelled reference compounds.

The radioactive residues of liquid samples were determined by liquid scintillation counting (LSC) using the scintillator Quicksate A containing 5% of water

Results and Discussion

O

The degradation behaviour of [pyrid] 2,6-C] fluopyrad pyrid] acetic acid was investigated in buffered focal drinking water at a projected dose of 1.0 mg.a. L. The hydrolysis conditions were chosen to mimic parterization (96°C at pH 4 for 20 min), baking, brewing, boiling (100 °C at pH 5 for 60 min) and sterilization (120 °C at pH 6 for 20 min).

The applied dose was defined as the applied active residues measured in the samples at zero time. The total amount of applied active substance was 0.99 mg/L. Based on the results of LSC measurements immediately after test termination a balance of radioactive residues was established for each experiment. The material balances anged between 90.2% and 93.1% of the AR the unshaken samples and between 95.2% and 97.1% of the AR for the shaken samples (Table 6.5.1-5).

The complete material balances demonstrate that no radioactive material dissipated from the test systems, and that small amounts of the test substance were present as volatiles in the gaseous phase of the samples 2



Conditions	Conditions of hydrolysis	% of applied dose after	mg a.s./L	% of applied dose after incubation*	mg a.s. (shaken
		incubation*		(shaken samples [#] )	samples [#] )
Pasteurization	pH=4, 90 °C,	91.1	0.90	97.1 🔊	0.96
	20 min			10 ⁹	
Baking, brewing,	pH=5, 100 °C,	90.2	0.90	95.4	0.95
boiling	60 min		Ĉ.s.		
Sterilization	pH=6, 120 °C,	93.1	0.92	<b>9</b> 9.2 Ù	Q.95 0
	60 min		v	Re le	

Table 6 5 1-5. TRR values in water samples after application of  $[nvridy]_2 6^{-14}C$  fluonyram-nvridy]

shaken samples: 5 mL acetonitrile were injected through the septa of the yessels; they the vessels were shaken # vigorously to solve volatiles into the liquid phase.

L,

Quantitative analysis of all test samples was performed by reversed phase HPLC with radio freetection. Confirmative HPLC-MS/MS analysis was performed exemplarily for the pH4/90 °C test series. 

a)

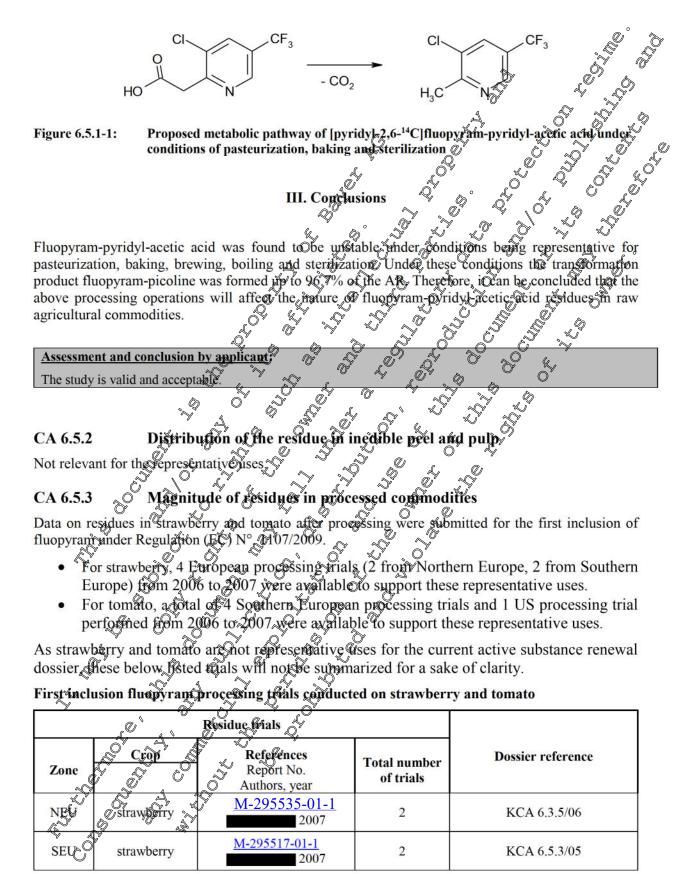
99.0% of the ARGIN the time zero The peak of fluopyram-pyridyl-acene acid represented 3.1% of samples, and 0%, 0% and 18.8% of the AR in the pasteurization, daking and sterilization samples, respectively. The formation of the transformation product Ruop fam-picoline was depended on the processing scenario. fluopyram-picoline was formed to 96.7%, 94.5% and 76.0% of the AR in the pasteurization, baking and sterilization samples, pespectively (Table 6 7.1-6 and Figure 6.5.1-1).

»Ô

Table 6.5.1-6:	Opantification of Auop am-poridyl-acetic acid and Gransformation products, expressed as % or applied radioactivity (% AR)
	expressed as % or applied radioactivity (% AR)

			<u> </u>	Y	NY N	si a			1	
	Rep. O No _v S	pH 4 0 k		p214 20 min 90 °C	pH 5 0 h	60 <b>m</b> in	pH 5 60/min	рН 6 0 h	pH 6 20 min	pH 6 20 min
			90 °C 4			100 °C	100 °C, shaken		120 °C	120 °C, shaken
fluopyram-	Mean	95 1	QKQ	D.O S	99.0	0.0	0.0	99.0	19.0	18.8
pyridyl-acetic acid (M40)						ð,				
	Mean	3.7 0	8998 , 8998 ,	96.7	0.0 0	89.4	94.5	0.0	73.9	76.0
4	Mean Q		1.3		ř.ø	0.7	0.9	1.0	0.2	0.4
Total %	Mean		91.1 Q	97.1	100.0	90.2	95.4	100.0	93.1	95.2
% AR in gaseous phase	Mean	WW .	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Q V		5.2			2.1	
AR in gaseous phase			~ ~ 7							







SEU	tomato	<u>M-295818-02-1</u> 2007	3	KCA 6.3.5/07
SEU	tomato	<u>M-298072-01-1</u> 2007	1	KCA 6.5.3/08
US	tomato	<u>M-299429-01-1</u> 2008	1	⁶ KCA 6.5.3/09
			Č V	⁶ KCA 6.5.3/0 ⁹ ⁶
Data Poin	L .	KCA 6.5.3/01	s do	× × × × ×
Report Au				
Report Ye		2008		0° ° 0° 0°
Report Tit		Determination of the residues	of•AE C <b>69</b> 6948, ir	on grope (burnen of grapes) and
1		bunch of grapes for vite pro- washings; pomace, dried; pom must; wine at 1st faste test wit SC) in the field on Northern Fr	ace wet; begy, w negatter low volu	Yon grope (broch of grapes) and d fractions (Sice; raw juice; asocd; retentate; Symace grape; c one spracing of AE C658948 (900
Report No	):	RA-3611/06		
Document		M-29682601-1	<u>~</u> \$. 0	
	(s) followed in	EU-Ref: Souncil Birective 91	414/EEC of July	B, 1990, Ann SII, par A, section
study:		6 and Annex In part Section		
2 L		Residues in or on Treated Pool Deviment 7029/x 95 rev. 5 ( Equivalent to USEPA @PTS	lucts, Food av Fe	
Deviations	s from current	vione Q S A		
test guidel	ine:		Č Š	
Previous e		yer evaluated and accepted gev. 1 to 01.3 of DAR B7 Au	wist 2012, (referen	Dices relied on)
GLP/Offic		Yes, conducted under GLP/Qt	ncially recognized	d teacing facilities
recognised facilities:	N Q	O O W X		
Acceptabi	lity/Reliability:	Yes of A AY	Å V	
Ę				
L L L				



Data Point:	KCA 6.5.3/02
Report Author:	
Report Year:	2008
Report Title:	Determination of the residues of AE C656948 in/on grape (bunch of grapes) and bunch of grapes for wine proc. and the processed fractions buice; raw juice washings; pomace, dried; pomace, wet; berry, washed; residue; pomace grape must;
Report No:	RA-3647/06
Document No:	<u>M-296549-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/41 EEC of July 9, 1991, Anne II, par A, section 6 and Annex III, part A, section 8
study:	6 and Annex III, part A, section 8
	Residues in or on Treated Products, Food are Feed EC Gui Once Working
	Document 7029/VI/95 rev 5 (1997-07-22); US-EgA OPPO'S Guideline No.
Deviations from current	
test guideline:	
Previous evaluation:	860.1520 Supplemental none yes, evaluated and acceptor rev. 1 to Vol.3 (SDAR by August 2012) (references reformed on)
GLP/Officially	rev. 1 to Vol.3 QUAR BY August 2018 (references relation), Yes, conducted under CLP/O@cially recognized testing facilities
recognised testing facilities:	
Acceptability/Reliability:	Yes Q' A A A A A

Balance studies on processing of grapes into grape wine were enduced to tetermine the transfer of fluopyram and its metabolites Fhippyrand benzamide. Thuopyram-pypdyl-acetic-acid and fluopyram-pypdyl-acetic-acid and fluopyram-pyridyl-carboxylic acid from bunch of grapes into processed fractions.

## Materialsand Methods

Wine was produced from red grapes obtained from 4 offerent trials located in Southern and Northern France in the 2006 season in order to determine the magnitude of the residues of fluopyram (AE C656948) and its metabolites fluopyram-PAA (B6S-A10139). Ouopyram-benzamide and fluopyram-PCA (AEC 657188) in grape processed commodities (juice, raw juice; washings; pomace, dried; pomace, wet; berry washed; retentate; pomace grape must wine at 1st taste test; wine) following lowvolume spraying of fluopyram 500 Sc).

## Fçeld part

In the field trials (study reference RA 2611/06, KCA 6.3.1/01 and RA-2647/06, KCA 6.3.1/02), two foliar spray applications with Ruopyram SC 300 - a suspension concentrate formulation containing 500 g/L fluopyram - were conducted at a single application rate of 250 g a.s./ha/application and water rate at 200 L/ha. The achieved total seasona rate was 0.500 kg a.s./ha. The applications were conducted at BBCH of 81 (for the first application and BBCH of 85-89 (for the second application).

For residue analysis, grape samples (bunches of grapes) were taken from the treated and the control plot on day 3 after the last application. Grape samples (bunches of grapes) for processing were taken from the treated plots and the control plots on the same day.

The field sub-samples from both trials were stored deep-frozen within 24 hours after sampling and until dispatch to the laboratory for logistics and preparation. All field sub samples were shipped by deep-freeze lorry and arrived in good condition. The samples for residue analysis were stored in a freezer at  $\leq$ -18°C with preparation of the examination samples.

The samples for processing were stored in a freezer at  $\leq$ -18°C or below until processing procedures.



The samples from processing were deep-frozen again immediately after the respective processing step. The processed samples were stored at  $\leq$ -18°C until preparation of the examination samples. For the preparation of examination samples of raw agricultural commodity and processed commodities the deep-frozen samples were shredded with dry ice in a cutter. Representative parts of the shredded samples were transferred into polystyrene boxes and stored at  $\leq$ -18°C until analysis.

wretransferred into polystyrene boxes and stored at ≤18°C until analysis.
Processing procedures
The processing of bunche of grapes into berries, washed; yashing water pomace, wet romacs, dried, retransferred into polystyre boxes and stored at ≤18°C until analysis.
The processing of bunche of grapes into berries, washed; yashing water pomace, wet romacs, dried, retransferred into polystyre boxes and stored at ≤18°C until analysis.
The processing of bunche of grapes into berries, washed; yashing water pomace, wet romacs, dried, retransferred into polystyre boxes and stored at ≤18°C until analysis.
The processing of bunches of grapes into berries, washed; yashing water pomace, wet romacs, dried, retransferred into polystyre boxes and stored at ≤18°C until analysis.
The processing of bunches of grapes into berries, washed; yashing water pomace, wet romacs, dried, retransferred into polystyre boxes and stored at ≤18°C until analysis.
The processing of bunches of grapes into berries, washed; yashing water pomace, wet romacs, dried, retransferred into polystyre boxes, and the industrial practice.
The processing procedures are outlined on the flow(flow) of the transferred into polystyre boxes, and the polytyre boxes, a



Diagram 6.5.3-1 and Diagram 6.5.3-2) below.

Processing of Bunches of Grapes into Berry, washed; Washing Water; Retentate; Pomace, wet; Pomace, dried; Raw Juice and Juice

The processing started in deep-frozen state. The bunches of grapes were destempted into berries stalks and stems. The waste of stalks and stems was disposed. The destemmed berries were washed for approx. 2 min in luke-warm standing water (ratio water/fruits = 2/1 (w/w)) by moving them around slowly. After washing, the berries were let to drain in a sieve. An aliquot of the obtained laboratory sample of berry, washed was filled into a plastic bag. The obtained laboratory sample of washing water was prepared by filling a portion into polystyrene boxes.

The washed berries remaining for further processing were crushed in a cutter to get thash. During mashing in two trials (R 2006 0650/8 TA and R 2006 0415/7 TA) the cutter was leaky; and portions of about > 1 kg were lost. The mash was pressed in a high-pressure pressento raw juice and ponace. Wet. The obtained laboratory sample of pomace, wet was prepared by filling an aliquot into a plastic bag. The laboratory sample of raw juice was prepared by filling an aliquot into a plastic bag. The laboratory sample of raw juice was prepared by filling an aliquot into a plastic bag. The laboratory sample of pomace, wet was dried in a fair-assisted over at about 100°C until the water content was nearly 10%. The obtained haboratory sample of pomace, sample of pomace of pomace dried was filled into a plastic bag.

Table 6.5.3- 1:	Water content	of pomače	, wet an	d poma	ce, dried	Ĵ,
-----------------	---------------	-----------	----------	--------	-----------	----

trials	Région @	V O Q Wate contract
R 2006 0415/7 CA	₩,	
R 2006 0415/7 TA	NEU ×	
R 2006 0650/8 TA	N.	
R 2006 0623/0 CA		
R 2006 0623/0 TA	SEU SEU	$\mathcal{A} = \mathcal{A} = $
R 2006 0622/2 TA		

The portion of raw juice remaining for further processing was depectinised by heating for approx. 30 sec to  $80 - 85^{\circ}$ C. The raw juice was cooled down to  $45^{\circ} - 50^{\circ}$ C using icewater. The pectolytic enzyme Novo Pectinex 3XL (20) µL/kg juice was added and the raw juice was left to stand for one hour at room temperature. Then the fuice was stored for about 20 hours (overnight) at 4°C, except in trial R 2006 0622/2 TA, where the raw juice was stored for 2 hours at room temperature until the following processing. After the cold storage, the staled clear juice was lifted up by a soup ladle. The restless juice with lees was separated by centrifugation for 10 mitrat 7000 rpm. The waste of lees was disposed. The Brix value of the coarsely find grape juice was determined. The coarsely fined juice was filtrated using a laboratory ultra-filtration set-up to obtain clear juice and retentate. The Brix value of clear juice and retentate was determined. An aliquot of the obtained laboratory sample of retentate was filled into polystyrene boxes. The filtrated juice was pasteen sed in a plate-heat-exchanger. After pasteurisation, the juice was collected in fractions. The Erix value of each fraction was determined to differentiate and combine the right fractions of grape juice without rates of water. The pasteurisation value is calculated (pasteurisation-time and temperature) and should be in a range of 2 to 5 (according to apple juice).

		ν
	A Région	Pasteurisation values
trials of	Region	Juice
R 2006 041 07 CA		2.1
R 2006 04 5/7 TA	<b>NEU</b>	1.9
R 2006 0650/8 TA		4
R 2006 0623/0 CA		3
R 2006 0623/0 TA	SEU	4.7
R 2006 0622/2 TA		3.8

## Table 6.5.3 2: Pasteurisation values



### CA : control sample

TA : treated sample

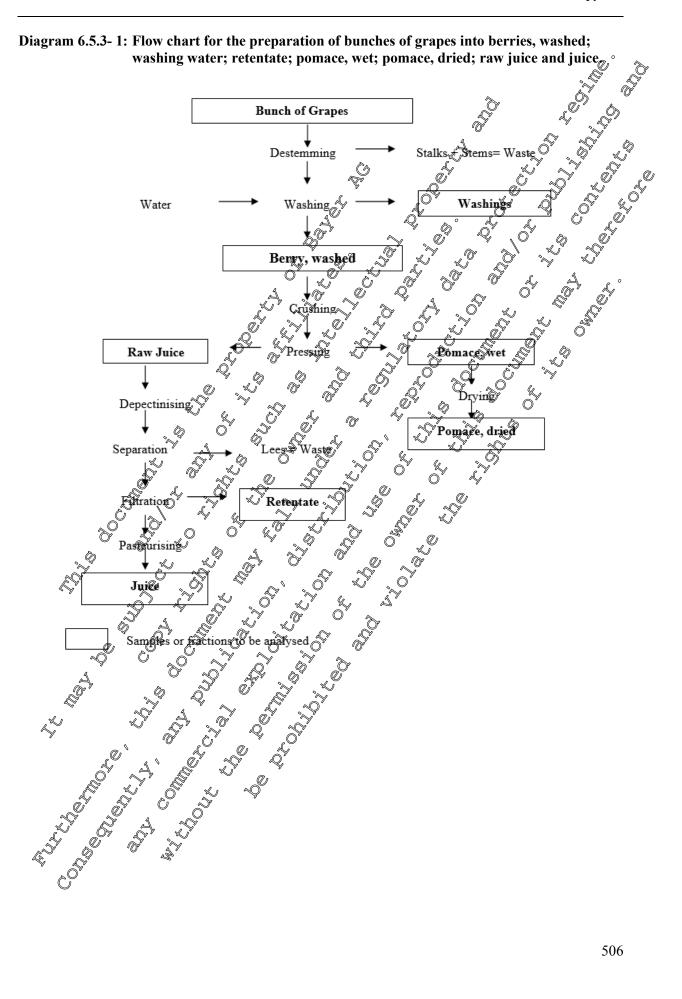
An aliquot of the obtained laboratory sample of juice was filled into polystyrene boxes. In addition, a small amount of the juice was taken apart for the determination of the pH-value and titratable acted. Ô

All aliquots of laboratory samples were stored deep-frozen at ≤-18°C for 1 to 1 days until haddoveroo preparation of the examination samples. n

Trial no.	Région	Sample material	Brix value	pH- value	(calculat	Total Asta ted as tarta $\rho$ in g/L 3.0 4.3 4.8 4.3	ric acid)
R 2006 0415/7 CA		Raw juice	~~ ×1			<u> </u>	
R 2006 0415/7 TA	NEU	Juice Raw juice	×15.9° ≪ n.¢2	2 3.6 ×		4.3%	- Sr
		Juice Raw juice	↓4,4 ° č) 、 0n.d.			Oi o d	<del>}*</del>
R 2006 0650/8 TA		Juice	15.2%	3.6		L 4.5	
R 2006 0623/0 CA		Raw whice	<b>D D D D D D D D D D</b>	× 3.0 Ø.9		<u> </u>	<u> </u>
R 2006 0623/0 TA	SEU	Raw juice	n.d.	3.8		$ \begin{array}{c}                                     $	<i>y</i>
R 2006 0622/2 TA	-	Rawjuice	nga.		ð d	9 4.0 V 24 9.8	
	<u> </u>	Juice	24.4°	<u> </u>	1_@	<u>¥.8</u>	
	~~ _			St was	5 5		
				' o ^r &			
	Ų "í	6, 5			U V		
le la	' à v				<u> </u>		
J. J				y Q 4			
					Ş		
					J.		
					J.		
					J.		
					Ţ		
					Ţ		
					Ţ		
					Ţ		
					Ĵ		
					Ĵ		
					¥.		
					Ĵ		
					J.		
					J.		
					J.		
R 2006 0623/0 CA R 2006 0623/0 TA R 2006 0623/0 TA R 2006 0622/2 TA							

Table 6.5.3- 3:	Determination of Brix Value, pH-value and titratable acid







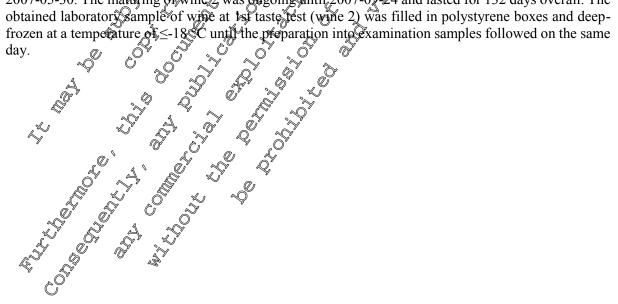
#### Processing of Bunches of Grapes into Must, Pomace, Grape; Wine at 1st Test Taste and Wine

The vinification started on 2007-03-28. The grapes were allowed to thaw. The partly thawn grape samples were weighed and subsequently crushed and destemmed in a grape crusher. A mash heating was performed by heating up the obtained mash with steam to a temperature of  $T = 82^{\circ}C$  for 3 mb while stirring. The mash was allowed to cool down. The mash was pressed in a cloth press, while increasing the pressure step by step from 0.2 to 2.0 bar. The obtained laboratory sample of pomace, grape was prepared by filling an aliquot into polystyrene boxes. The obtained must was filled into vessels and a hyposulfite solution (100 mg hyposulfite per litre must) was added. To prevent a later protein haze in the wine, 2 g/L of the fining agent bentonite was added to the wine. The must was allowed to clarify. After clarifying overnight, the must was decanted from the lees. An arquot of the obtained laboratory sample of freshly decanted must was filled into polystyrene boxes on 2007-03-29. The density of the obtained must was determined. No sugar was added prior to fermentation.

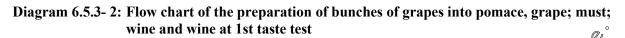


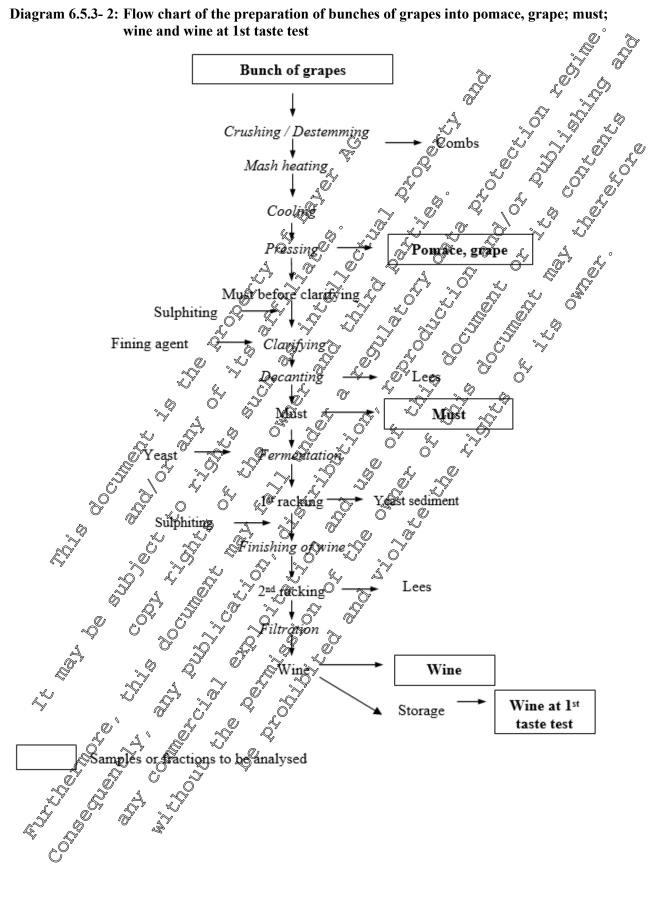
1 abic 0.3.3- 4. D	clisity of white	
trials	Région	$\frac{M_{\mu st} Dearsity in Oe}{\sqrt{2}} \sqrt{2} \sqrt{2} \sqrt{2} \sqrt{2} \sqrt{2} \sqrt{2} $
R 2006 0415/7 CA		
R 2006 0415/7 TA	NEU	
R 2006 0650/8 TA		$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
R 2006 0623/0 CA		
R 2006 0623/0 TA	SEU 🖉	
R 2006 0622/2 TA	Ś	
	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
	Ĉo	

The fermentation was started by addition of 20 g/100 L of pure-culture yeast to the must. During the fermentation, the loss of weight due to the conversion of sugar, into CO2 was monitored. The first racking was done 29 days after start of fermentation on 2007-03-29. After removal of the yeast sediment, 50 mg/L of potassium hyposulfite was added to the young wine and the finishing of the wine was started. A second racking was not done. The wine was filtered on 2007-05-15. A portion of the obtained laboratory sample of wine (wine 1) was filted in polystyrene boxes and stored deep-frozen at \leq -18 °C until shipment to Monheim. For the preparation of wine at 1st taste test (wine 2), a portion of the laboratory sample of wine 1 and the sample for preparation of wine 2 were delivered in Monheim on 2007-05-30. The maturing of wine 2 was origoing until 2007-09 24 and lasted for 132 days overall. The obtained laboratory sample of wine at 1st taste test (wine 2) was filled in polystyrene boxes and deep-frozen at \leq -18 °C. The laboratory sample of wine 1 and the sample for preparation of wine 2 were delivered in Monheim on 2007-05-30. The maturing of wine 2 was origoing until 2007-09 24 and lasted for 132 days overall. The obtained laboratory sample of wine at 1st taste test (wine 2) was filled in polystyrene boxes and deep-frozen at a temperature of \leq -18 °C until the preparation into examination samples followed on the same day.











Residue analysis

Residues of fluopyram and its metabolites were determined by LC-MS/MS according to method , 2007, M-295145-03-1, see MCA section 4.1.2). Full details and acceptable 00984/M001 (validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues were extracted from 10 g of sample material (pomace, wet; pomace, dried and poprace, grape: 5 g) by two successive extractions using a high speed blender with a mixture of acconitrile. water (80:20; v:v).

Subsequently, the raw extracts were diluted 10-fold by adding international solutions:

- One dilution and an additional clean-up@step performed under a@dic conditions Ô Ó determination of FLU-PCA)
- Another dilution performed under basic conditions for determination of fluopyram, FLUbenzamide and FLU-PAA)

Residues were quantified by reversed-phase chromatography coopled with tandem mass spectrometry (MS/MS) with electrospray ionisation. Que injection in positive electrospray ionisation allowed the determination of fluopyram, FLU-benzanide and FLICPAA. Another injection in begative electrospray ionisation allowed the determination of FLQ-PCA under different conditions.

The Limit of Quantitation (LOQ calculated and expressed as floopyram parent equivalents for fluopyram and its metabolites), defined as the lowest validated fortification level, was 0.01 mg/kg in all matrices for all analytes. All residues are calculated as parent fluopyram.

The quantification was done by internal standardization using isotopically stable labelled internal standards.

Findings 🚽

No apparent residues above the DOQ were prosent in the control samples. In order to check the performance of the method, recovery determinations were concurrently performed to the analyses of control and treated samples in each set of analyses. Concurrent recoveries were obtained during the conduct of the residue studies RA-2611/06, RA-2612/06 and RA-2647/06 (KCA 6.3.1/01 to 03) and corresponding processing studies (RA-3611/06, RA-3612/06 and RA-3647/06). All data of the method performance and recoveries are shown in the tables below.

The mean concurrent becoveries were within the acceptable range of 70% - 110% in all tested matrices. The RSD values (although bot all could be calculated) were ≤ 20 %.

Ô

Ô

The storage period of deep-frozen processed samples ranged between 2 and 125 days.

Table 0.5.5- %.	Concurrent Recov		or independent	i anu its metab	ontes			
Portion	Matrices covered	A STATE	Fortification		Recov	ery (%)		
analysed		'n	level (mg/kg) *	Individual recoveries	Min	Max	Mean	RSD
Fluopyram (Al	E C6369485 × ×	Ą,						
		, <u>3</u>	0.01	108; 111; 102	102	111	107	4.3
Bunch of	bunch of grapes;	4	0.10	91; 105; 100; 92	91	105	97	6.9
grapes S	berry, washed	Q.	1.0	90; 93	90	93	92	
			Over	all Recovery (n	= 9)		99	8.0
	juice S	3	0.01	96; 92; 95	92	96	94	2.2
Spaice O	raw juice; washings;	3	0.10	99; 95; 87	87	99	94	6.5
	retentate		Over	all Recovery (n	= 6)		94	4.4
≥O [®]	pomace, dried;	2	0.01	95; 105	95	105	100	
Pomace, dried	pomace, wet; pomace,	2	1.0	96; 98	96	98	97	
romace, dried	grape;	1	2.0	97			97	
	raisin;	1	10	86			86	

\bigcirc coveries of Elizopysam and its metabolites



Portion	Matrices covered		Fortification		Recov	ery (%))	_
Portion analysed		n	level	Individual	Min	Max	Mean	RSD
anaryseu			(mg/kg) *	recoveries		IVIAX	Witan	, Q°
	raisin waste			all Recovery (n	= 6)		96	<u>^6.4</u>
		1	0.01	100	(D	100	· 🏊
Must	must	1	0.10	97			97	<u>_</u>
Widst	must	1	0.50	94				~~ <u>~</u>
				all Recovery (n.		, 	<u>_</u>	¢ 3.1 🐒
Wine at 1 st	wine at 1st taste test;	2	~	م 97; 87	87	97 🛒	y 92	\$
taste test	grape wine	2	0.10 🚿	98; 96	96	98 ⁰	<u>90</u> ′	K)
	0 1		(0).*	<u>all Recovery (n</u>	= 4)	<u>×</u>	5	\$3.4
Fluopyram-py	ridyl-acetic-acid (BCS-A	A10			° · · ·			<u>ĭ_</u> @
		3	0.01V	95; 83, 86		<u>* 95</u>	88	7
Bunch of	bunch of grapes;	4	ر 0.10 °	101; 80; 80;	2 80 0	1001	~ <u>\$</u> 6	J.7
grapes	berry, washed			<u>२</u> 83 ८		Ň		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
	<i>, , , , , , , , , ,</i>	2		<u>č 111</u> 080 ~	<u>80</u>	0111	Ç 96 🗳	0
	• •	AL I		all Recovery (n			89	125
I	juice;			67 , 92; 85	. 89 [°] ≰,90	9 7	91 ⁸	Q
Juice	raw juice; washings; retentate	Ø\$).	× 0.10 €	 № 91; 91,090 № Валахини (л. 100) 		Ø1	91	D
	<u> </u>	20		all Recovery (n			<u>v 91</u>	4.2
	pomace, dried;		<u> </u>	85,92	85,7	9 <u>~</u> 3 67	<u>89</u> , 185	
Demons duited	pomace, wet; pomače,	B Nî	© 1.0 ° 2.0	6583; 87 ^O	83		0	
Pomace, dried	grape;		2.0	96 ⁹ 85 0	· ·	$\beta^{}$	Ky	
	raisin;		× *			0		
	raisin waste	- North		all Recovery in		- Q	88	5.7
	N A	٥ĵ ١	\$0.01 £	01	6 ²		87	
Must	must 🖉 🖉 🦉		0.10	0 [°] 92 V 95 5	~~	D)	92	
					<u>-</u>		95	
		Ŝ	- Quel	all Recovery (n	= 3)	00	91	4.4
Wine at 1 st	wine at vst taste test;	2	~ 0.01	90;77 890,95 <	89	90 95	84	
taste test 🔬	Ogrape Wine			4 V		95	92	
\bigcirc				all Recovery (n	= 4)		88	8.7
Fluopyram-pe	nzamide (AE F148815)	<u></u>		M2. 100 02	02	112	102	10.4
		0°3	0.01	13; HO9, 92	92	113	102	10.4
Bunch of	bunch@f grapes;	4		<u>394; 8</u> ©91; 90	87	94	91	3.2
grapes	berry, washed	.40°	¥.0 &	<u>1</u> 01; 93	93	101	97	
		$\mathcal{O}_{2}^{\mathbb{Z}}$	Over	all Recovery (n	= 9)	104	96	8.3
L	juice;	* 5	0.04	91; 103; 104	91	104	99	7.3
Juice	raw juce; washings:	20	000	91; 106; 95	91	106	97	8.0
¥		Q.		all Recovery (n		00	<u>98</u>	6.9
A A	pomace, dried;	<u>752</u>	\$ 0.01 150	85; 99	85	99	92	
. .	pomace, wet; pomace,	2		91; 93	91	93	92	
Pomace, dried	graper a raisin;	Ê	× × 27.0	103			103	
<i>i</i> √j [™]		Q,	~~10	93			93	
	raisin waste	1		all Recovery (n	1		94	6.7
Ś	A & X	1 #	Q [°] 0.01	95			95	
Must	must &		0.10	89			89	
Ś		٩ ٩	0.50	94			94	
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~				all Recovery (n	· · · ·	10-	<b>93</b>	3.5
Wine at 1 st O	wine at 1st taste test;	2	0.01	87; 105	87	105	96	
taste test	The grage wine	2	0.10	95; 111	95	111	103	
				all Recovery (n	= 4)		100	10.7
Fluopy@m-py	ridyl-carboxylic-acid (A						~	
Bunch of	bunch of grapes;	3	0.01	83; 103; 86	83	103	91	11.9
grapes	berry, washed	4	0.10	79; 96; 85; 89	79	96	87	8.2
0	,	2	1.0	70; 79	70	79	75	



Portion	Matrices covered		Fortification					
analysed		n	level (mg/kg) *	Individual recoveries	Min	Max	Mean	RSD
			Over	all Recovery (n	= 9)		86	<b>A</b> 1.4
	juice;	3	0.01	97; 86; 95	86 (	<b>9</b> 7	93 @	6.3
Juice	raw juice; washings;	3	0.10	102; 102; 106	102	106	103	2.0
	retentate		Over	<b>98</b>	<u>7.2</u>			
	pomace, dried;	2	0.01	91; 111	<b>(79</b> 1	111 .	Q01	Q K
	pomace, wet; pomace,	2		چ 97; 105	۶ <b>9</b> 7 و	105 🛒	J 101	- ¢
Pomace, dried	grape;	1	2.0 🚿	* 99 ⁽			<b>9</b>	
	raisin;	1	10 🔍	85 _د 0 [%]		2		
	raisin waste		Øver	. 98 (	<b>9.6</b>			
		1	0.0	<u>96</u>	Â	× 0	96	
Must	must	1	°6∕210		ľ		100	~~~~~
Musi	must	1	×0.50	<u>√</u> 101 ×	×-	ĎĿ.	<b>*1</b> 01	<u></u>
			Over 🔬 Över	all Recovery (n	<b>⇒</b> 3) ′	V ,	🚄 99 🏹	2.7。
Wine at 1 st	wine at 1st tests test:	2 🔎	0.01 <u>0</u>	୰ 103≩107	102	107 [©]	105	ŧ,
taste test	wine at 1st taste test;	Ž	~0.10 ~ ^y	<b>D9</b> 0; 10 <b>4</b>	<u>.</u> 100	1QA	102	\$ <del>9</del> -
laste test	grape wine	Ø	ر 🖉 🖉 🖉 ver	all Recovery (n	∉Ă)	S	<b>104</b>	2.8

FL: fortification level RSD Relative Standard F

* some RSDs were not calculated as there were only two individual recoveries of Final determination as: fluopyram Residues calculated as: fluopyram

Final determination as: FLU-benzamide Residues calculated as: fluopyram Final determination as: FLU-PCA Residues calculated as: fluopyram Final determination as: FLU-PCA Residues calculated as: fluopyram

Final determination as: FLU-PAA Residues calculated as: flaopyram

, Ç O In bunch of grapes used for juice and wine production residues of fluopy am were between 0.36 and 0.58 mg/kg. Residues of fluoryram in the final products ince and wine were 0.01 mg/kg and 0.06 -0.08 mg/kg respectively. Residue values of fluops am in juice, wine and the processed by-products are summarised in Table 6.5.3 9 and Table 6.5.3 10.

During processing for vice production a mean of 77% of the absolute residue was recovered after destemming in perries washed and the washings. On further processing, a major part counting for 35% of the absolute residue remained in the pomace, whereas the residue to raw juice only accounted for 8% of the initial absolute residue After altration and pasteussation ho residues above the LOQ were detected in the final product, price. Õ × i  $\bigcirc$ 

With wine processing a mean of 43% of the initial absolute residue remained in the grape pomace, and 16% were recovered in must. Rermenting and filtration further reduced the residue concentration of fluopyram so that the final product whe only contained 8% and wine at first taint test 10% of the initial absolute residue.

Processing factors (PF) were calculated by dividing the fluopyram residue in grape processed commodifies by the floopyran residue in the raw agricultural commodity (RAC) bunch of grapes. Processing factors calculated for the individual grape processed commodity samples are summarized in the tables below. Q,

- Concentration of fluopyram residues was observed only in dried pomace, wet pomace and grape pomace and its mean processing factors calculated based on four residue trials results were 6.4, 3.2 and 3.4, respectively. For the other matrices, no concentration of fluopyram was observed  $\hat{\mathcal{O}}$ Š
- Concentration of fluopyram-benzamide residues was observed only in dried pomace, wet pomore and rape pomace and its mean processing factors calculated based on four residue trials results were 2.75, 1.25 and 1.25, respectively. For the other matrices, no concentration of
- ft opyram-benzamide was observed (PF < 1.0),
- Concentration of fluopyram-pyridyl-carboxylic-acid residues was observed only in dried pomace, wet pomace and grape pomace and its mean processing factors calculated based on



four residue trials results were 2, 1 and 1, respectively. For the other matrices, no concentration of fluopyram-PCA was observed (PF < 1.0),

<ul> <li>Concentration o</li> </ul>		· · · ·		was not o	bserved.		2		N N N
Fable 6.5.3- 6: Proc	essing fact	ors for fl	uopyram		4	de la constante de la constant			
	R 2006 France	0650/8	R 2006 France		R 2006 ( France S		<b>R 2006</b> France S	62340	Mean
Sample material	Residues (mg/kg)	PF*	Residues (mg/kg)		Rosidues	PE		PF*	D PF
Bunch of grapes (RAC)	0.51		0.58		0.36	<u>6</u> <u>Y</u> _	<b>√ 0.58</b>	Å.	-
Juice	<0.01**	0.02	<6.01**	0.02	<0.91**	0.03	<0.0 ⁰ **	0.02	0.02
Raw Juice	0.06	0.1	&_0.06 Ø	0.1	×0.05 «	0,10	°0,09 °	€ ⁷ 0.2	0.1
Washings	0.05	0.1	0.06 [®]	e0.1	0.030	Ø	£ 0.02	0.03	0.1
Pomace, dried	3.0	6.0 🔬	278	© 4.8 ~	2.7	7.5	0 4.20	<i>#</i> 2	6.4
Pomace, wet	1.6	3.1%	×1.3 ~	× 2.2	A.4 (	3.9	2.1	3.6	3.2
Berry, washed	0.30		°∼y 0.38 ©	.0.5	0.18	0.5	Ø.43 Å	0.7	0.6
Retentate	0.05	Q.1 &	0.05	~0.1 °	0.00	<b>.</b> 1	0.08	0.1	0.1
Pomace, grape	2.0	Ç 4.0 P	° <b>1</b> >6	[∞] 2.7~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	3.3	2,1,2	3.6	3.4
Must	0.11	02	©0.12 🏷	02	Q.11 O	0.30	0.13	0.2	0.2
Wine at 1 st taste test (wine 2)	0.10	×.9.2	0.08	Q.1	Q 0.07		^{&amp;} ∕0.10	0.1	0.2
Wine (wine 1)	0.08	V 0.2 V	of \$06	or 0.1 [™]		Q 0.2 🔊	0.08	0.2	0.2.
Processing factor of	calculated	acconding	to th	ne follo		iation 🔊			

Ő

Table 6.5.3- 6:	Processing factors for fluopyram
1 abic 0.3.3 - 0.	1 I UCCSSINg lactors for huopyram

Residue concentration in the processed product [ PF

Residue concentration in the RAC

 $\bigcirc$ Remark: Processing factors of a calculated from the corresponding residue of centrations using mrounded values. For this reason, deviations can occur when the round a values given in comm for levels of residues of fluopyran in relevant matrices are used for recalculation. RAC: Raw Agriculture Commodio **: Values below LOO which were set to the LOO for the calculation of processing factors

#### Ş Processing factors for flugpyram benzamide Table 6.5.3₅

	d n d n		(°		1 Alian and a second se				
	<b>R 2006</b> 0		R 2006		🕅 🕅 🕅 🕅 🕅 🕅	622/2	R 2006 0	623/0	
Sample meterial	Erance N		» France		🎽 France S	South	France S	South	Mean
Sample material	Residues	PF≪ 0°	Residues	DE*	Residues	PF*	Residues	PF*	PF
	∢ (mg/k∰ [∛]		(mg/kg)	PF*	(mg/kg)	гг.	(mg/kg)	ГГ.	
Bunch of grapes (RAC)	∑ ^{&gt;} <0.4€1	<i>.0</i> -	~~ 0.0 <b>2</b> ~~	Ċ,	<0.01	-	0.02		-
Juice	<b>0</b> .01_ °≈	~		0.5	< 0.01	-	0.01	0.5	0.5
Raw Juice	<0.01 <0.01	Q.	<b>\$</b>	0.5	< 0.01	-	0.02	1	0.75
Washings	<0.00		×\$0.01*	0.5	< 0.01	-	<0.01**	0.5	0.5
Pomace dried	<0.61	-	° 0.057	2.5	0.02	-	0.06	3	2.75
Pomace, wet	AQ.01	y - ô	0:02	1	< 0.01	-	0.03	1.5	1.25
Berry, washed	×0.01×	Q	<b>0</b> .02	1	< 0.01	-	0.02	1	1
Retentate	<0,0	<i>©</i> -	0.01 گ	0.5	< 0.01	-	0.01	0.5	0.5
Pomace, grape	< <b>Q</b> 01 (*	Ş - 4		1	< 0.01	-	0.03	1.5	1.25
Must a N	@0.01	-0-	0.02	1	< 0.01	-	0.02	1	1
Wine at As taste test		Ż	0.02	1	< 0.01		0.02	1	1
(wine 2)	()	-	0.02	1	<0.01	-	0.02	1	
Wine wine 1	\$9.01	-	0.01	0.5	< 0.01	-	0.01	0.5	0.5
*Processing @ factor	calculated	accordin	g to	the fol	lowing e	quation:			

caleylated according @ factor *Processing Residue concentration in the processed product  $\left[\frac{mg}{kg}\right]$ 

 $\mathbb{O}^{\mathbb{V}}$  Residue concentration in the RAC  $\left[\frac{mg}{kg}\right]$ 

Remark: Processing factors were calculated from the corresponding residue concentrations using unrounded values. For this reason, deviations can occur when the rounded values given in column for levels of residues of fluopyram-benzamide in relevant matrices are used for recalculation.

RAC: Raw Agriculture Commodity



**: Values below LOQ which were set to the LOQ for the calculation of processing factors.

Samula matarial	R 2006 0 France N		R 2006 ( France		R 2006 0 France S		R 2006 0 France	ି Mean	
Sample material	Residues (mg/kg)	PF*	Residues (mg/kg)	PF*	Residues (mg/kg)	PF*	Residues (mg/kg)		PF
Bunch of grapes (RAC)	<0.01	-	0.02	<u>_</u>	<0.01	» -	°0,04 •	9° - K	í -
Juice	< 0.01	-	< 0.01**	Ø.5	<0.0	-	0.01	0.25	&A
Raw Juice	< 0.01	-	< 0.01**	0.5	<0.01	-	0.029	\$5	0.5
Washings	< 0.01	-	<0.01**	0.5	£0.01	- *	<0.0 **	Ø.25 \$	0.4
Pomace, dried	< 0.01	-	0.04	2	~Q<0.01, ° <0.00		0.08		2
Pomace, wet	< 0.01	-	0.042	1 🕿	<0.0	-Q, [*]	00.040	10×	1
Berry, washed	< 0.01	-	0.01	。 0.5 0	<0.01	<i>𝔅</i> - 𝔅	0.02	A.5	0.5
Retentate	< 0.01	-	9.01	0.5 0 0.5		- 9	0.02	0.5	0.5
Pomace, grape	< 0.01	-	0.02	Q	\$0.01 <0.01 <0.01	0 ^y	Ø.04	≥ 1 ₂ °	1
Must	< 0.01	- 4	0.02		-0.01	\$ ⁻	0.03	0.05	0.9
Wine at 1 st taste test (wine 2)	<0.01		2~9.02 C		60.01	7 - 5	n	0.05	1
Wine (wine 1)	< 0.01	o [™] Accordin	g to	29.5 ×	o <0.01 TowingO en	- Contraction of the second se	0.02	0.5	0.5

#### Table 6 5 3 9. Processing factors for fluonyram-nyridyl-carboyylic-acid

PF =

Residue concentration in the RAC  $\left[\frac{mg}{kg}\right]$ 

Remark: Processing factors were calculated from the correst ording residue concentrations using undounded values. For this reason, deviations can occur when the rounded values given in collary for the correst ording residue of Gropyram-PCAin relevant matrices aroused for recalculation. RAC: Raw Agriculture Commodity **: Values below LOQ which were set to the LOQ for the calculation of processing pictors.

Ø

As no residue were detected for fluepyram-pyrid acetic acid (BCS AA10139), no processing factors were calculated.

Conclusion

The study was conducted according to the relegant godelines The results of control samples, and recovery samples were in the expected range. Ô

Mean processing factors between 3.2 and 6.4 were calculated for puopyram in pomace (wet, dried and grape). Processing factors below 1 were calculated for fluopyram in the other processed commodities.

Mean processing factors betweer 1.25 and 2.75 were calculated for fluopyram-benzamide in pomace (wet, dried and grape). Processing factors below 1 were calculated fluopyram-benzamide in the other processed compodition. Ô 0 Ô

Mean processing factors between V and 20 vere a culated for fluopyram-PCA in pomace (wet, dried and grape). Processing factors below 1 were calculated for fluopyram-PCA in the other processed commodities.

Assessment and conclusion by applicant:
Assessment and conclusion by applicant:
The study scaceptable. a so so

BAYER

Page 514 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application rate g per treatment		per treatment		per treat				Growth stage at last treat- ment		on grape		Growth stage at ampling (d) Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Auopyram Au		OF PU	PHI (	29 ¹ ¹ ¹ ¹ ¹ ⁰ and all ¹ ¹ ¹ ⁰
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./h L	(c)	ي (d) گ		» (d)	faiopyram	PCA	) benzamiqe	.1	, í					
2006 0650/8 650-06 rance, north -71850 harnay les facon (Rhone- lpes) urope, North 006	Grape Pinot noir /PG161.49; red variety	1) 01.04.2002 2) 07.06.2006 - 15.06.2006 3) 10.09.2006 - 15.09.2006 - 15.09.2006 - 15.09.2006	pe .	0.0°			tati	owner Junden juicer washingen pomace, dried pomace, wer bery, washed,	24 89 89 91 91 91 91 91 91 91 91 91 91 91 91 91	0.06 0.06 0.06 0.06	<0001 <0.01 <0.01	<0.01 <0.01	<0(00)	2 3 7 14 21 28	(g) RA-2611/06 (h) Fluopyram 500 SC (i) Spraying (j) Analytical method: 00984/M001 (k) LOQ: 0.01 mg/kg (l) Method Validation Data 00984/M001, (m) Storage: wine at first taste test: 380 days wine: 323 days, washings: 379 days, retentate: 379 days, retentate: 379 days, pomace, wet: 379 days, pomace, grape: 323 days, pomace, dried: 379 days, juice: 379 days, bunch of grapes: 200 days, berry, washed: 379 days				

Page 515 of 801 2021-02-26



Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	pe	blication r treatm		Dates of treatment / Application interval	Growth stage at last treat- ment	Portion analysed	Growth stage at Campling		ক্ষি	DP ^{CT} ves (mg/kg)	tect i	PHI (days)	e 9 Bill Betails on trial
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./h L	(c)	(d)		(d)	fuopyram	PCA	OFLU- benzamite 0.02000 0.02000	PLU-PAA	C(e)	efo ^r (f)
R 2006 0415/7 0415-06 France, north F-37270 Athée sur Cher (Centre) Europe, North F 2006 (a) A	Grape Gamay; red variety	1) 01.01.1995 2) 08.06.2006 - 15.06.2006 3) 18.09.2006 3) 18.09.2006	\$ ^e	cog				retentate pomace, grape møst	089 89 t	0.50 0.50 0.50 0.56 0.06 0.06 1.3 0.35 1.6 0.12	0.02 0.02 0.03 0.03 0.03 0.03 0.03 0.03		<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01		<ul> <li>(g) RA-2611/06</li> <li>(h) Fluopyram 500 SC</li> <li>(i) Spraying</li> <li>(j) Analytical method:</li> <li>00984/M001</li> <li>(k) LOQ: 0.01 mg/kg</li> <li>(l) Method Validation Data:</li> <li>00984/M001</li> <li>(m) Storage:</li> <li>wine at first taste test:</li> <li>376 days</li> <li>4 wine: 319 days</li> <li>washings: 375 days</li> <li>retentate: 375 days</li> <li>pomace, wet: 375 days</li> <li>pomace, dried: 375 days</li> <li>pomace, dried: 375 days</li> <li>punch of grapes: 188 days</li> <li>berry, washed: 375 days</li> </ul>
(b) O (c) Y (d) E G gu	niy if relevant ear must be indica ither growth stage reenhouse	ated Character of Broad		DIR (g)	SNOT	ks may include: Gin ation which mytabol reference blast the thinnent	saric conditionities are inclu	ons; Reference to a ided	naiytical meth	od and	(j) M (k) LO	plication method ethod information Q idue in control	(m) #	! based P based	e (max) I on date of analysis d on production date a available



Page 516 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram

#### Results of processing trials conducted with fluopyram on grape Table 6.5.3-10:

OD Analyte 1: Fluopyram AE C656948 (determined as AE C656948, calculated as AE C656948), Analyte 2: AE C657188 (determined as AE C657188, calculated as AE C656948), Analyte 3: AE C656948-benzamide/ AE F148815 (determined as AE C656948-benzamide/ AE F148815, calculated as AE C656948), Analyte 4: AE C656948-pyridyl-acetic acid, calculated as AE C656948)

4^{e°}

Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Ар	plication er treatm		Dates of treatment / Application interval	Growth stage at last creat ment	Portion analysed	Growth stage at sampting		Residu		or c it c	OD PHI (days)	Details on trial
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	i g tu	ement		(d)	fluoreram	FLÖ GEA	FLU- beužamide	FLACPAA	(e)	(f)
R 2006 0622/2 0622-06 France, south F-30290 Laudun (Languedoc- Roussillon) Europe, South F 2006	Grape Grenache Noir; Red variety		0 ² 0 ²	0 ²⁰		01.08.2006/0 12.09.2006/4 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2		Gunch of grapes Unice raw jurge washings pomace, dued pomace, wet Gerry, washed retentate	85 89 89 89 89 89	0.17 0.44 0.29 0.23 0.35 0.35 0.35 0.35 0.35 0.35 0.35 0.3	<pre>&gt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01 &lt;0.01</pre>	\$0.01 <0.01 <0.001 <0.01 <0.01 <0.01 \$	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01		(g) RA-2647/06 (h) Fluopyram 500 SC (i) Application method: Spraying, low-volume (j) Analytical method: 00984/M001 (k) LOQ: 0.01 mg/kg (l) Method Validation Data: 00984/M001 (m) Storage: wine at first taste test: 376 days wine: 319 days washings: 376 days retentate: 376 days raw juice: 376 days pomace, dried: 376 days pomace, dried: 376 days juice: 376 days juice: 376 days bunch of grapes: 175 days berry, washed: 376 days
	Ċ°.	ج	j'. V'												516

9. D.J.

BAYER

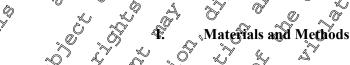
Page 517 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	p	plicatior er treatn		Dates of treatment / Application interval	Growth stage at last treat- ment	Portion analysed	Granda extage at sampling		Resid	ves (mg/kg)	Uber		9 1 Me J.D.d.
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	(c)	(d)		(d)	Buopyram	PCA	FIN- Benzamide	DELU-PAA	≜ ^O (e)	€ 0 ¹ (f)
R 2006 0623/0 0623-06 France, south F-31620 Fronton (Midi- Pyrenees) Europe, South F 2006	variety	I' DON	K Du	0 6				Puice raw inter washings pomace, wet berry, washed retenate pomace, grape must withe at first withe at first	89 89 89 89 89 89 89 89 89 89	0.01 0.02 42 0.43 0.43 0.43 0.13 0.10 0.08	0.02 0.02 0.04 0.05 0.06 0.06 0.06	0.01 0.02 0.02 0.02 0.02 0.02 0.02 0.02	<0.01 × <0.01 × <0.01 × <0.01 × <0.01 × <0.01 × <0.01 × <0.01 × <0.01 × <0.001 × <0.000 × 50 × 0.000 × 50 × 0.000 × 50 × 5	3 7 14	(g) RA-2647/06 (h) Fluopyram 500 SC (i) Application method: Spraying, low-volume (j) Analytical method: 00984/M001 (k) LOQ: 0.01 mg/kg (l) Method Validation Data: 00984/M001 (m) Storage: wine at first taste test: 387 days wine: 330 days washings: 387 days retentate: 387 days retentate: 387 days pomace, grape: 330 days pomace, dried: 387 days pomace, dried: 387 days must: 330 days juice: 387 days bunch of grapes: 186 days berry, washed: 387 days
<ul> <li>(a) Acc</li> <li>(b) Onl</li> <li>(c) Yes</li> <li>(d) Eitt</li> <li>G great</li> </ul>	ording to CODE y if relevant r must be indicat er growth stage c enhouse	X Classification / Guid ed lescription BBCHA F field F JBC F field F JBC JUC JUC JUC JUC JUC JUC JUC JUC JUC JU		out out	Days after Regarks n Study refet prior clas	last application (1 nay inorfile: Clima n value metaboli pice t reatment (1)	abel pre () ntic contribut Sure includ	west interval, PHI, t ns; Reference to ana ed	ınderline) lytical methoc	l and	<ul><li>(i) Appl</li><li>(j) Meth</li><li>(k) LOQ</li></ul>	nulation type lication method od information ue in control	(l) (m) #		max) n date of analysis on production date



Data Point:	KCA 6.5.3/03
Report Author:	
Report Year:	2008
Report Title:	Determination of the residues of AE C656948 in/on table grape (bunch of grape 9)
	and the processed fractions (raisin; raisin waste; washing) after spraying of ALC C656948 (500 SC) in the field in Spain, Portugal, Italy and Greece
	C656948 (500 SC) in the field in Spain, Portugal, Italy and Greece
Report No:	
Document No:	<u>M-296512-01-1</u>
Guideline(s) followed in	M-296512-01-1 EU-Ref: Council Directive 91/414/EEC of July 5, 1991, Ann II, par A, section 6 and Annex III, part A, section 8 Residues in or on Treated Products, Food and Feed EC Guidance Working Document 7029/VI/95 rg 5 (1997-07-22); US-07 A OPPES Guideline 10.
study:	6 and Annex III, part A, section 8
	Residues in or on Treated Phoducts, Food a Feed EC Guidance Working
	Document 7029/VI/95 rg 5 (1997-07-22); US-OFA OPPES Gualeline Jo.
	860.1520 Supplemental
Deviations from current	none of the transformed and the second secon
test guideline:	
Previous evaluation:	yes, evaluated and accepted
	rev. 1 to Vol.3 of DAR \$7 August 2019 (references reped on 2 , 5
GLP/Officially recognised	Yes, conducted under GLP/2) ficially recognised testing facilities of O
testing facilities:	
Acceptability/Reliability:	Yes y y y y y y

The study included fort supervised field residue trials with grape conducted in Southern Europe (Spain, Portugal, Italy, and Greece) in the 006 season in order to determine the magnitude of the residues of fluopyram and its metabolites Phopyram benzamido fluopyram ovridyleacetic-acid and fluopyram-pyridyl-carboxylic-acid in table grapes and in processed fraction and processing by-products (raisin; raisin waste; washings) following spaying of fluopyram(500 Sc).



#### Field part

In the field trials (KCA 6.3.1/03), two foliar spray applications with fluopyram (500 SC) - a suspension concentrate formulation containing 600 g/b fluopyram - were conducted at a single application rate of 250 g a.s./ha/application and water rate at 600-1000, L/ha. The achieved total seasonal rate was 0.500 kg a.s./ha. The application were conducted at BBCH of 81(for the first application) and BBCH of 85-89 (for the second application).

For residue analysis, table grape samples (bunches of grapes) were taken on day 3 after the last application. Table grape samples (bunches of grapes) for processing were taken on the same day. A table grape sample (bunches of grapes) for processing of control material was taken from trial R 2006 0417/3. The field sub samples from a trials were stored deep-frozen within 24 hours after sampling. The samples for residue analysis and for processing were stored in a freezer at  $\leq$ -18°C until preparation of the examination samples and processing procedures.

The samples for processing were stored in a freezer at  $\leq$ -18°C or below until processing procedures.

The samples from processing were deep-frozen again immediately after the respective processing step. The processed samples were stored at  $\leq$ -18°C until preparation of the examination samples. For the preparation of examination samples of raw agricultural commodity and processed commodities, the deep-frozen samples were shredded with dry ice in a cutter. Representative parts of the shredded samples were transferred into polystyrene boxes separately for analysis (UP samples) and archiving (UR samples) and stored at  $\leq$ -18°C until analysis.



#### **Processing procedures**

The processing of the samples of bunches of grapes into raisins was performed in the Food Processing Laboratory (FPL) of BCS-D-ROCS in Monheim and simulated the industrial practice at a laboratory scale.

Processing procedures are outlined on the flow chart (Diagram 6.5.3-3) below

#### Processing of Bunches of Grapes into Raisins

Damaged and unripe berries were sorted out. The bunches of grapes were destemmed before drying

In trial R 2006 0651/6 the whole berries were already removed from the stalks. In trial R 2006 04  $\frac{97}{3}$  about 90 % of the whole berries were already removed from the stalks. The desteroined berries and the sample of raisin waste were dried at a temperature of 60 to 65 °C m a fan-assisted oven until a water content of approx. 10 – 15 % was achieved.

The dried berries were washed in lukewarm standing water by moving the paround slowly (ratio dried berries / water = 1/2 (w/w)). During washing the dried berries absorb water. After washing the water content should be in a range between 9 and 15 % Depending on the sugar content, the raises absorb more water than desired (up to 23 %).

 $\sim$ 

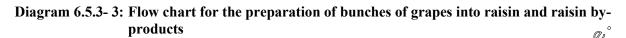
The washed raisins, the raisin waste and the washing water were sampled,

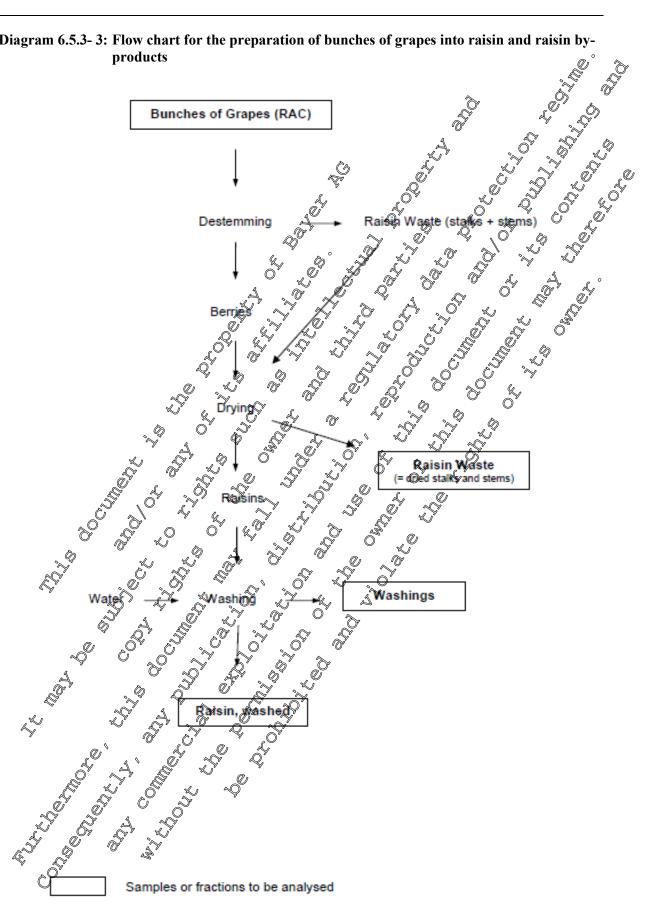
&?

Table 6.5.3-11:	Water content 🔞	raisias du	ring the	processing
-----------------	-----------------	------------	----------	------------

Trial	Water Content Safter Drying	Time of Drying	Water Content afto Washing
R 2006 0417/3 C	6 0 ¹ 14 % 0 ¹	27 h	2 16 %
R 2006 0417/3 T	× 16%	@ 37ch	£ 22 %
R 2006 0624/9 T	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	26 h 0 ^	۶» ۱9%
R 2006 0651/6 🔊 🔍		2 2 32 h	23 %
R 2006 0652 T	0 00 % 0	45h	16 %









#### **Residue analysis**

Residues of fluopyram and its metabolites were determined by LC-MS/MS according to method , 2007, M-295145-03-1, see MCA section 4.1.2). Full details and acceptable 00984/M001 ( validation data to support this method are presented within document M-CA , which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues were extracted from 10 g of sample material (raisin and raisin waste: 5 g) by two spece extractions using a high speed blender with a mixture of acetonitrile:water (80:20; v.9.

Subsequently, the raw extracts were diluted 10-fold by adding internal standard solutions.

One dilution and an additional clean op step performed ander acidio conditions for determination of fluopyram-PCA)

Another dilution performed under basic conditions (for determination of fluopyram, FLU-

Residues were quantified by reversed-phase chromatography coupled with tondem mass spectrometry (MS/MS) with electrospray ionisation. One injection in positive electrospray ionisation allowed the determination of fluopyram, FLU-bencamide and FKU-PAA. Another injection in negative electrospray

The quantitation was carried out by internal standardization using internal stable labelled standards. The Limit of Quantitation (LOQ, calculated and expressed as floopyron parent equivalents, for fluopyram and its metabolites), defined as the lowest validated fortification level, was 0.01 mg/kg in all matrices

r deter softwe electrospins addition using infinal stable labels, add as fleopy an parent equivalent ed fortification fivel was 0.01 me and fluopy and parent equivalent ed fortification fivel was 0.01 me and fluopy and a fluopy and the fluor ed fortification fivel was 0.01 me and fluopy and the fluor ed fortification fivel was 0.01 me and fluopy and the fluor ed fortification fivel was 0.01 me and fluopy and the fluor and fluopy and the fluor addition for the fluor



#### II. Findings

No apparent residues above the LOQ were present in the control samples. In order to check the performance of the method, recovery determinations were concurrently performed to the analyses of T control and treated samples in each set of analyses. Concurrent recoveries were obtained during the conduct of the residue studies RA-2611/06, RA-2612/06 and RA-2647/06 (KCA 6.3.1/01 to 03) and corresponding processing studies (RA-3611/06, RA-3612/06 and RA-3647/06, KCA 6.55/01 1003). All data of the method performance and recoveries are shown in the 1 abie 0.3.3-12. The mean concurrent recoveries were within the acceptable range of 70 % – 110% in all tested matrices. The RSD values (although not all could be calculated) were  $\leq 20$  %. The storage period of deep-frozen processed samples is displayed in Table 6.5.3-04.

Table 6.5.3- 12:	<b>Concurrent recoveries</b>	of Floopvram	and its	metabolites

Portion	Matrices covered		Fortification		Recov	erty (%)	× .	*
analysed		n	level	🗘 Indixîdual 🖒	Min	Max		നഞ്
anaryseu			(mg/kg) *	recoveries	WIID	Max	Mean	RSD
Fluopyram (Al	E C656948)	ź	$\sim$ $\sim$	jà là		Z.	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	S.S.
	( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( )	Ø3	¢≫ 0.01	≈108; 11,1 <b>9</b> 102 _s	<b>©</b> Í02	<b>A</b> 111 .	A107 (	<b>4</b> .3
Bunch of	bunch of grapes;	4	y and 2	Ç 91; 1 <b>65</b> ; 100; Ç	91	105	97©)	6.9
grapes	berry, washed	. @			Å	Ø	<u>k</u> i	
		Č,		90; 93 <u></u>			°≈9/2	
		ال الم		all Recovery (n 96; 02, 95	<b>€⁄9)</b> 92	96	<b>99</b> 94	<b>8.0</b> 2.2
Juice	juice;	30		90, 01; 93 99, 95; 8 <u>7</u> ~	92 .8Ø	90 (	94	6.5
Juice	retentate 0	2		all Recovery (n	<u> </u>		94	4.4
	×,	2	\$ 0.0b	\$ 95: 105 ×	95	105	100	
	pomace, dried; pomace, o	2		96,498 (	96°	98	97	
Pomace, dried	wet; pomace, mape; 🗸	10	\$.0 ×	97 OV	÷		97	
,	raista,	$\sim$	10	86 g	a;		86	
	Tagsin wasae	$\sim$	Sover	al Recovery (n	₹6)		96	6.4
. (		1	0,04	× 000			100	
Must	muso o	1%	<b>\$</b> 10	~ ^{\$\$} 97 @			97	
Îvîtust 🔘	inuage is a	<u>_</u> 1	× 0.50 m	94 🗸			94	
		þ″		al Recovery (n	· · ·		97	3.1
Wine at 1st	wine al 1st taste test;	2	<u>06</u> Y «		87	97	92	
taste test	grape wine of	<u>2</u>	\$ <del>0</del> ,10	<b>3</b> %; 96	96	98	97	
		۶ ۲		all Recovery (n	= 4)		95	5.4
Fluopyram-py	ridyl-aceticacid (BCS	<u>.</u>	01(39)			0.5	00	
		3	<u>001</u>	95; 83; 86 101; 80; 80; 83	83 80	95	88 86	7.1
Bunch of Q	bundly of grapes;	4¥ Ø.	1.0	111; 80	80	101 111	<u>86</u> 96	
grapes		4_74 1		all Recovery (n	••	111	<b>89</b>	12.5
	juice: A	3.¢		97; 92; 85	85	97	91	
Juice	raw price; washings;	R.	°≈Ø.10	91; 91; 90	90	91	91	
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	retentate	Ą,		all Recovery (n	= 6)		91	4.2
		2	J 0.01	85; 92	85	92	89	
Å	Comace, dried pomace	2 &	Q 1.0	83; 87	83	87	85	
Pomace, drie	wet: pomace grape; 🗸 v raisin;	Þ	2.0	96				
	arsin waste	-Qĩ	10	85				
				all Recovery (n	= 6)	1	88	5.7
	r a sý	1	0.01	87			87	
Must V	most	1	0.10	92			92	
	L'	1	0.50	95			95	
<u> </u>		2		all Recovery (n		00	91 84	4.4
Wine at 1st	wine at 1st taste test;	2	0.01 0.10	90; 77 89: 95	77 89	90 95	84 92	
taste test	grape wine	2		all Recovery (n	• /	75	92 88	 8.7
		I	Over	an Accovery (II	- 4)		00	0./



luopyram-b	enzamide (AE F14881										
		3	0.01	113; 100; 92	92	113	102	10,40			
Bunch of	bunch of grapes;	4	0.10	94; 87; 91; 90	87	94	91	£2			
grapes	berry, washed	2	1.0	101; 93	93	101	97	Š (
			Over	all Recovery (n		<u>></u>	96	8.3			
	juice;	3	0.01	91; 103; 104	91~	104	99.	7,2,7			
Juice	raw juice; washings;	3	0.10	91; 106; 95	910	106	27	~8,0 \$~6.9			
	retentate		Overall Recovery (n = 6)								
	pomace, dried; pomace,	2	0.01	85; 99 🦼	₩ ⁸⁵	99 🦼	🏷 92 🗞	× ~			
	wet; pomace, grape;	2	1.0	91;93	91	93	92	-O ^v			
Pomace, dried	raisin:	1	2.0	103 Q		Ð	163				
	raisin waste	1	10	93		~~- 0	~Q93	0 ^v %			
				all Recovery (n	<u>= 6)</u>	<u>k 7</u>	<u>94</u> (€ 6.7 ©			
		1	10.9	<u>95</u>	~~	0	95	Ø			
Must	must	1	0.10	@ 89	<i>m</i>	~~	\$89	~~			
111000		1	× 0.50	<u>~ 94</u>	KJ 17-1	Ç*-	* 94	···			
				all Recovery (p		0° ,	93 🛁	3.5 •			
Wine at 1 st	wine at 1st taste test;	2	, 0701	07,9105	87	105©	960	Ċ,Ÿ			
taste test	grape wine	2	0.10	95; 111	<u></u>	<u>k</u> 1,1	103	Q#-			
		Q"		all Recovery (n.	₹ 4)	<u></u>	\$100	10.7			
Fluopyram-py	ridyl-carboxylic acid	-		ý _n y v			<u>y</u> ka				
	4	3 @		83, 103; 86	83	103	<u>91</u>	11.9			
Bunch of	bunch of grapes; 🔗	A	@0.10 	79,96; 85,089	09	ØĞ	°~8⁄7	8.2			
grapes	berry, washed	£_2	0° 1.0 S	~ 70; 7 9	70 /	079	75				
		*		all Recovery (8		<u> </u>	[≫] 86	11.4			
	juice;	30	× 6,01 ~	97, 86; 95	860	97	93	6.3			
Juice	raw juice; washings,	<u>j</u>	0.10	102; 102; 106	Q^2	106	103	2.2			
	retentate 🗇	-4		all Recovery (n*		S.	98	7.2			
	pomace, dried pomace	2	0.0	91 11	91	2111	101				
	wet bomace, grape;	20	<u> </u>	97, 105	9¶_″	105	101				
Pomace, dried	ratsin;	Ť	2.0	<u> </u>	@		99				
	raisin waste	۹I		85 ⁰ ~	Ş		85				
~		,		all Recovery (n	= 6)	1	<u>98</u>	9.6			
C		1%		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			96				
Must 🖏	must		<u>~0.10</u>				100				
		p <u>1</u>	0,50	e kolo			101				
- É	<u>, 0 , 0 , %</u>			all Re@very (n :		107	99	2.7			
Wine at 1st	wine at 1st thate test	$\overline{\mathbf{O}}$	\$ <u>\$</u> \$0,01	103; 107	103	107	105				
taste test	grape wine	j¥_	0.10	Ť00; 104	100	104	102				
	I. RSD - Relative Standard Dev	۲.	V Over	all Recovery (n	= 4)		104	2.8			

FL: fortification level, RSD - RSDative Standard De fration * some RSDs were bot calculated as three were only two individual recoveries given Final determination as: fluopyram Reclues calculated as fluopyram Final determination as: FLU-benzamide Residues calculated as fluopyram Final determination as: FLU-PCA Residues calculated as: fluopyram Final determination as: FLU-PCA Residues calculated as: fluopyram Final determination as: FLU-PCA Residues calculated as: fluopyram

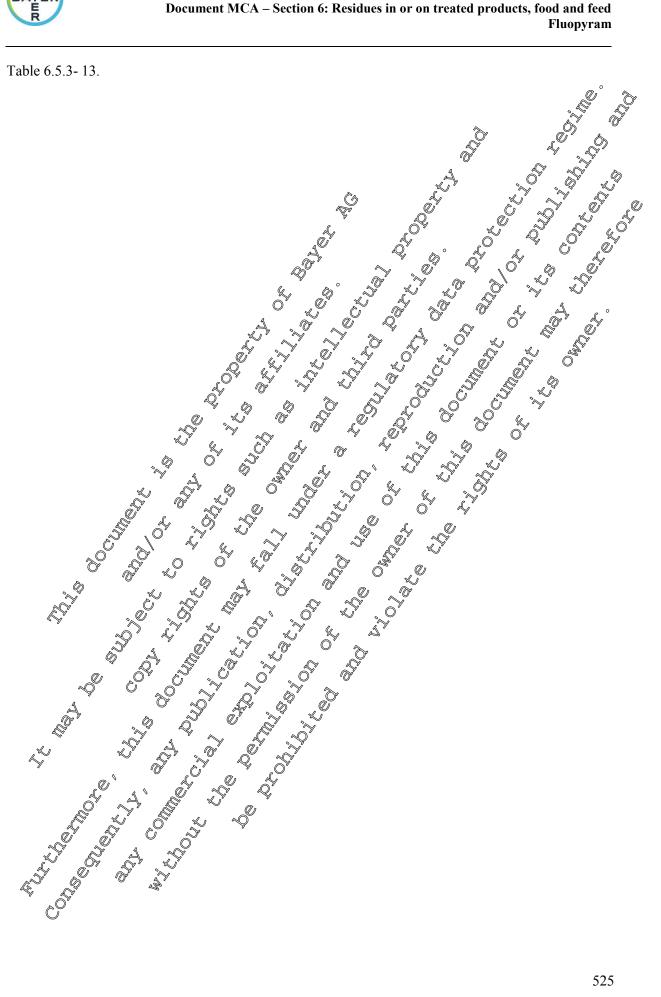
, Z

During processing for raisin production a mean of 7% of the absolute residue was recovered with r. waste. Anajor part counting for 59% of the initial absolute residue remained in the dried and was raisin to adding to values between 0.96 mg/kg and 2.1 mg/kg in the final product. Residue value fluopyram in bunch of grapes, raisin, raisin waste and washings are summarised in fluopyram in bunch of grapes, raisin, raisin waste and washings are summarised in In bunch of grapes used for raisin production residues of fluopyram were between 0.30 and 0.66 mg/kg. During processing for raisin production a mean of 7% of the absolute residue was recovered with raisin waste. Advajor part counting for 59% of the initial absolute residue remained in the dried and washed raisin Cading for values between 0.96 mg/kg and 2.1 mg/kg in the final product. Residue values of



<text> , the second And the second of the second o PF, processing factor) were calculated by dividing the fluopyram residue and fluopyram metabolites in grape processed commodities by the fluopyram esidue and its metabolites in and the second the sec the bunch of grapes (raw agricultural commodity: RAC). Since residues of fluopyram-PAA were \$0.01







10

Table 6.5.3- 13: Sum	mary of residue	s in grape ma	trices and proc	essing factors	for fluopyram	and its metab	olites	re ^{gi}	and and
trial	R 2006	0417/3	R 2006	0624/9	R ⊴006 ()651/6	R 2006)652 ³ 4 × 1	09
Sample material	Residues (mg/kg)	PF*	Residues (mg/kg)	PF	Residues	PROTO	Residues (mg/kg)	PF*SIL	Mean PF
Fluopyram (AEC65694				. L		10 ² 0,9		JU . CI	
Bunch of grapes	0.55		0.32		» 00.66 A	×,>	~Q0.30	P AL	"C -
Raisin	1.1	2.1	2.1	(O.S	1.9	2.8	Ø 0,96 O ♥	C3.2 £	3.7
Raisin waste	4.6	8.3	5.3	17 £\$	6, 1 3	\$ 9.1 20		\$ 11 (^C *	11.4
Washings	0.02	0.04	0.03	₿ <u>0.1</u>	s ~0.01** √	0.02	0.02		0.1
Fluopyram-benzamide	(AEF148815)		4. D	i t ^ĝ	Te HDA	~0 ² 10	10 I	. I	
Bunch of grapes	0.03		, ⊗0.01 _©	01	A0.02 🔨	× ×	.×.0.01 _8		-
Raisin	0.07	2.8	<u>Դ</u> Ծ.03 Օ ^Դ		2 ⁵⁰ 0.07	2317	CL 0.04	\$\$.5°	3.0
Raisin waste	0.29	11	V 0.06	5.8 x	0,28	0 ⁰ 16 vi	A A	JL 11	11.0
Washings	<0.01**	0.400	Ø:01** S		≈0.01** ¢\$	S AO	11 0.01** O	1.0	0.8
Fluopyram-pyridyl-car	coxylic-acid (AEC	C657488)		O _{Ne} .	ç X	. Â _ AO	C , tp		
Bunch of grapes	0.07	0 31	≶0.01 √	~~	0.02	, ⁰⁵	£ 0.01		-
Raisin	0.17	22	0.02	6.9.1	<u>)</u> 0.07	28	◎ ₩ 0.03	2.5	4.0
Raisin waste	1.9	27 👋	0.16	29 N	0.59	× 25 ×	0.39	33	27.0
Washings	0.01	0.1	\$9 .01** £		Ø.01**	.0.A.	<0.01**	0.8	0.6
Fluopyram-pyridyl-ace	tic-acid (BCS-AA	10139	NV a		Vit - 1	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			
Bunch of grapes	< 0.01	le le	< <u>6091</u>	9.7	<u> 1</u> 00	¢	< 0.01		-
Raisin	<0.01	NR V	≪√<0.01	NRO	0.01 5	NR	< 0.01	NR	-
Raisin waste	<0.010	O BALL	ST <0.00 Th	NR NR	> <0.0®	NR	< 0.01	NR	-
Washings	001	C NR JUL	\$0.01		$\sqrt{0.01}$	NR	< 0.01	NR	_

C Residue Koncentration in the processed product $\left[\frac{my}{ka}\right]$ *Processing factor calculated according to the following equation \bigcirc Residue concentration in the RAC $\left[\frac{mg}{ka}\right]$

Remark: Processing factors were calculated from the corresponding vesticulation $M^{a} = \bigcirc$ *Residue concentration in the RAC* $[\frac{mu}{kg}]$ **Remark:** Processing factors were calculated from the corresponding vesticulation of the corresponding vesticulation

Processing factors between 2.1 and 6.5 (refsin), between 8 3 and 17 (raisin waste) and between 0.02 and 0.1 (washings) were calculated for AE C656948. Processing factors between 26 and 3 7 raisin), between 55 and 16 (raisin waste) and between 0.4 and 1.0 (washings) were calculated for FLU-benzamide. Processing factors between 2.4 and 6.9 (raisin), between 25 and 33 (raisin waste) and between 0.1 and 1.0 (washings) were calculated for FLU-benzamide.



Conclusion Ш.

III. Conclusion
The study was conducted according to the relevant guidelines. The results of control samples, and recovery samples were in the expected range.
Concentration of fluopyram and its two metabolites (FLU-benzamide and FLU-PCA) was observed in most of the tested matrices (PF>1), except for washing water.
Accompany and annalucian by annihilanty
The study is acceptable.
H. Cnclusion

BAYER

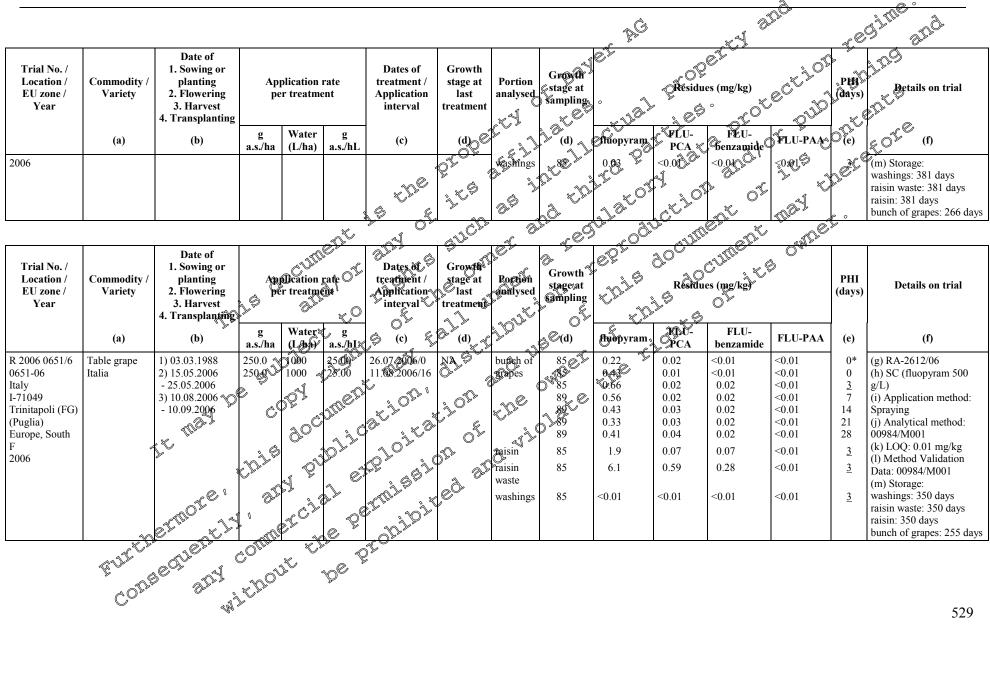
Page 528 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Table 6.5.	3-14: Re	sults of proces	ssing tr	ials co	nducted	d with fluop	oyram on		E BOS	er pg	PTOP	erti	ection	, re Ligh	9 ¹ 10 ² and 110 ⁹ a
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting		plication er treatm		Dates of treatment / Application interval	Growth stage a last treatment	Portion analysed	Orowth stage at sampling	e 	LE BERN	Orp.	j.	OPHI (days)	C Details on trial
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	*OLLC	10)°	1 (\$	(d)))	fluopyram	FLU-O	benzamide	FLU-PAA	(e)	(f)
R 2006 0417/3 0417-06 Spain E-03688 Hondón de las Nieves (Comunidad Valenciana) Europe, South F 2006	Table grape Italia	L. P.			2102 20	5 5 201	011 011 10 11 011	waste washingo	89 89 89 89 89 89 89 89 89 89 89 89 89 8	0.021 0.90 0.55 0.16 0.12 0.02 1.1 4.6 0.02	0.06 0.02 0.02 0.05 0.05 0.03 0.04 0.17 1.04 0.17	0.02 0.03 0.03	<0.01 <0.01 <0.04	$ \begin{array}{c} 0^{*} \\ 0 \\ 3 \\ 7 \\ 14 \\ 28 \\ 3 \\ 3 \\ 3 \\ 3 \\ 3 \\ 3 \\ 3 \\ 3 \\ 3 \\ 3$	(g) RA-2612/06 (h) SC (fluopyram 500 g/L) (i) Application method: Spraying (j) Analytical method: 00984/M001 (k) LOQ: 0.01 mg/kg (l) Method Validation Data: 00984/M001 (m) Storage: washings: 322 days raisin waste: 322 days raisin: 322 days bunch of grapes: 207 days
R 2006 0624/9 0624-06 Portugal P-2580-347 Passinha- Alenquer (Ribatejo e Oeste) Europe, South F	Table grape Cardinal	1) 15.03.2006 2) 10.05.2006 - 22.05.2006 30.15.07.2006 - 30.07.2006 -				103 08 5006/0 31 07 2006/8 2 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0	eg at	bunch of grapes	85 85 89 89 89 89 85 85 85	0.06 0.35 0.32 0.22 0.34 0.28 0.18 2.1 5.3	<0.01 <0.01 <0.01 <0.01 0.02 0.02 0.02 0.02 0.10	<0.01 <0.01 <0.01 <0.01 0.01 0.01 0.01 0	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	$ \begin{array}{c} 0^{*} \\ 0 \\ 3 \\ 7 \\ 14 \\ 21 \\ 28 \\ 3 \\ 3 \\ 3 \end{array} $	(g) RA-2612/06 (h) SC (fluopyram 500 g/L) (i) Application method: Spraying (j) Analytical method: 00984/M001 (k) LOQ: 0.01 mg/kg (l) Method Validation Data: 00984/M001
	COr	N.	L.P.												528

Page 529 of 801 2021-02-26



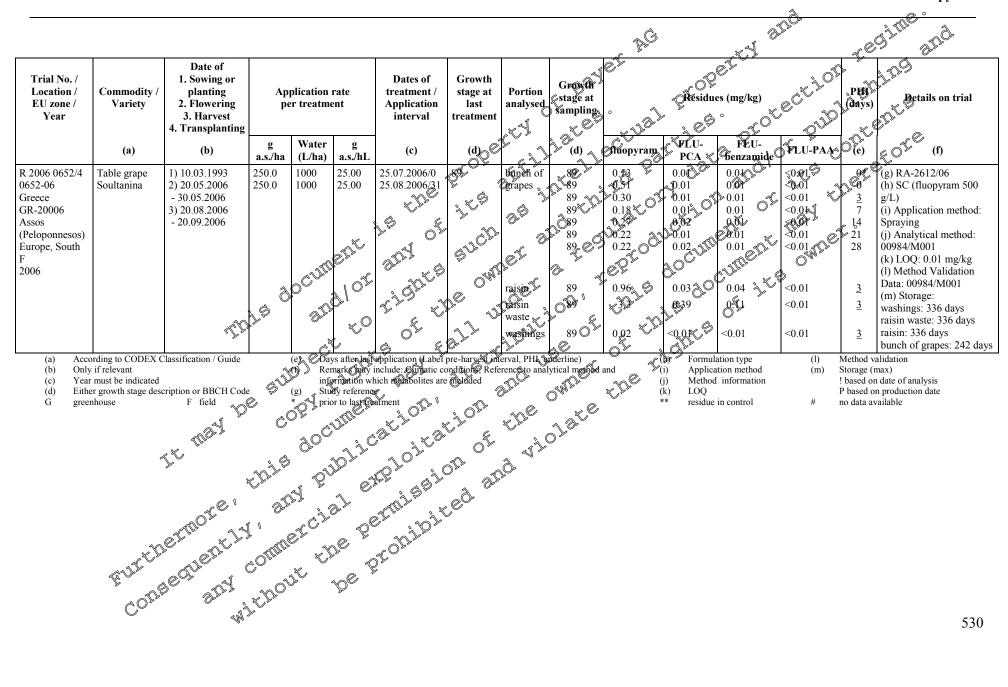
Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram



Page 530 of 801 2021-02-26

BAYER

Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram





Data Point:	KCA 6.5.3/04
Report Author:	
Report Year:	2008
Report Title:	AE C656948 500 SC - Magnitude of the residue on grape Occessed comodities
Report No:	RAGMP042
Document No:	<u>M-298571-01-1</u>
Guideline(s) followed in	EPA Ref.: OPPTS 860.1520;
study:	PMRA Ref.: DACO 7.4.5
Deviations from current	none
test guideline:	none
Previous evaluation:	yes, evaluated and accepted
	rev. 1 to Vol.3 of DAR B7August 2012 (reference relie On)
GLP/Officially recognised	Yes, conducted under GBP/Officially resignised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes V C R & C A A C

The study included one supervised residue trial with grape conducted in North America (USA) in the 2006 season in order to determine the magnitude of the residues of theoryram (APC656948) in bunch of grapes and the processed fractions (washed/ruits, heated/pulce, jelly, and raisin) following two spray applications of fluopyram (500 SC).

J. Materials and methods

Field part

In the trial, two air blast applications with fluopyram (500 SC) - a suspension concentrate formulation containing 500 CL fluopyram - were conducted at a single application rate of 1.25 kg a.s./ha/application and water rate at 519 523 P/ha. The achieved total seasonal rate was 2.50 kg a.s./ha. The applications were conducted at BBCH of 85 (for the first application) and BBCH of 89 (for the second application), with a 14 day interval between the two applications. This application rate was equivalent to five times (5X) the total maximum proposed Jabel rate for a single growing season

One control and one treated bulk grape samples were collected at a 7-day PHI. Bulk grape samples were harvested by hand first from the control plot tollowed by the treated plot. Grapes were sampled from the adjacent inner facing half of the two plot rows. Each bulk sample consisted of 200 lbs (91 kg) of grapes. The samples were put into labelted containers in the field, placed in a pick-up truck, surrounded with frozen plastic bottles of water, and hand delivered to the processing facility the same day.

Progessing procedures

The samples were harvested and band delivered at ambient temperatures to The National Food Laboratory, bc. for sub-scorpling and processing. The samples arrived in good condition and were placed in a cool storage room at 18 ± 5 °C Prior to processing, a random sub-sample of the control and treated back grapes were collected for analysis, and the remainder of the grape samples were used to generate the required processed commodities of raisins and grape juice. In addition, samples of washed fruit and jelly were generated for use in the dietary risk assessment for fluopyram. Processing was performed using proceedings which simulated commercial processing practices.

Details Pprocessing of the control and treated grapes are presented on flow chart diagrams and material balance summaries. The sub-samples were shipped to Bayer CropScience via freezer truck for analysis.



Food processing involves the use of water to start up and shut down certain unit processes. Water is mixed with the food product when it is introduced into the running machine and again when the food product is exhausted. To minimize water dilution of the food product in this study, some of the product may be discarded at each end of the process. Therefore, weight losses may result when diluted product is discarded. Or weight losses may occur if product is spilled or not fully receivered from processing equipment. Weight gains may result if the sample contains additional water. This is a normal part of food processing, especially small batch processing. The term "material balance" generally refers to showing a balance of a constant, measurable quantity, such as total solids, through a unit process or a series of unit processes. Since a total solids assay was not performed on all samples, a mass balance is not an accurate term. Therefore, this report presents weight distributions as measured throughout the processing operations. These weight distributions are presented on the flow charts below on Diagram 6, 28-4 p Diagram 6.5.3-7.

Processing of the Control and Treated grapes begation August 30, 2006 The initial weight of the Control and Treated grapes was determined. Fraction samples of raw unwashed grapes from Control and Weated were collected. The fraction samples were as will be by taking grapes from each of the bags delivered for each sample. The fraction samples were bagged weighed, labeled, and placed in the freezer. Grapes for sun drying of Control and Treated raisins were removed and were taken to sundrying. Control and Treated grapes for wash as in the home were washed under tunning water, the samples were bagged, weighed, labelled, and placed in the freezer

Crushing/Destemming

Grapes for processing into grape juice from Controland Treated samples were ontially passed through the crusher/destemmer. The crusher/destemmer crushes the betries and separates the stems from the crush (crushed berries and juice). The crush was collected, weighed and transported to the depectinization step. Stems were collected, weighed and discarded.

Depectinization

Each crush was transferred to a spam-jacketed kettle for the depectinization step. Novozyme Pectinex 3XL pectinase may was added to each yoush at a level of approximately 0.06 % by weight. The enzyme-inoculated crush was then heated and held for approximately 2 to 3 hours. The target temperature for the enzyme treatment was approximately $49 - 60 \,^{\circ}$ C. The Crushed Control grapes were heated to 57 - 60 °C fot a period of 746 minutes during the enzymatic depectinization process. The Crushed Preated grapes were reated to 60 - 58 of for a period of 121 minutes during the enzymatic depectinization process. S

Extraction

The 2 depectivized pape wish spirities were passed through a screw press at the depectinization temperature. For each slupp, the extracted, undarified juice was collected, weighed, and transferred to a steam-jacketed kettle. The wet pomace was collected, weighed, and discarded.

Juice Clarification and Argol Settling

Each unclarified juice batch was place into a steam-jacketed kettle for heating. The unclarified juice was heated to inactivate the peclinase@nzymeand cooled prior to placement into refrigerated storage for argol settling Control juice was heated to 87 °C and cooled to 24 °C. The Treated juice was heated to 88 °C and then cooled to 24 °C. Cooled, unfiltered juice samples from Control and Treated were collected, weighed, and placed in refrigerated storage for argol settling.

Juice Filtrati

Argo settling for the Control and Treated juice samples took place under refrigeration at -1 °C to 2 °C; settling time was 26 days for Control juice and 25 days for Treated juice. Upon completion of the argol settling process, the argol-settled juice was filtered to prepare clarified juice for canning, concentrating, and jelly making. Upon completion of the argol settling process, the argol-settled juice was filtered to prepare clarified juice for canning, concentrating, and jelly making. The Millipore filter was set up using



filter paper and was precoated with approximately 2 % of diatomaceous earth filter aid (Celite 545), based on the weight of juice filtered. The juice was filtered through the filter using air over pressure.^A portion of the filtered juice was transferred to Juice Canning and a portion was transferred to felly Making.

Single Strength Juice Canning

A portion (4.5 kg for Control and 3.9 kg for Treated) of the filtered juice was weighed, placed in a steam of jacketed kettle and heated to canning temperature. Hot juice was filled into plastic jars and sealed. Hot filled plastic jars were held inverted for 7 minutes before poling. When cool, the jars were dried, weighed, labelled, bagged, and placed in the freezer. Control fiftered and clar hed single strength of juice was heated to 92 °C, filled into plastic jars, and bed for 7 minutes prior to cooling. Reated iltered and clarified single strength juice was heated to 92 °C, filled into plastic jars and held for 7 minutes prior to cooling.

Grape Jelly Preparation

A portion of the filtered juice (1.3 kg for Control and 1.3 kg for Reated) was weighed and placed into a steam-jacketed kettle. The pH of the juice was adjusted to about 20 with citric acid. Control juice required 36.0 g of citric acid, and Treated juice required 42.6 g. Sugar (2.9 kg) and pectin (34.4 g) were added to the Control filtered juice. The mixture was heated to boiling and the place winto plastic jars and sealed. The fill temperature was 104 °C. The jars were held inverted for 5 minutes and then cooled in running water. The jars were then labelled and placed into the freezer. Sugar (2.7 kg) and pectin (32.2 g) were added to the Treated filtered juice. The mixture was heated to

boiling and then placed into plastic jars. The fill temperature was 105 °C. The jars were held inverted for 6 minutes and then cooled in ronning water The jars were then labelled and placed into the freezer.

Sun Drying of Grapes

For sun drying, grape bunches were spread out on stainless steel drying trays (on the pilot plant/low bay roof). Each sample of grapes was physically separate oto avoid cross contamination. Drying started on August 30, 2006 On Qotober 34, 2006 the moisture of the sun-dried grapes was 12.8 % for the Control and 14.6 % for the Treated; this was within the specified moisture range of 12 to 16 %, so the Control and Treated raisins were collected and transferred to sweat box storage.

"Sweat Box" Moisture Equilibration

The Control and Treated dried grapes were placed into separate plastic bags (acting as a "sweat box"), weighed, and place in the $19 - 27^{\circ}$ C storage room until they were removed for destemming and further processing. Control and Treated dried grapes were placed into the 19 - 21 °C storage room on October 31, 2006 and were both removed on November 2, 2006.

Destemming and Cap Stem Removal

The destemming and cap stem removal copsists of separating the dried grapes from the stems and then removing the residual cap stems by hand. This process was performed only on enough dried grapes to obtain approximately 2.7 3.6 kg of sample for the Control and Treated samples. The remaining dried grapes and the stems were discarded. The Control sample was frozen from November 2, 2006 to November 3, 2006 to make the cap stems more fragile and easy to remove. The Treated sample was frozen from November 2,2006 to November 6, 2006 to make the cap stems more fragile and easy to remove.

Dried Grape Washing and Behydration to Raisins

Washing and rehydrating of dried grapes was accomplished by placing destemmed dried grapes into a stainless seel mesh basket and immersing them into fresh water for 1 to 2 seconds. After this immersion, excess@arface water on the rehydrated raisins was drained before weighing the sample. The moisture for the Control and Treated samples was determined to be 18.1 % and 18.7 %, respectively. Samples of



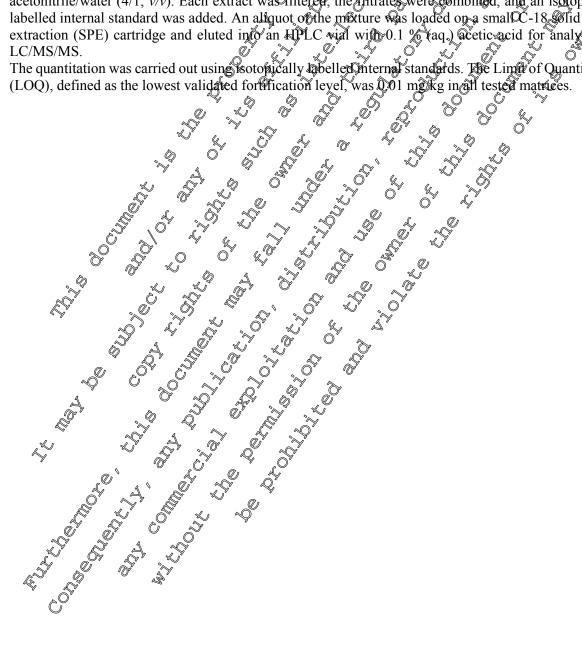
raisins were bagged, weighed, labelled, and placed in the freezer on November 8, 2006 for both the Control and the Treated sample.

Residue analysis

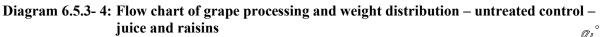
To prepare samples for analysis, the grape raw agricultural commodity sub-samples and the grape processed commodities of raisins and washed fruit were homogenized with dry ice. All samples were returned to frozen storage immediately following homogenization, and the samples always remained in frozen storage except during sub-sampling for analysis. Grape juice and jelly were analysed as received from the processor.

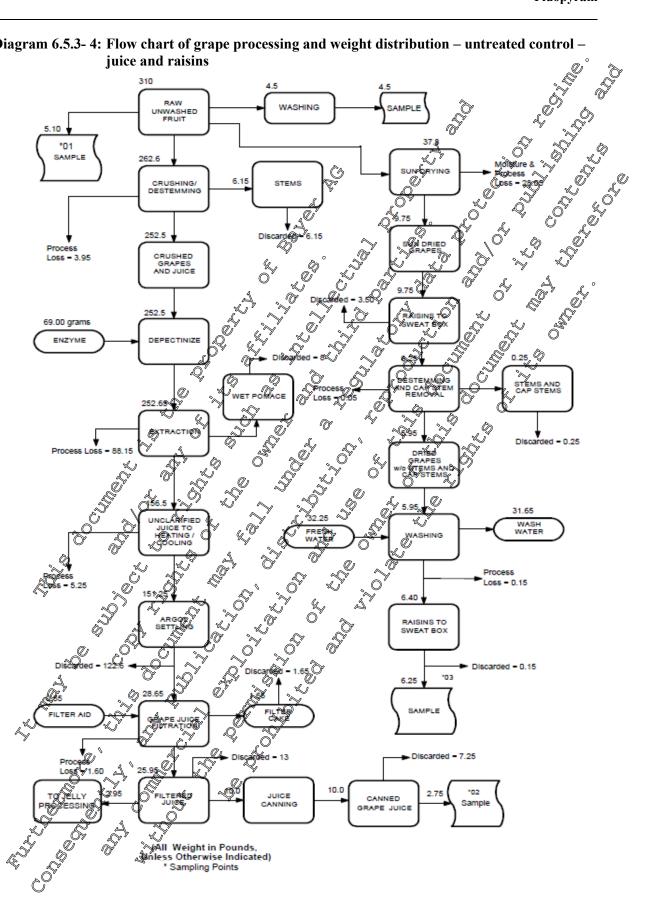
The residue data for grape raw agricultural commodity and grape processed commodities were obtained using the analytical method for determining the fluoporam residue in plant 00984 05/0**Q**)2002 2007, No. GM-001-P07-01, M-283301-01-1, see MCA section 4.1.2) with modifications (L. M-297568-01-2)

Briefly, a 5-g aliquot of the crop matrix was extracted by blending twice, each time with a mixture of acetonitrile/water (4/1; v/v). Each extract wastiltered, the Artrates were combined, and an isotopically labelled internal standard was added. An aliquot of the mexture was loaded on a small C-18 solid phase extraction (SPE) cartridge and eluted into an HPLC will with 0.1 % (aq.) acetic acid for analysis by LC/MS/MS. The quantitation was carried out using isotopically labelle Cinternal standards. The Lingu of Quantitation

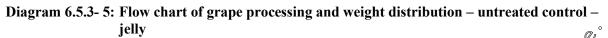


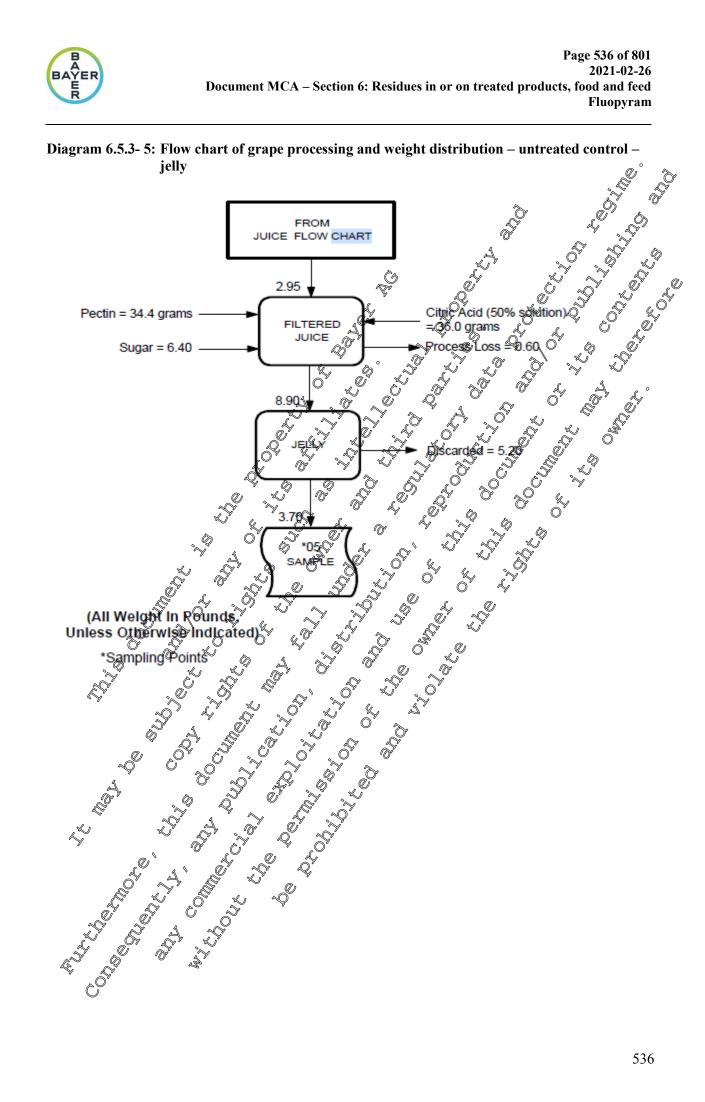




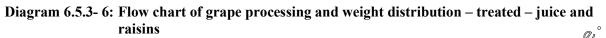


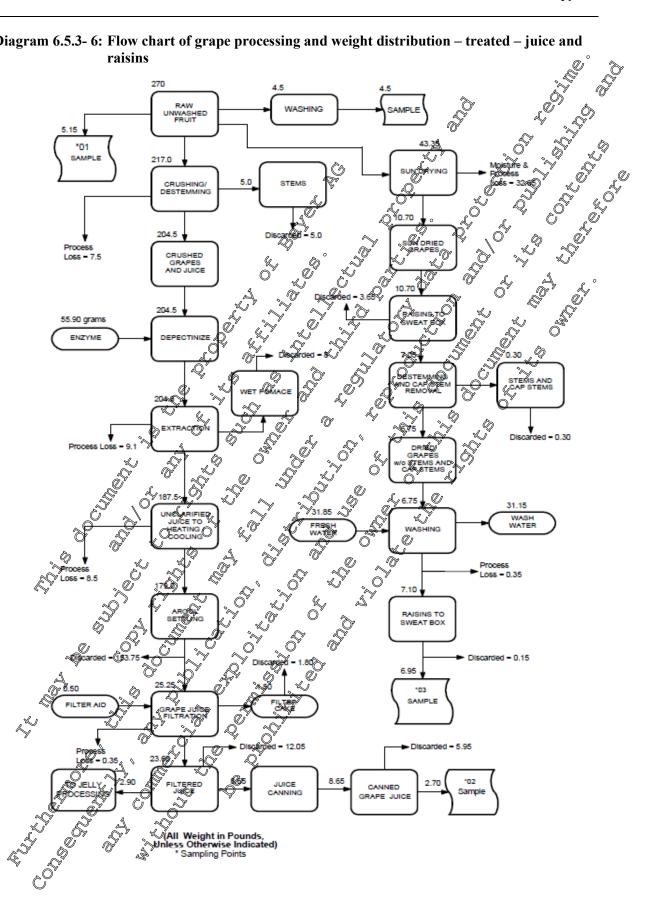




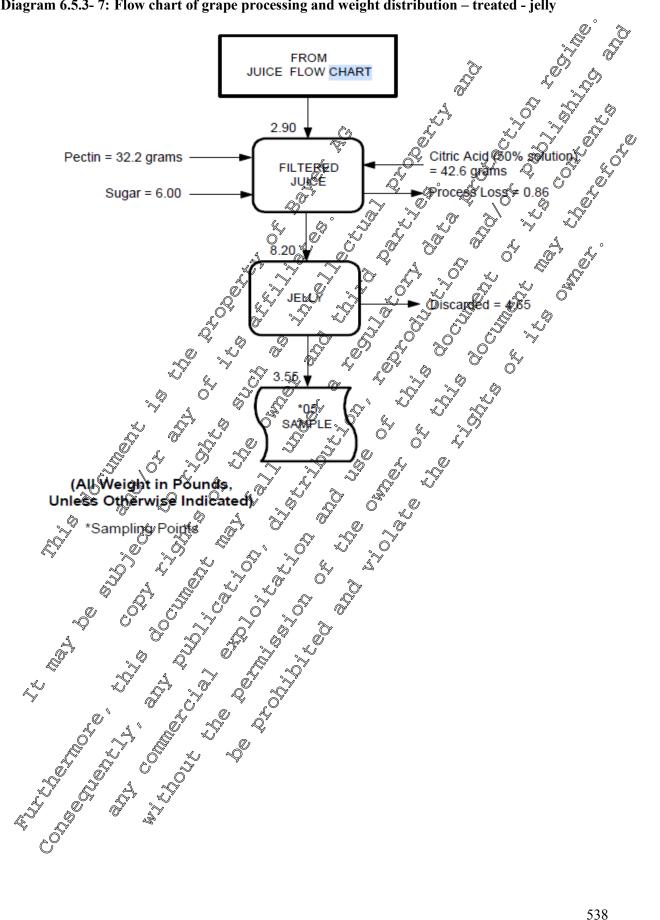
















II. Findings

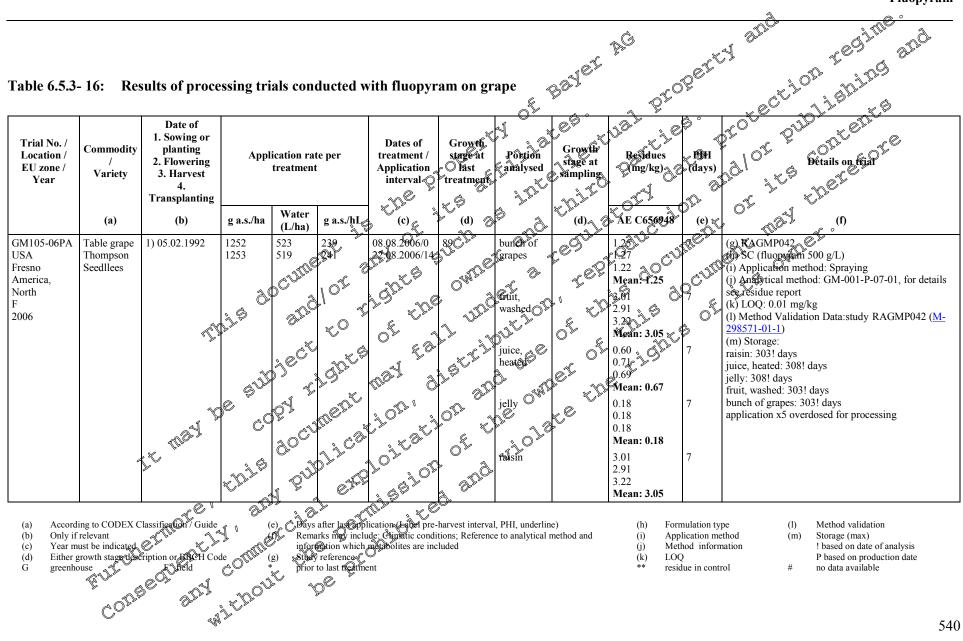
No apparent residues above the LOQ were present in the control samples. In order to check the performance of the method, recovery determinations were concurrently performed to the analyses of T control and treated samples in each set of analyses. Concurrent recoveries well obtained during the conduct of this study. All data of the method performance and recoveries are shown in the tables below. The mean concurrent recoveries were within the acceptable range of 70 % $-\frac{1}{2}$ 10% in all tested matrices. The RSD values (although not all could be calculated) were ≤ 20 %. The grape RAC samples analyzed in this study were held in frozen storage for a maximum of 10 monos (300 days) prior to extraction. The grape processed commodities in this study were also analyzed within 10 months (299 days) of generation The mean fluopyram residue level in fresh grapes collected at PHV 7 was 1.25 mg/kg/in grape raisu 3.05 mg/kg, in grape juice 0.67 mg/kg, in washed ruit 0.96 mg/kg, in elly 0.18 mg/kg. Processing factors (PFs) were calculated by dividing the Muopytam residue of grape processed commodities by the fluopyram residue in grape fruit RAC Commodity samples are suffimarized Processing factors calculated for the individual grope processed in the tables below. Processing factors for fluopyram were for mashed fruit) and 2.4 (for raisin). The study was conducted according to the relevant goidelines. The results of control samples, and recovery samples were in the expected range. Concentration of fluopyram was observed in raisin (PF>1). Assessment and conclusion by applicant: The study is acceptable K, Concurrent recoveries of fluopyrad Table 6.5.3 Recovery (%) Fortification Portion analy Individual (mg/kg) Max RSD Min Mean & recoveries ð Fluopyram (AE 6 1140109; 89; 92; 89 115 102 10.5 94; 102; 115 Fresh fruit 99; 101; 99 101 99 100 1.2 104; 93; 107 93 107 101 7.3 Juice 101; 99; 101 99 101 100 1.2 0.01 95 103 4.7 95; 103; 95 98 2.00 97 96 96 0.6 96; 97; 96 0.01 88; 98; 84 84 98 90 8.0 3 2.00 91; 93; 90 90 93 91 1.7 3 5.00 103; 95; 96 95 103 98 4.5

FL: fortification level, RSD - Relative Standard Deviation

Final determination as: fluopyram Residues calculated as: fluopyram

BAYE

Page 540 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram





	RAG	MP042	
Sample material	Residues (mg/kg)	PF*	
Fluopyram (AE C65	6948)	Ğ	
Grape (RAC)	1.25 1.27 1.22 Mean: 1.25		cessing factors for fluopyram
Raisins	3.01 2.91 3.22 (Mean: 3.05		
Grape juice	0.71 0.69 Mean: 9.67		cessing factors for fluopyram
Fruit, washed	0.92 0.97 0.97 Mean: 40.96		
Jelly	Q 0.Q Q Q.18 Q 0.18 Q 0		
Processing factor	calculated according to	the totowing equation	$\frac{2}{2} PF = \frac{2}{2}$
Residue concentratio	$\frac{1}{n \text{ othe RAC}} \begin{bmatrix} \frac{mg}{kg} \end{bmatrix} $		₩ ^y
	0.90 0.97 0.97 Ntean: 0.96 0.18		

 Table 6.5.3-17:
 Summary of residues in grape matrices and processing factors for fluopyrame



New studies

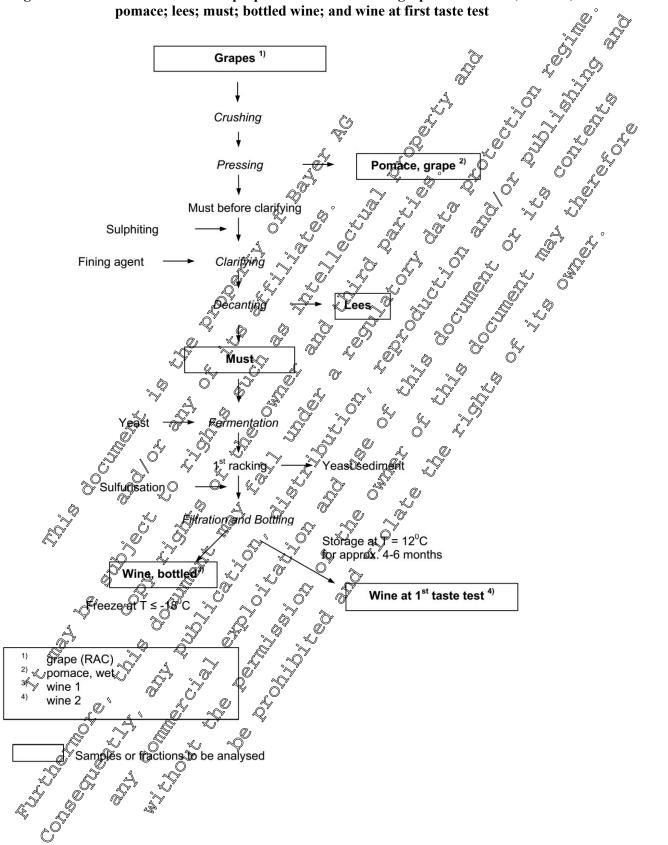
Data Point:	KCA 6.5.3/10
Report Author:	
Report Year:	
Report Title:	Determination of residues of AE C656948 in/on grape and processed fractions
	after spraying of fluopyram SC 500 in the field in Germany
Report No:	08-3077
Document No:	M-352682-01-1
Guideline(s) followed in	EU: Council Directive 91/414/EEC, Annex II, part A, section and Annex III part
study:	A, section 8; EC guidance working document 9029/VI/95 reg 5 (1997-07-22)
Deviations from current	
test guideline:	
Previous evaluation:	yes, evaluated and accepted
GLP/Officially recognised	Yes, conducted under GLROfficially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes A A A A A A A
Data Point:	Yes, conducted under GLROfficially recognised testing facilities (Yes (KCA 6.5.3/11 @ 2
Report Author:	
Report Year:	
Report Title:	Amendment no y to report No: 08-3081- Determination of residues of AE
200F 200	C656948 in/on grape and processed fractions after spraying of fluopyram SC 500
	in the field of France (South)
Report No:	
Document No:	M-35200-02 %
Guideline(s) followed in	EU: council Directive 91/414/EEC, Sinnex of, part of, section 6 and Annex III, part
study:	A, section & EC graidance working document 7029/VI/95 rev. 5 (1997-07-22)
Deviations from current	pone
test guideling:	
Previous evaluation:	yes, evaluated and accepted and accepted and accepted and accepted and accepted acce
~~~~	
GLP/Officially recognised	Yes, conducted order GLP/Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability	Yes v v
	Yes 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7
A to	

# Test system:

Balance studies on processing of grapes into grape wine were conducted to determine the transfer of fluopyram and its metabolites fluopyram-pyridyl-acetic acid, fluopyram-benzamide and fluopyram-pyridyl-carboxylic acid from bunch of grapes into processed fractions.

Wine was produced from red grapes obtained from two different trials located in Germany and Southern France. The processing of burch of grapes into washed berries, wet pomace, lees, must, bottled wine and wine at  $0^{4}$  taste test was performed at Weinstr. Nord 27, D-67487 Maikammer/Germany. The processing simulated the industrial practice on a laboratory scale. A flow chart to describe the production of grape price is presented in Diagram 6.5.3-8.







Samples were analysed according to the analytical method 00984 (1997), 05/02/2007, M-283301-01-1, see MCA section 4.1.2). Full details and acceptable validation data to support this method, are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues were extracted from 10 g of sample material (raisin and raisin wasters g) by two-succe extractions using a high speed blender with a mixture of acetonitrile:water (80.20; v:v).

Subsequently, the raw extracts were diluted 10-fold by adding internal standard solutions.

- One dilution performed under acidic conditions for determination of fluopyram-PC
- Another dilution performed under basic conditions (for determination of fluor) ram • benzamide and FLU-PAA)

Residues were quantified by reversed-phase chromanography coupled with tandem mass spectrometry (MS/MS) with electrospray ionisation. One injection in positive electrospray ionisation, allowed the determination of fluopyram, FLU-benzamide and FLUpPAA, Another injection in regative electrospray ionisation allowed the determination of FLU-PCA under different conditions.

The quantitation was carried out by internal standardization using internal stable labelled standards The Limit of Quantitation (LOQ, calculated and expressed as fluopyram parent equivalents for fluopyram and its metabolites), defined as the lowest validated fortification level, was 0.0 mg/kg in all matrices for all analytes. All residues are calculated as parent fluopyram The storage period of deep frozen processed samples ranged between and 264 day e,  $\mathcal{A}$ 

Table 6.5.3- 18:	Recovery results f	or fluopyram	in bunch o	oferapes a	and process	d materials of
	wine production		°		× .0	

	Sample Matrices FL				
		Single Values	Mean	RSD	LOQ
Report No.	N N Imake	g 5 × (%) 0 0	Value ~[%]	[%]	[mg/kg]
Analyte: fluc	pyration of the second s		Ø		
	Pomaço Pomace, 0.10	102, 104, 167, 106, 404, 169 7	105	2.4	
(Ča		98, 10, 99, 103, 102, 104	101	2.3	0.01
		ll Recovery (n = 2)	103	3.1	
08-3077& 08-3081	Wine at 2 0 ft	, 199, 111, 111, 1102, 104, ∠106, 104, Δ	107	4.0	
	wine at 1 st tast		105	1.0	
	1 st taste test 5 test grape 1.0	97 97 P	93	_	0.01
<u></u>	wine Si 50	AT7 0	117	-	
	June Sveral	h Recovery (n = 12)	106	5.8	

FL: fortification level, RSD - Relative Standard Deviation * some RSDs were not calculated as there were only one prdividual recoveries given Final determination as: fluopyram Residues calculated of. fluopyram

Recovery results for fluopyram-pyridyl processed materials of wine production Recovery results for fluopyram-pyridyl-acetic acid in bunch of grapes and Table 6.5.3-



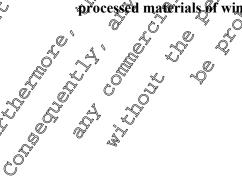
Report No.	Sample Material	Matrices covered	FL [mg/kg]	Single Value	es Mean Value [%]	RSD	LOQ
Analyte: flue	opyram-pyr	idyl-acetic a		[/ <b>0</b> ]			<u>, rae o</u>
			0.01	78, 84, 78, 81, 78, 7		3.Q	Ś
08-3077	Pomace .	Pomace, lees, must	0.10	70, 72, 72, 77, 78, 8	30 75	5,4	30.01
		ices, inust	Overall R	Recovery (n = 12)	77	5.0	
		<b>XX</b> 7. 4	0.01	76, 82, 75 72, 79, 8		۲.0%	
	wine at 1 1 st taste tt test g	Wine at 1 st taste test;	0.10	78, 74, 74	5 75 Ø	ক্সা	
			1.0	71	Ô ^Y , ZP	3 - 🖉	0.00
		grape	5.0	890 ⁻⁷ ~	× ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	Ĵġ	<u></u>
		wine	Overall	ecovery (n = 12)	J 0 77 5	~7.6	S -

Standard * some RSDs were not calculated as there were only one individual rece Final determination as: FLU-PAA Residues calculated as: the opyram

Recovery result for fluopyrand-benzamidein bunch of grapes and processed Table 6.5.3-20: materials of wine production

(U)

Internation of the production       FL       Single Values       Merrin (RSD)       LOQ         Report No.       Material       covered       FL       Single Values       Value       RSD       LOQ         Analyte: fluopyram-benzamide       Img/kg       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       1%1       <						° N	
Analyte: fluopyram-benzamide $0.01$ $107$ $108$ $103$ $4.1$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.01$	Report No.		covered	KFL     Single Values       V     Single Values	value (	1	
Analyte: fluopyram-benzamide $0.01$ $10^{\circ}_{0}108,104,96402,103$ $003$ $4.1$ Pomace       Pomace $0.01$ $10^{\circ}_{0}108,104,96402,103$ $003$ $4.1$ Pomace       Pomace $0.01$ $0.01$ $10^{\circ}_{0}108,104,96402,103$ $003$ $4.1$ 0.01 $0.01$ $0.01$ $10^{\circ}_{0}99,98,96,99,97,96,96$ $4.97$ $1.3$ $0.01$ 08-3077       wine at $1^{\circ}_{1}$ taste $0.01^{\circ}_{1}$ $103^{\circ}_{9}99,98,100,102,1008,102,1008,102,1008,102,1008,102,1008,102,1008,102,1008,100,102,1008,100,102,1000,102,100,102,100,102,100,102,100,102,100,102,100,102,100,102,100,102,100,102,100,102,100,102,100,102,100,100$						[%]	[mg/kg
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Analyte: flu	opyram-ben	zamide			Т	r
08-3077 $08-3077$ $08-3077$ $08-3077$ $08-3077$ $08-3077$ $08-3077$ $08-3077$ $08-3077$ $0.017$ $0.017$ $103-99, 98, 100, 102, 1006$ $102$ $0.017$ $103-99, 98, 100, 102, 1006$ $102$ $3.6$ $0.017$ $103-99, 98, 100, 102, 1006$ $102$ $3.6$ $0.01$ $101$ $0.01$ $0.01$ $0.01$ $0.01$		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Por a s		3 . 1903	4.1	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Pomage	lees, must		₫ 97	1.3	0.01
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Ĵ,	Ô ^Y ÌY			4.5	
$\begin{bmatrix} 1 & \text{st} \\ \text{test} \\ \text{test} \\ \end{bmatrix} \begin{bmatrix} 1 & \text{test} \\ \text{grand} \\ \text{grand} \\ \text{st} \\ \text{test} \\ \end{bmatrix} \begin{bmatrix} 1 & 1 & 1 & 1 \\ 1 & 0 \\ \text{st} \\ st$	08-3077				102	3.6	_
$\mathbb{C}^{\mathbb{C}}$ test $\mathbb{C}$ graph $\mathbb{C}^{\mathbb{C}}$ but $\mathbb{C}^{\mathbb{C}}$ but $\mathbb{C}^{\mathbb{C}}$ but $\mathbb{C}^{\mathbb{C}}$ but $\mathbb{C}^{\mathbb{C}}$	, Oj		1 st taste	A.10 \$7108, 108, 108	106	2.7	
			test;		101	-	0.01
C: fortification level, RSD - Reneve Standard Decation some RSDs were not calculated as there were only one individual coveries oven nal determination as: FLU tenzanide Residue calculated as: fit opyram       104       5.7         Cable 6:3.3-21:       Recovery results for floropyram-pyridyl-carboxylic acid in bunch of grapes and processed materials of wine production       9		~~~~	wine 🖇	5.45° NY9 4 X	119	-	
: fortification level, R&D - Reputve Standard Devation some RSDs were not calculated as there were only one individual Goveries given nal determination is: FLUGenzamide Residues calculated as: fit opyram rable 6.3.3-21: Recovery results for floopyram-pyridyl-carboxylic acid in bunch of grapes and processed materials of wine production			S S	Qverall Recover Q(n = 12)	104	5.7	
	`able 6. <b>3</b> .3-	21: Reco	very result essed materia	for thropyron-pyridyl-carboxylic rials of wine production	e acid in bunc	h of gra	pes and





Report No.	Sample Material	Matrices covered	FL	Single Values	Mean Value	RSD	
			[mg/kg]	[%]	[%]	[%]	[mg/kg]
Analyte: flu	opyram -pyi	ridyl-carbox	ylic acid		~	Ć	N O
			0.01	104, 96, 82, 91, 94, 85	~ ⁹ 2	8.6	Ś
08-3077	Pomace .	Pomace, lees, must	0.10	87, 82, 74, 91, 94, 90	86	8,4	<u>ک</u> 0.01
		ices, must	Overall R	Recovery (n = 12)	89	8.8	
		W	0.01	89, 93, 10, 81, 95, 98, 96	' 93 🕺	7.9	
	wine at	Wine at 1 st taste test;	0.10	100, 102, 105	102	25	
	1 st taste te test gr		1.0	96 JO	20	~~- °	
		grape	5.0	ko vie	407 Ó	Ċ,	<u></u>
		wine	Overall R	$ecovery (n = 12)^{\circ}$	<u>6</u> 97	~	Š

* some RSDs were not calculated as there were only one individual re Final determination as: FLU-PCA Residues calculated as; floopyram

C

### **Findings:**

In bunch of grapes used for juice and wine production residues of fluopyram were at 0.25 and 0.88 mg/kg. Residues of fluopyram in the funal product whe at A taske test were 0.17 mg/kg and 0.71 mg/kg respectively. Residue values of fluop@am in wing and the processed by-products are summarised in Table 6.5.3-  $22^{\circ}$ . Ś Ŵ

With wine processing, 56 70% of the initial residue remained in the grape pomaee, and 49 - 74% was recovered in must. Fermenting and fibration further reduced the residue conceptration of fluopyram so that the final product wine contained 32 - \$9% and wine at first taint test 35 - \$2% of the initial residue. C.S.

Residue of flugyram and metabolites in bunch of grapes and processed Table 6.5.3 commodities of wine production Ĩ

	, , , , , , , , , , , , , , , , , , ,	i al				
Country	Cróp 🚫	DACT	Residues (m	rg@kg) expressed	as AE C65694	48 equivalents
Study No.	Crôp Portion analysed	(days)	🗢 fluopyram	FLU~pyridyl-	FLU-	FLU-pyridyl-
Trial No.	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			acetic acid	benzamide	carboxylic acid
Germany	bunch of grapes	3≪∫	× 0.88	∞ < 0.01	0.01	0.03
08-3077	bung of grapes	Ŷ	َ [*] 2.2 ⁹	< 0.01	0.03	0.07
08-3077-01 🚕	dees of	°≈y3 ~	2,22	< 0.01	0.03	0.14
4	must 🔗 🗸	× 3 Q	<b>0</b> .95	< 0.01	0.03	0.03
A A A A A A A A A A A A A A A A A A A	Wine bottled	Ъ.	ిస్త్రి 0.65	< 0.01	0.02	0.02
	Wine bottled wine at 14 taste test	<u>∧</u> 3	C 0.51	< 0.01	0.02	0.03
Southern	bunch of grapes	~~~ 3 _ C	0/25	< 0.01	< 0.01	< 0.01
France	pomace 🔊 🔊	× 3 ×	0.84	< 0.01	0.01	< 0.01
08-3081	legs	<u>s</u>	0.29	< 0.01	< 0.01	< 0.01
	must A	×3	0.17	< 0.01	< 0.01	< 0.01
J.	Winebottled	3	0.16	< 0.01	< 0.01	< 0.01
<u> </u>	wine at 1st taste test	3 🖇	0.17	< 0.01	< 0.01	< 0.01
	0 $1$ $1$ $1$ $1$					

DALT - Qays after last application

Ċ An average processing factor of 0.7 was calculated for the transfer of fluopyram from bunch of grapes into wine The transfer factors of fluopyram into wine and the processed by-products are summarised in Table 6.5.3-23.



#### Transfer factors for the residue of fluopyram in processed commodities of Table 6.5.3-23: wine production $a^{\circ}$

	Transfer	factors for residues of f	uopyram
Sample material	08-3077-01 Germany	08-3081-01 France South	Mean S
pomace wet	2.6	3.4	03.2
lees	2.5	1.2	1.9 7
must	1.1	0.7	
Wine bottled	0.7	064	X DY LY OY
wine at 1 st taste test	0.8	5.7	0 40.8 0

* Values below LOQ which were set at LOQ for the calculation of transfer factors

#### **Conclusion:**

Consective and in the section of the , L Ś Conclusion: Residues of fluopyram concentrate in wet pomace out are reduced in must and wine. This result comparable to the data presented in EFSAs "Conclusion on the peer review of the posticide ris

			di di	1 Col	~~y	≪J'	$\sim$	$\sim$	S d		9
1	Assessment and conclusion	1 by app	licant:		Ô	2	ð .	$\sum_{i=1}^{n} e_{i}$			
	The study is acceptable.			n a		, , , , , , , , , , , , , , , , , , ,		ð	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	& Í	



Data Point:	KCA 6.5.3/12
Report Author:	
Report Year:	2010
Report Title:	Determination of the residues of AE C656948 and trifloxy probin in/on grape and the processed fractions (must; pomace, grape; wine at bothing and wine at first taste test) after spraying of AE C656948 & CGA279202 SC 500 in the field in France (South) and Italy
Report No:	08-3204
Document No:	<u>M-384844-01-1</u>
Guideline(s) followed in	EU: Council Directive 91/414/EEC of July 150991, Annex & part & Section 6
study:	and Annex III, part A, section 8; EC guidance working document 7029/VI/95 rev of 5 (1997-07-22)
Deviations from current test guideline:	
Previous evaluation:	yes, evaluated and accepted
GLP/Officially recognised testing facilities:	Yes, conducted prider CDP/Officially recognised testing facilities
Acceptability/Reliability:	Yes Q Q Q Q Q Q Q Q Q

. Materials and Methods

The study included two supervised tesidue trials with grape, conducted in the field in southern Europe (southern France and italy) in the 2008 season. The purpose of this study was to determine the magnitude of the residues of fluonoram and its metabolites thropyram-bergamide (AE F148815, alias FLU-benzamide), fluopyram pyridyl-acetic acid (BCS-AA10139, alias FLU-PAA) and fluopyram-pyridyl-carboxylic acid (AE G557189, alias FLU-PCA) in on grape (burch of grapes) and its processed fractions of wine (must, pomace, wine at bottling and wipe at first taste test).

# Field part

In each field trial from study 08-2204, the treated plot was sprayed twice at BBCH growth stages from 81 (beginning of repening: berries begin to de clop variety specific colour) to 85 (softening of berries) with AEC656948 & C6A279302 S6 500, a suspension concentrate (SC) formulation containing 250 g/L fluopyram (AEC656948) and 250 g/L friflox strobin (CGA279202). The application rate was 50 g a.s. fluopyram/ha using a pray volume of 200500 L Ga. The interval between applications was 14-15 days and the pre-harvest interval was 24 days. All treatments were made at the scheduled rates.

Bunch of grape samples were taken 14 days after the last treatment at BBCH 89. The sample 08-2204-03-0003F for processing for trial/08-3204-02 was not receipt at the processing laboratory and a new sample was taken at DACT21. Samples for processing were shipped to processing laboratory in fresh conditions and then were stored in a cold room (5-10°C) until processing on the next day.

The grapes were crushed and after taking a laboratory sample of the must, the crushed grapes (=must) were transported by car at ambient temperature for the flash vacuum-expansion (CIRAD, Montpellier, France). The must and fiquors obtained after vacuum-expansion were grouped together in a stainless steel tank and transported by car at ambient temperature to the processing laboratory to start the alcoholic fermentation.

Directly after processing the laboratory sample wine at first taste test was stored in a cold room (approx. 5-10°C) until shipment by courier at ambient temperature to the laboratory for preparation of the examination samples. The other laboratory samples were stored deep-frozen after sampling at  $\leq$ -18°C until deep-frozen shipment in boxes with dry ice. The laboratory sample wine at first taste test was stored



Q,

Ľ

for approximately 6 months at 12°C and then stored deep-frozen until preparation of the examination samples. The other laboratory samples were stored in a freezer at  $\leq$ -18°C until preparation of the examination samples where the deep-frozen lab samples were shredded with dry ice in a catter. Representative parts of the shredded lab samples were transferred into polystyrene boxes separately for analysis (examination samples) and archiving (retain samples) and stored for analysis or archiving at s-18°C until analysis.

#### **Processing procedures**

The processing procedures followed industry procedures adapted to esidue studies in small volume The red wine grape specimens were processed into red wine with thish vacuum-expansion of the must Ő

#### Crushing-stemming

The grape specimens were crushed and stemmed with an electric crusher/stemmer. The crushed grapes (= must) were recovered in a stainless steel tank and weight. Two 0. Dkg must subspecimens were collected into plastic bottles, labelled and frozen (2-18°C)

#### Flash vacuum-expansion

With regards to the oxidation, the must was sulphited by addition of potassium netabisulphite at a level of 0.04 g/L. The must volume was estimated by division of the weight of the grapes with a coefficient a) depending on grape variety: 1.3 (for the two trials). 6

The crushed grapes were transported in car at ambient temperature to GJRAD, Montpollier, France for the flash vacuum-expansion. ×, m

The crushed grapes were heated by portions of about 2 kg with water steator at approx. 90°C for 5 min in a steam heating chamber, then decanted quicklein a secure vessel. The first vacuum expanded portion (between 1.649 kg and 1.914 kg) was discarded  $\bigcirc$ 

As the flash vacuum expansion equipments a single exemplar for the trial No 08-3204-01, the untreated specimen was processed Defore the treated specimen with a great cleaning between each specimen to avoid all contamination.

The obtained amount of vacuum expanded mustors dependent on different parameters, notably, the lost during the manipulation and the addition of the injected water steam whill 10% of weight in supplement. When all amount of grapes was wacuute expanded, the obtained must and liquors were grouped together in a standers steel taple and than sported in a car a Cambient temperature at the processing laboratory to start the alcoholic formentation. A

### Alcoholic fermentation

The necessary quantity of otassium metabisupplite was weight and diluted in approx. 10 times its weight in distilled water. The necessary quantity of enzymes was weight and rehydrated in a volume of must equal to 10 times its weight. The accessary quantity of yeast was weight and rehydrated in a sugared water (the mixture equalled 10 times the weight of the yeasts used).

Potassium metabised phite (0.06 g/D), perfolytic enzymes (0.02 g/L) and yeasts (0.10 g/L) were added to the must in the tank and mixed The pH of the Dnust was measured using a pH-meter.

For the trial No@8-3204-01, as the alcohol content estimated from the refractometric degree was judged insufficient toproduce normal quality wine, white crystallised sugar was added. For the control sample (8.2%) and reated sample (8.0%) from 08-3204-01, 34 g/L of sugar were added to the must during alcoholic@ermemation, in order to increase the probable alcohol content of each specimen to 2%. The progress of the alcoholic ferguentation (AF) was followed each working day by measuring the density and temperature of the must. The density and temperature were measured using a mustimeter, which was plunged into a 250-mL measuring cylinder containing the must.

The alcodolic fermentation was considered to be completed when the density of the must was stabilized under the value 1000 (998 for control and treated samples from trial 08-3204-01 and 996 for treated sample from trial 08-3204-02).



#### Pressing

The stainless steel tanks were weighed after alcoholic fermentation. The wine was run off to the tank (free-run wine) end the solid part was pressed with a water press to recover the maximum quantity of wine. The pressed wine was added to the free-run wine and all the wine obtained was weighed. The we pomace obtained was weighed and two 0.1 kg wet pomace sub-specimens were aken and packaged into plastic bags, labelled and frozen (s -180C). The remaining pomace was discarded.

#### Malolactic fermentation

The malolactic fermentation was carried out in absence of air into demijohns, at ambient temperature with a direct inoculation of lactic bacteria: leuconostoc oenos (0.01 gR) to accelerate this process, The wine unused was weighed and discarded.

The progress of the malolactic fermentation was followed-up one or two times each week chromatography on paper. 1

botassium metabis@phite~was added to After the malolactic fermentation was complete, 0.10 g/I wine.

#### Clarification-Cold storage

The natural clarification lasted four days for all speciments. The wine was packed The obtained malolactic fermentation wine and lees were weighed. Lees were discarded. 0.162/L of dry gelatine and 0.04 g/L of potassium metabisulphice were added to obtained wine, to mprove the charification.

The wine was kept into demijohns and stored in a cold room (5-10°C) to be stabilized with regard to tartaric deposits and so that classification could be achieved

To remove impurities (solid material), the wing was racked. The racked wine and sediments were weighed. Sediments were discarded.

#### Filtration

The racked wine was filtered using staintess steef filtration unit with 10 liter capacity under pressure using nitrogen (3 hars magimum) The filtration was carried out over cellulose filter plate of 90 mm dameter and 2.5 µm of porosity. After

this operation, the specimens received 0.40 g/L of potassium metabisulphite, which protects the wine from oxidation.

On the same day, two 0.1 kg red wine sub-spectmens were conflected into plastic bottles, labelled and frozen (≤-18 °C) and two 0.75 I fed wine subspecimens were collected into glass bottles, labelled and



n of the must **BUNCH OF GRAPES (RAC) CRUSHING-STEMMING** Potassium metabisulphite FLASH VACUUM-EXPANSION 90° @ 5 Pectolytic enzymes Potassium metabisulphite Yeasts Sugar COHOLIC FERM (trial No 08-3204-01) SSING Wet pomace X  $\bigcirc$ Lactic bacteria Potassium metable Gelatine + potas ARIFICATION COLD STORAGE ð TION Potassium metabisulphite TTLING Red wine ഹ Red wine *) Samples opfractions to be analysed: -Artust - Wet mace = Pomace, grape RAC = RawAgricultural - Red wine = Wine at bottling Commodity - Red wine *) = Wine at first taste test (kept after bottling at standard wine storage temperature (between ca. 5 and 10°C)

Diagram 6.5.3-9: Flow chart of the red wine processing with flash vacuum-expansion of the must



# **Residue analysis**

Residues of fluopyram and its metabolites were determined by LC-MS/MS according to method. , 2007, M-295145-03-1, see MCA section 4.1.2). Full details and acceptable 00984/M001 ( validation data to support this method are presented within document M-CA 4 which complet with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues were extracted from 10 g of sample material by two successive extractions using blender with a mixture of acetonitrile:water (4:1; v:v).

Subsequently, the raw extracts were diluted 10-fold by adding internal standard solutions:

- One dilution and an additional clean-up stop were performed under ocidic Conditions determination of FLU-PCA
- Another dilution was performed under basic conditions for defermination of fluopfram, benzamide and FLU-PAA

Residues were quantified by reversed-phase Phromatography coupled with tandom mass spectrometry (MS/MS) with electrospray ionisation. One injection infloositive electrospray ionisation allowed the determination of fluopyram, FLU-benzamide and FLU-PAA. Another injection in regative electrospray ionisation allowed the determination of FLU PCA under different conditions.

The quantitation was carried out by Onternal standardization using stable-labeled internal standards in pure solvent.

for fluopyram and its metabolites, all calculated as The Limit of Quantification (LQQ) was 0.01 mg/kg parent equivalents and for all matrices?

Finding

During the course of this study, the method performance was shecked by concurrent recoveries. Details on concurrent recovery that are shown Table 6.5.9- 24 to Table 6.5.3 27. The average recoveries were within the acceptable range of 90 - 110%. If applicable, the RSD values were always below 20%. The overall RSD values where at 22.9% and 28.1% for pust and pomace, grape, respectively.

The levels of residues of fluopy am and its metabolizes in the processed samples are summarized in Table 6.5 2 29. No residues above the LOQ were found in the control samples. The results were not corrected for concurrent recoveries.

The residue level of Pluopyfam in Ounch of grape (RAC for the calculation of the processing factors) was at 0.04 mg/kg in trial 08-2204-02 (processing trial 08-3204-01). The sample 08-2204-03-0003F for processing of trial 08-3204-02 was not receipt at the processing laboratory and a new sample was taken at DALT21. On fortugately to RAC sample taken on DALT 21 is available, and therefore for calculation of the transfer factors, the reside value of the must was used for the RAC value. The must was obtained after crusping and stemping of the bunches of grapes, and therefore residue levels are not expected to differ significantly from those in the RAC. This is also confirmed by the results of trial 08-3204-01, where for all analytes for must the same residue value as for the RAC was found. The residue level of fluopyram in must (RAC for the calculation of the processing factors) was at 0.07 mg/kg in trial 08-3204-02. Residues values of Mapy can ranged from 0.01 to 0.28 mg/kg in processed commodities.

For both meabolites fluggyram-benzaroide and fluopyram-pyridyl-acetic-acid, residue levels were always <0.01 mg/kg with one exception for pomace, grape where residues of fluopyram-benzamide were at 0.02 mg/kg in trial 08-3204002.

For flaopyrate pyrider-carboxylic-acid, residues ranged from <0.01 mg/kg to 0.03 mg/kg.

The processing factors (PF) were calculated based on the residue level in the treated processed commodely and residue level in the RAC specimens (bunch of grape for trial 08-3204-01 and must for trial 08=3204-02). When residues in the RAC and in the processed fractions were both <0.01 mg/kg a processing factor could not be calculated. The proposed processing factors are summarised below in



### Table 6.5.3-28.

The analyses were done after a maximum frozen storage period of 361 days for bunch of grapespand processed commodities.

#### **III.** Conclusions

Two residue trials were conducted in southern Europe in 2008. Grapes were treated twice at growth stage from BBCH 81 to BBCH 85 (pre-harvest interval of 14 days) with a dose rate of 2 x fr g a. state

Bunch of grape samples from red grape varieties were processed in order to obtain red wine. The samples (RAC and processed fraction) were analysed for the residues of the res metabolites FLU-benzamide, FLU-PAA and FLU PCA. The processing study was conducted according

inde the second The results of the study indicate that residues of thopyray and is metholite FLU-benzamide rentain to a large extent in wet pomace after pressing with processing factor at 3.4 apt >2.0, respectively of at 1.0 was found in must for fluopyram and FLUPCA and in wet pomace for FLC-PCA. Residues of fluopyram (PF at 0.34 at bottling and 0.1st taste test) and FDU-PCA (PF 0.84 botting and at 0.84 at 1st taste test) are very low in wine



	Portion		Fortification	Recov	very (%)		, P D
Study	analysed	n	level* (mg/kg)	Individual recoveries	Min	fax Mean	RSD S
08-3204		2	0.01	101; 102	101	02 102 4	F - A
	Grape / must	1	1.0	84	84 8	34 - 🖓	
		3	Overall	Å.	\$84 1	02 396	-1 <u>9.6</u> -1 <u>9.6</u> - 5
	Grape /	2	0.01	<b>96</b> ; 98	96 9	97 0	
	pomace,	1	1.0	83 04	83 8	<u>i</u> j	
	grape	3	Overall		83	8 92	8.8
	Grape / wine	2	0.01	102; 105	102 <b>Q</b> Í	05 <u>0</u> 104 g	) - ¢
	at first taste	1	0.10 🦿	° 103 ° (	s n	08) ×	t de la companya de l
	test	3	Overall O		Ø102 f	05 <u>1</u> 03	A1.5

	Table 6.5.3- 24:	Recovery results for fluopyram in processed commodities into wine
--	------------------	-------------------------------------------------------------------

* some RSDs were not calculated as there were only two individual yecoveries given

1 D. Iorunounon level, R.	SD Relative Standard Deviation		. 🤍		
* some RSDs were not ca	alculated as there were only two	o individual secove	ries/given	A. N	
Final determination as: fl	luopyram Residues calculated a	s; fluopýram			
	<u> </u>			,0° , ()	
T 11 ( 5 2 35				a 0 V	
Table 6.5.3-25:	Recovery results for	' fluøpyram-t	benzamide0	m processed	ommodities into wine
		400 • •			

				4	~ //	(( ))	e.	· ."	5 14 1	
Study	Portion analysed	n Ø	Rortification level* (mg/kg)	Individ	lual recor	Recove	er 0(% Min		`~> ∳Yean	RSD
08-3204		2	× 0.005	Ó (	067; 72 ^{**}	- A	67	72	70	-
	Grape / musť 🕉	1	0.30		104	К ^и	<u>J</u> Ø1	161	-	-
	2	<i>S</i>	Øverall O	- A		y w	67 📎	<b>91</b> 01	80	22.9
	Grape	2	S 0.00		67; 67	O,	67\$	67	67	-
	Domase ()	1	0.50	\$ \$	1005	\$ \$	<b>A</b> Ø6	106	-	-
	grape	3	Qverall		à.	4 1 1	v [×] 67	106	80	28.1
	Grape Øwine *	$\sqrt{2}$	0.005		77;80	L.	77	87	82	-
		1 🗶			100	Ø	100	100	-	-
E S	test O	ð	Overall	. 0	Ĵ, Ĵ	)*	77	100	88	13.1

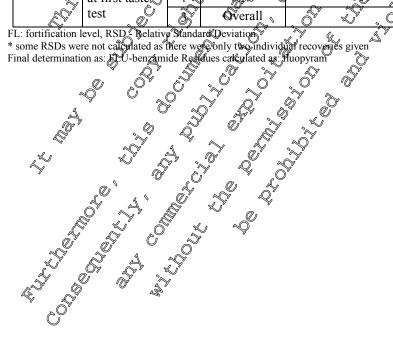




Table 6.5.3- 26:	Recovery results for fluopyram-pyridyl-acetic acid in processed commod	lities
	into wine	a,°

	Portion		Fortification	Recov		
Study analysed		n	level* (mg/kg)	Individual recoveries	Min	
08-3204		2	0.007	93; 93	93 ^{°O} 93	93
	Grape / must	1	0.70	105	105 105	
		3	Overall		93 105	97 7.1 0
	Grape /	2	0.007	83; 97	83 97	90,57 - 67 , 67
	pomace,	1	0.70	3 ⁰ 93 ⁵	°93 Ø	
	grape	3	Overall		83 🖉 97	6 ⁹ 91 7.9
	Grape / wine	2	0.007	₀88; 1 <b>00</b> ×	88 109	994 -
	at first taste	1	0.70 🔘		J10 190	
	test	3	Overalk		88 110	Ö102 Ö12.1

					6. V A	- V	4		A R	
F	L: fortification l	evel, RSD - Relativ	e Standard I	Deviation 🖉 😞			A	. O ^v 🐇		Ŕ
*	some RSDs we	re not calculated as	there were o	only two individu	al recovories	given	No.	N C	×,	L.
F	inal determination	on as: FLU-PAA Re	esidues calc	ulated as: fluxpyr	am 🗶	Å 4		S. O'	Ş	$\odot$
				Ň Y	~~~ .	~~ ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Ž v		, a	
			1	S O	× *	v N	×		Ş. 41	
		<b>AF</b> D	- Ç	) A o Com ()	» »		.0.	õ. õ	°~.	
	Table 6.5.3-	27: Recove	ry resul	ts for fluopy	ram-pyr	idy-eart	<b>exylic</b>	scid in Dro	cessed	
		commo	dities in	tôwine	O ^v	L h	S .	° Or	×	
			1.2	″ ∧(>		<i>"</i>	" (h		V	

	Portion	×)'	Fortification level*	d o A	Recovery	(%) (	2	
Study	Portion	À	level* (mg/kg)	Individual recov		Iin Max	Mean	RSD
08-3204	Graper must	Ĩ.	~0.006			34 103	94	-
	Grape must	/ 1 👡	03 0 <i>3</i> 0	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		08 108	-	-
		3≪∕	Qverall		¢, ⁽ )	34 108	98	12.9
		, O2	00.006	A 298; 106 S		08 106	102	-
<i>D</i>	Grape / 5 s	¹	\$ 0 <u>,6</u> 0 ~	y % 113	× 1	13 113	-	-
In all and a second sec	grape	20	Querall		× 9	08 113	106	7.1
K.	Grape / wine	Ż	ر 0.00¢¢	98; 10 <b>3</b>	9	08 103	101	-
	at first taste	¥ 1	\$ 0.60	103	1	03 103	-	-
	test	the second	Qverall 📈		9	08 103	101	2.8

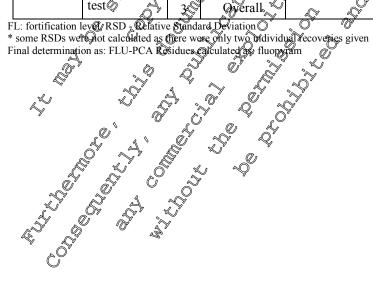


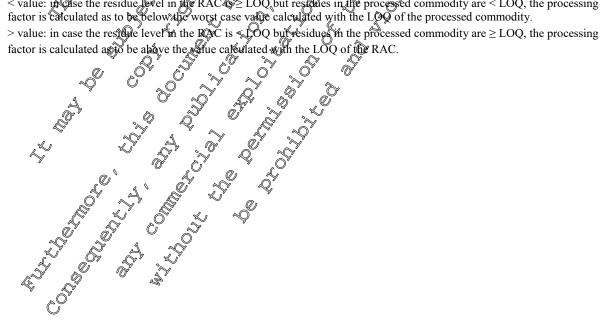


Table 6.5.3- 28:	Summary of residues in grape and proposed processing factors for fluopyram and its	5
	metabolites for grape (Tested GAP: 2 × 50 g a.s./ha at BBCH from 81 to 85)	,

					ia at BBCH fro	
Trial	08-320	04-01	08-32	04-02	Proposed	
Sample material	Residues (mg/kg)	PF	Residues (mg/kg)	PF	PF (mean, if applicable	
Fluopyram					$\mathcal{O}_{\lambda}$	
Bunch of grapes (RAC)	0.04	-	0.09		A.	
Must	0.04	1.0	0.07	م 1.0	.K0″	
Pomace, grape	0.11	2.8	0.28	4.0	Ø3.4	
Wine at bottling	0.01	0.25	0.03	♥ 0.43	Q 0.34	
Wine at 1 st taste test	0.01	0.25	0.03	0.43	0.34	
Fluopyram-benzamide			4	Ą		
Bunch of grapes (RAC)	< 0.01	-	.01	~>>		
Must	< 0.01	n.c	° رۆلەكەرچى «	li je	$\begin{array}{c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & & \\ & & & & \\ & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & $	
Pomace, grape	< 0.01	n.c	O″0.022°	2.0	× 20.0 m	í de la comercia de l
Wine at bottling	< 0.01	n.c 🔬	<0,01	0 n.c Q	n.c 🔊	ON DY AN
Wine at 1 st taste test	< 0.01	n.¢	× \$0.01	n n n n n n n		
Fluopyram-pyridyl-car	boxylic-acid	I 🔊 ,	°~".©"	. 4		
Bunch of grapes (RAC)	0.01	<u> </u>	0,02	~~-~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		
Must	0.01	C 1.0 ~	10.03	V 1.0	<u>مَنْ 1.0 مَنْ الْمَنْ /u>	
Pomace, grape	0.01 🖉	1.0	ു 0.03 🏷	1.0 0,67	2 ^{1.0} 2 ⁵ 0 1.0	
Wine at bottling	<0.0	. <b>≪J</b> .0	© 0.02 0.02	@.67	<0.84	P &
Wine at 1st taste test	0.01	~~~1.0 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.02	1,0° 0,67 ~0.67 ©	§ @9.84	
Fluopyram-pyridyl-ace	tic-acid	×1.0	×0.01	y 🍫		Ô
Bunch of grapes (RAC)	°\$0.01 ℃	ŝ	~0.01	≺		$\mathcal{Q}^{*}$
Must	₹<0.04	n.c	P. < 0, 00/	n.c 🥼		r
Pomace, grape	/ <0,01	n.c	<0,001	≫ n.c 🔊	$ \begin{array}{c}     \text{I.c} \\                                    $	
Pomace, grape       Wine at bottling	_<0.01 🖏		<u>گ</u> 0.01 ک	nc	[∪] _{n.c} [~] ∀	
Wine at 1st taste test	€0.01	shič i	<0.01°	()).C	n 🖉	

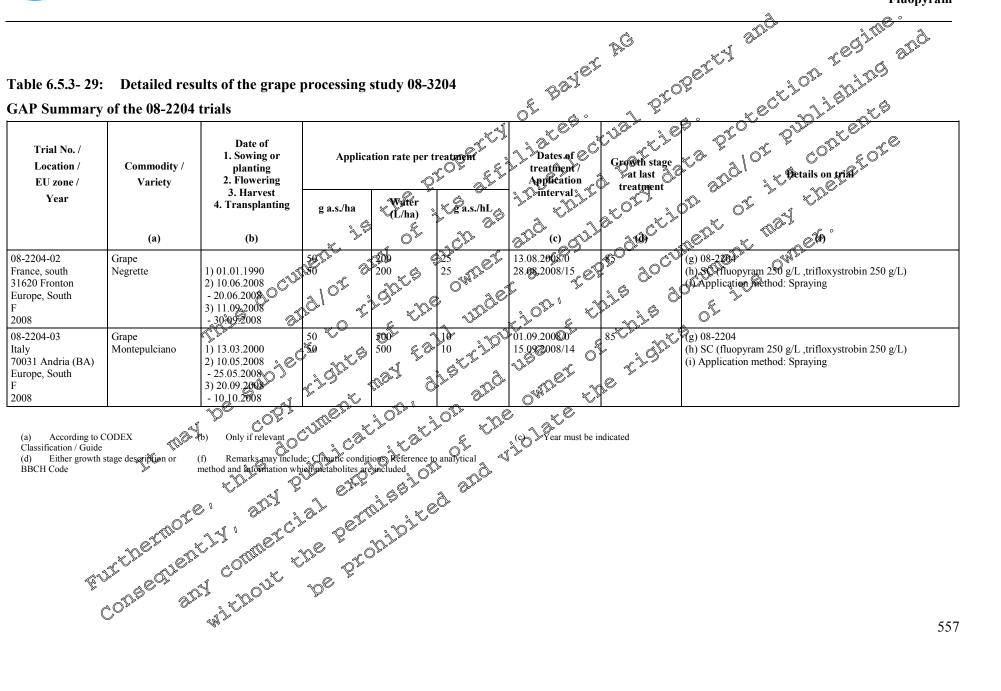
Notes: for trial 08 3204-02, since no RAC (Raw Agricultural Commodity) sample with DALT 21 is available, the residue value of the must was taken as the RAG value for calculation of the transfer factor. PF (processing factor) = residue concentration in processed commodity (mg/kg) / residue concentration in the RAC (mg/kg) n.c: no processing factor can be calculated (residues <LOD in RAC and in processed commodity)

< value: in the residue level in the RAC  $S \ge LOQ$  but restricts in the processed commodity are < LOQ, the processing factor is calculated as to be below the worst case value calculated with the LOQ of the processed commodity.



BAYER

Page 557 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram



BAYER E R Page 558 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

											<u> </u>
							AC BC		C.C.J. OLOC	regit	and and
Trial No. / Location / EU zone / Year	Commodity / Variety (a)	Portion analyzed	Growth stage at sampling (d)	fluopyram as fluopyram	Resi FLU- benzamice	FLU-pxridyl- carboxylic-acid	FIC-pyridyl- neetic acid as flugpyram		rty and protect	Details on trial Details on trial Details on trial CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f) CO(f	59 5 ⁹
08-2204-02 France, south 31620 Fronton Europe, South F 2008	Grape Negrette	Processing into wir most pomace, grape wine, bottled	2110 E D. C. 2110 E D. C. 0 Prial 08-33 89 5 0 05 8	04-01) 0.04 ©11	<0.01 j + 1 g u C U 0 M D 20 U <0 M D 20 U <0 M D 20 U 20 U			0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	(g) 08-3204 (i) Analytical meth (k) LOQ: 0.01 mg (i) Method Varda (m) Storage: wine Dottled: 268 wine at first taset pomace grape: 33 must 304 days gunch of grapes: 3	0 days	001
		WIL -									558

BAYER

Page 559 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram A

									2	°
							PG		STA SIDE	reginne and
Trial No. / Location /	Commodity / Variety	Deutien en elected	Growth stage at sampling		Resi	dues (mg/kg)	ALC'T	PHQ [©] (days)		Details of Prisit
EU zone / Year	(a)	Portion analyzed	(d)	fluopyram as fluopyram	FLU- benzamide as fluopy@m	ELU-pyridyl- earboxylic acto as floopyram	FLU-pyridyl- aceix acid as theopyram	× '> (e)	PTOT P	LOR EDV
08-2204-03 Italy 70031 Andria (BA) Europe, South F 2008	Grape Montepulciano	bunch of grapes	89	0.09 2 5 0 2 6 0 2 6 0		Elle J. D. E. B. B. D. C. E. E. E. E.	2001 DEC	Ctilon Ctilon	<ul> <li>Analytical pactor</li> <li>Analytical pactor</li> <li>LOQ (0.01 mg/k)</li> <li>(1) McBod Validati</li> <li>(1) McBod Validati</li> <li>(1) Storage:</li> <li>(1) McBod Validati</li> <li>(2) Wine, bottled:</li> <li>(2) Storage:</li> <li>(2) Wine, bottled:</li> <li>(2) Storage:</li> <li>(2) Storage:</li> <li>(3) Storage:</li> <li>(4) Storage:</li> <li>(5) Storage:</li> <li>(4) Storage:</li> <li>(5) Storage:</li> <li>(1) McBod Validati</li> <li>(1) McBod Validati</li> <li>(2) Storage:</li> <li>(3) Storage:</li> <li>(4) Storage:</li> <li>(4) Storage:</li> <li>(5) Storage:</li> <li>(5) Storage:</li> <li>(5) Storage:</li> <li>(5) Storage:</li> <li>(6) Storage:</li> <li>(7) Storage:</li> <li>(8) Storage:</li> <li>(9) Storage:</li> <li>(1) Storage:</li> <li>(1) Storage:</li> <li>(2) Storage:</li> <li>(3) Storage:</li> <li>(4) Storage:</li> <li>(5) Storage:</li> <li>(5) Storage:</li> <li>(6) Storage:</li> <li>(7) Storage:</li> <li>(7) Storage:</li> <li>(8) Storage:</li> <li>(9) Storage:</li> <li>(9) Storage:</li> <li>(9) Storage:</li> <li>(9) Storage:</li> <li>(9) Storage:</li> <li>(1) Storage:</li> <li>(1) Storage:</li> <li>(1) Storage:</li> <li>(2) Storage:</li> <li>(3) Storage:</li> <li>(4) Storage:</li> <li>(5) Storage:</li> <li>(4) Storage:</li> <li>(5) Storage:</li> <li>(5) Storage:</li> <li>(6) Storage:</li> <li>(7) Storage:</li> <li>(7) Storage:</li> <li>(8) Storage:</li> <li>(9) Storage:</li> <li>(9) Storage:</li> <li>(1) Storage:</li> <li>(1) Storage:</li> <li>(1) Storage:</li> <li>(1) Storage:</li> <li>(2) Storage:</li> <li>(3) Storage:</li> <li>(4) Storage:</li> <li>(5) Storage:</li> <li>(6) Storage:</li> <li>(7) Storage:</li> <li>(7) Storage:</li> <li>(7) Storage:</li> <li>(8) Storage:</li> <li>(8</li></ul>	d: 009800001 g Data: : 00984/M001 ays Vine at first taste test: 98 days, Go's, must: 335 days 3 days
		Processifie into win	CFrial 08-32		2400 240 240 21000	der x zon		<u> </u>	* sample for proces 320402 was not rec a new sample was ta	ceipt at the processing laboratory and
		pomace, grape wine, bottled wine at first taste	89 V C 89 V 89 V	0.07 0.07 0.03 0.06 0.03	<0.01 × 0.02 × <0.01 × <0.01 ×		<0.01 <0.05 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	21* 21* 21* 21*		
(a) According to CC Guide	DEX Classification /	(e) Days afte		(Label pre-harves	stemerval, PHI, ur	terrine) (lfb)	Formulation type	()	od validation	
<ul><li>(b) Only if relevant</li><li>(c) Year must be incomented in the incomentation of the</li></ul>	licated I	(I) Remarks method and information	on which metabo	litegate included	O ^D		Application method Method	Bunch of gra	ge (max) pes: between deep-freez	
(d) Either growth sta Code G greenhouse	age description or BBC	H (g) Study fefa	erence C st treatment		o data data data data data data data dat	inform (k) **	LOQ residue in control	Processed co	and date of last extraction mmodities: between the g and date of last extract	ir
Ē.	irthermo	nonse, grape wine, bottled wine at first have test (c) Ibuys afte (f) Remark method and H (g) Study of provide and to office and the state of the state	the period	5. 7. 0. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1.	~					
(C	J [~]	W L								5



Data Point:	KCA 6.5.3/13
Report Author:	
Report Year:	2012
Report Title:	Processing Study - Determination of the residues of AE C636948 and feather amido in/on grape and the processed fractions (must; pomace, grape; wine at bottling and wine at first taste test) after low-volume spraying of Fluopyram SC 560 and Fenhexamid WG 50 in the field in France (south)
Report No:	
Document No:	<u>M-440382-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/#14/EEC of July 15, 1991, Amer II, part A, print 6
study:	and Annex III, part A, section 8; Residues ioor on Treated Products, Food and Feed; EC Guidance working document 7029/VI/95 rev.5 (1997-07-22); EC Guidance working document 7035/VI/95 rev.5 (1997-07-22)
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes & O Y & Y & Y & Y

J. Materials and Methods The study included two supervised tesidue trial with grape, conducted in the field in southern Europe (southern France) in the 2009 season. The purpose of this study was to determine the magnitude of the residues of fluopyram and its metabolites fluopyram-benzarrade (AE F14\$815, alias FLU-benzamide), fluopyram-pyrid acetic acid (BCS AA10139, alias FLU-PAA) and fluopyram-pyridyl-carboxylic acid (AE C657188 alias FEU-PCA) in/on grape (bunch of grapes) and its processed fractions of wine (must, pomace, wine at bottling and wine at first taste test).

# Field part

In field trial 09-2240-01-T?, the weated plot was sprayed once at BBCH growth stage 67 (70% of flowerhoods faller with fenhex mid WG 50, water dispersible granules formulation and 60 days later once at BBCH \$1 (beginning of ripening; berries begin to develop variety-specific colour) with fluopyram SC \$00, a Suspersion concentrate (SC) formulation containing 500 g/L fluopyram. In field trial 09-2240-01-T2, the treated plot was prayed once at BBCH growth stage 67 with fluopyram SC 500 and 60 days later once at BBCH 81 with fembexand WG 50. The application rates were 300 g a.s. fluopyran/ha using a spray volume of 200 Sha. All treatments were made at the scheduled rates.

Bunch of grape samples were taken 49 days after the last treatment at BBCH 89 (last treatment was done with fluopyram on trial - 1 and with fenhexand on trial -T2).

Samples for processing were hipped to processing laboratory in fresh conditions and then were stored deep frozen until processing.

After processing the processed samples (except "wine at first taste test") were stored at  $\leq$  -18°C in a freezer at the processing laboratory until shipment to laboratory logistics in Lyon (France) either deepfrozen in polystyrene boxes with dry ice or by courier at ambient temperature (wine at first taste test). Than, samples were transported deep-frozen or fresh (wine at first taste test) to the laboratory for preparation of the examination samples.

# Processing procedures



The processing study simulated industrial practice at a laboratory scale. The red wine grape specimens were processed into red wine with flash vacuum-expansion of the must according to the standard operating procedures in use in the processing laboratory.

#### Crushing-stemming

The grape specimens were crushed and stemmed with an electric crusher/stemmer. The crushed grapes (= must) were recovered in a stainless steel tank and weight. Two 0.1 kg must sub-speciments were collected into plastic bottles, labelled and frozen ( $\leq$ -18°C)

#### Flash vacuum-expansion

With regards to the oxidation, the must was sulphited by addition of potassium metabisulphite  $a^{1}$  le of 0.04 g/L. The must volume was estimated by digrsion of the weight of the grapes with a coefficient depending on grape variety: 1.4. Ø

The crushed grapes were transported in car at ambients temperature to CIRAD, Montpellier, France for the flash vacuum-expansion. Õ

The crushed grapes were heated by portions of about 2 kg with water steam at approx 90° Cofor 5 prin in a steam heating chamber, then decanted quickly in a vacuum vesset As the flash vacuum expansion equipment is a single exemplar, the untreated specimen was processed before the preated specimens with a great cleaning between each specimer to avoid all contamination and for each specimer, approximately 1 kg of crushed grapes was vacuum expanded and discarded. The obtained amount of vacuum expanded must is dependent on different parameters, notably, the lost during the manipulation and the addition of the injected water steam until 19% of weight in supplement. When all amount of grapes was vacuum expanded, the obtained must and liquors were grouped together in a staffless steel tank and transported in a car at ambient temperature at the processing aboratory to start the alcolodic fermentation.

### Alcoholic fermentation

The necessary quantity of potassium metabisulphite was weight an diluted in approx. 10 times its weight in distilled water. The necessary quantity of eroymes was weight and rehydrated in a volume of must equal to 10 mes its weight. The necessary quantity of yeast was weight and rehydrated in a sugared water (the mixture equalled H) times the weight of the yeasts used).

Potassium metabisum hite (0.06 g/L), pectolytic enzymes (0.02 g/L) and yeasts (0.10 g/L) were added to the must in the tank and taixed The phof the must was measured using a pH-meter.

The progress of the alcoholic fermentation (AF) was followed each working day by measuring the density and temperature of the must. The density and temperature were measured using a mustimeter, which was plunged into a 250-ml measuring a linde Containing the must.

The alcoholic fermentation was considered to be completed when the density of the must was stabilized under the value 1000 093 for control sample and 094 for treated samples -T1 and -T2).

### Pressing A

The stainless steel tanks were weighed after alcoholic fermentation. The wine was run off to the tank (free-run wine) and the solid part was pressed with a water press to recover the maximum quantity of wine The pressed wine was added to the free in wine and all the wine obtained was weighed. The wet pomace obtained was weighed and two 0.1 key wet pomace sub-specimens were taken and packaged into plastic bags, labelled and frozen ( $\leq 18^{\circ}$ C). The remaining pomace was discarded.

# Malolactic Vermentation

The matolactic fermentation was carried out in absence of air into demijohns, at ambient temperature with a direct proculation of lactic bacteria: leuconostoc oenos (0.01 g/L) to accelerate this process. The wine unused was weighed and discarded.

The progress of the malolactic fermentation was followed-up one or two times each week by chromatography on paper.

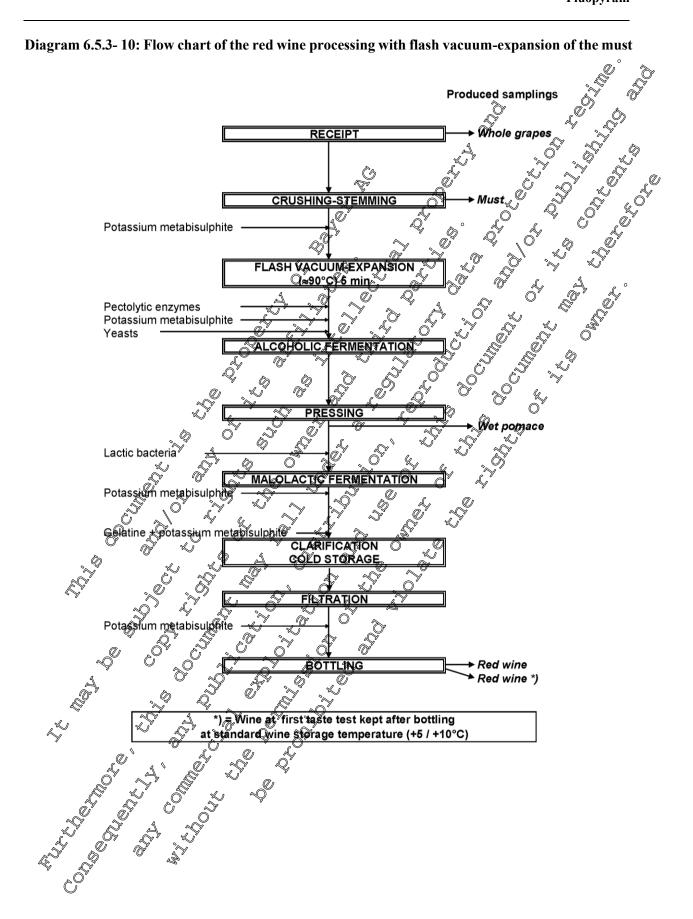
After the malolactic fermentation was complete, 0.10 g/L of potassium metabisulphite was added to wine.



### Clarification-Cold storage

The natural clarification lasted four days for control sample and treated sample -T1 and five days for treated sample -T2. The wine was racked. The obtained malolactic fermentation wine and less were weighed. Lees were discarded. 0.10 g/L of dry gelatine and 0.04 g/L of potassium metabisulphite were added to obtained wine, to improve the clarification. The wine was kept into demijohns and stored in a cold room (5-10°C) to be stabilized with regar tartaric deposits and so that clarification could be achieved. To remove impurities (solid material), the wine was recked. The racked wine and sediment e de la companya de l weighed. Sediments were discarded. Filtration The racked wine was filtered using a stainless steep filtration unit with \$10 liter capacity under pressure using nitrogen (3 bars maximum). Filter equipment was used for control and treated samples. After rom oxidation. The filtration was carried out over cellulose filter place of 90 mm diameter and 20 µm of porosity. After this operation, the specimens received 0.1 (g/L of potas frum metabisulphite, which protects the spine





#### Diagram 6.5.3-10: Flow chart of the red wine processing with flash vacuum-expansion of the must



# **Residue analysis**

Residues of fluopyram in/on plant material were determined by HPLC-MS/MS according to BCS method 01207 based on the QuEChERS multi-residue method (S., 11/12/2013, M-424756) 02-1, see section MCA 4.1.2).

Analytical method BCS 01207 is based on the QuEChERS multi-residue method. Extraction of residues was done with acetonitrile/water (4/1, v/v) by shaking. The residues of fluoryram, FLU-benzamide and FLU-PCA were extracted together but separately to FLU-PAA.

An aliquot of the extracts was taken, and stable-labelled internal standards were added excepted for FLU-PAA where the stable-labelled internal standard was added at the beginning of the extraction procedure. The final extracts were subjected to LC-MS/MS. The quantification was performed by internal standardization using stable-labelled internal standards in pure solvent for fluodyram FLU-benzanide and FLU-PCA. The quantification was performed with matrix matched standards with internal standard for FLU-PAA.

The Limit of Quantification (LOQ) was 0.01 mg/kg for fluopyran and its metabolites all calculated as parent equivalents and for all matrices.

During the course of this study, the method performance was checked by concurrent recoveries. Details on concurrent recovery data are shown in Table 6.5.3-30 to Table 6.5.3-33.

No average recovery or RSD value can be calculated. The overall average recoveries  $(2 \le n \le 3)$  were within the acceptable range of 70 = 110% with one overall RSD value below 20%

The levels of residues of fluop ram and its metabolites in the processed samples are summarized in Table 6.5.3-35. No residue above the LOQ were found in the control samples. The results were not corrected for concurrent recoveries

The residue level of fluopyrant in bunch of grape (RAC for the calculation of the processing factors) ranged from 0.02 mg/kg (trial 09-2240-01-72) to 0.16 mg/kg (trial 09-2240-01-T1). Residues values of fluopyram ranged from <0.01 to 0.46 mg/kg in processed combodities.

For all metabolites, residues levels were always <0.01 mg/kg/with the exception for wet pomace where residues of FLU-pyridy-carboxylic-acid were at the LOQ level (0.01 mg/kg) in trial 09-3240-01-T1.

The processing factors (PF) were calcolated based on the residue level in the treated processed commodity and residue level in the RAC specificens (banch of grape). When residues in the RAC and in the processed fractions were both <0.00 mg/kg a processing factor could not be calculated. The proposed processing factors are summarised below in Table 6.5.3-34.

The analyses were done after a maximum frozen storage period of 527 days for bunch of grapes and 818 days for processed commodities.

Two residue totals were conducted in southern Europe in 2009. Grapes were treated once with fluopyram SC 500 at a growth stage BBCH 67 or BBCH 81 with a dose rate at 1 x 300 g a.s./ha. All applications were at the required rates.

Bunch of grape samples from red grape varieties were processed in order to obtain red wine. The samples (RAC and processed fraction) were analysed for the residues of fluopyram parent compound and its metabolites FLU-benzamide, FLU-PAA and FLU-PCA. The processing study was conducted according to GLP.



The results of the study indicate that residues of fluopyram remain to a large extent in wet pomace after pressing with processing factor at 4.5. PF at 1.0 was found in must for fluopyram and in wet pomace, for FLU-PCA.

Assessment and conclusion by applicant: The study is acceptable.

N N Table 6.5.3-30: Recovery results for fluopyram in processed commodities in the

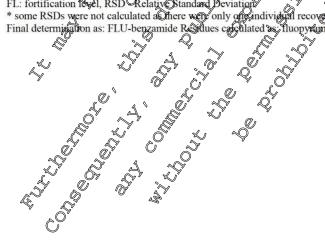
Study	Portion analysed	n	Fortification level* (mg/kg) (	^o Individual recoveries		Max Me	An RSD	
09-3240	Grape / must,	1	0.01		110	10 8-	-	4
	wine, wine at	1	0.1	. 0 . 86 . 9	80	- 00	0'-~	r" ôf
	1 st taste test	2	Overall		80 .	199 <b>98</b> 109 <b>5</b> -	' <u>k</u>	
		1	<b>B</b> 01 &	2 109 × 109 ×	P109	109 0-	Ş -	Õ
	Grape /	1	L ⁰ 0.1	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	1000 1 09	1005 -		
	pomace	1	Q 05	3 3.99 8	09		°∼γ	
		3	Qverall			109 210		

FL: fortification level, RSD - Relative Standard Deviation * some RSDs were not calculated as there were buly one individual recoverie given Final determination as: fluopyram Relatues calculated as fluopyram Ì

Ø Receivery results for fluopyran benzamide in processed commodities into wine Table 6.5.3-31:

Study	Portion O	n (	Portification level*	& recoveries	Min	(%) Max	Mean	RSD
09-3240	Grape must,	1	0.01	\$ \$02 0	192	102	8 <b>-</b> 8	4
	wine, wine at	1%	y fin C		76	76	2 <b>3</b> 40	-
	1 st taste test	J.S.			76	102	89	
	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	1	$\sim 0.0 \mathcal{V}$	¢r %92 ↔	92	92	25.75	-
	Grape pontace	100	Overall	74.0	74	74	8 9	-
		Ì	overally	, ⁶ ⁶	74	92	83	-

FL: fortification Rel, RSD Relative Standard Deviation * some RSDs were not calculated a Dinere way only any individual recoveries given Final determination as: FLU-benzamide Residues calculated as: fluopykun





Recovery results for fluopyram-pyridyl-acetic acid in processed commodities Table 6.5.3- 32: into wine \hat{a}

	Portion		Fortification	I	Recovery	(%)			
Study	analysed	n	level (mg/kg)	Individual recoveries	Min	Max	Mean	RSD	
09-3240	Grape / must,	1	0.01	81	81	81	-	Ţ.	
	wine, wine at	1	0.1	73	73	\$73	- ,	≫- `	
	1 st taste test	2	Overall	₩.	730	81	77		
		1	0.01	<u>بر</u> 70	, ÎN	70	Č.	Ĩ,	
	Grape / pomace	1	0.1	م لاً '70	ر 10 ک	。70	<u></u>	<u> </u>	
	poniaco	2	Overall		76	°70 🖗	700	- 0	

FL: fortification level, RSD - Relative Standard Deviation

* some RSDs were not calculated as there were only one individual recoveres given Final determination as: FLU-PAA Residues calculated as: fluop ram

Ø

Table 6.5.3-33: Recovery results for Huopyram-pyridyl carboxylic acid in processed commodities into whe ~ .\$ Ø \bigcirc

				~ <u>~</u>	. 7	Ŵ	Ĩ	~	Ŭ Å	Ş
Study	Portion analysed	n	Fortification Q level (mg/kg)		lividuat	»″	0	(%) (%) (%)	Mean	RSD
09-3240	Grape / must, wine, wine at 1 st taste test »		0.01 0.15 Overall	Ő.	81 ⁵ / 183	- L L	810 810 81	81 83	- 0 \$2 \$2	-
	Grape / S		× 0.01	ð	83 384 0	0	83 84	83× 84	-	-
		2	V Overall			Ô	83 🔊	8 4	84	-

FL: fortification level KSD - Relative Standard Deviation * some RSDs were not calculated as there were only ona natividual recoverie Driven Final determination as: FLVOPCA Residues calculated as: fluopyram L.

Summary of residues in grape and proposed processing factors for fluopyram Table 6.5.3-34: and its metabolites for grape ~0

1 ested GAP: 1 × 300 g a.s./na at BBCH 50 (-12) or 81 (-11)										
Trial	0993240	-01-T1 🔊	09+3240	-01-T2	Proposed					
Sample material	Residues (mg/kg)		Residues (mg/kg)	PF	PF (mean if applicable)					
Fluopyram	? Q									
Bunch of grapes (RAC)	0 .16	> -	<u>∘_0.02</u>							
Must	~0.09°~	0,06	% 0.03	1.5	1.0					
Pomace, grape	0° 0.46	2.9	0.12	6.0	4.5					
Wine at bottling	0,05	© 0.31 Q	0.01	0.50	0.41					
Wine at 1st tage test	9 .03	0.19	< 0.01	< 0.50	< 0.35					
Fluopyram benzamide*	Ó ×	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~								
Bunch of grapes (RAC)	U <0,000		< 0.01							
Must A A	\$9 .01	n.c	< 0.01	n.c	n.c					
Pomace, grape	°~~0.01	n.c	< 0.01	n.c	n.c					
Wine at bottling	<0.01	n.c	< 0.01	n.c	n.c					
Wine at Q st taste test	< 0.01	n.c	< 0.01	n.c	n.c					
Fluopyram-pyridyl-car	boxylic-acid	*								
Bunch of grapes (RAC)	0.01		< 0.01							
Must	< 0.01	<1.0	< 0.01	n.c	<1.0					

'	Tested GAP:	1 × 3	Øg	a. <u>s</u> /ha	at BB	CH ₂ 67	(-T2) or	81 ((-11)	6	

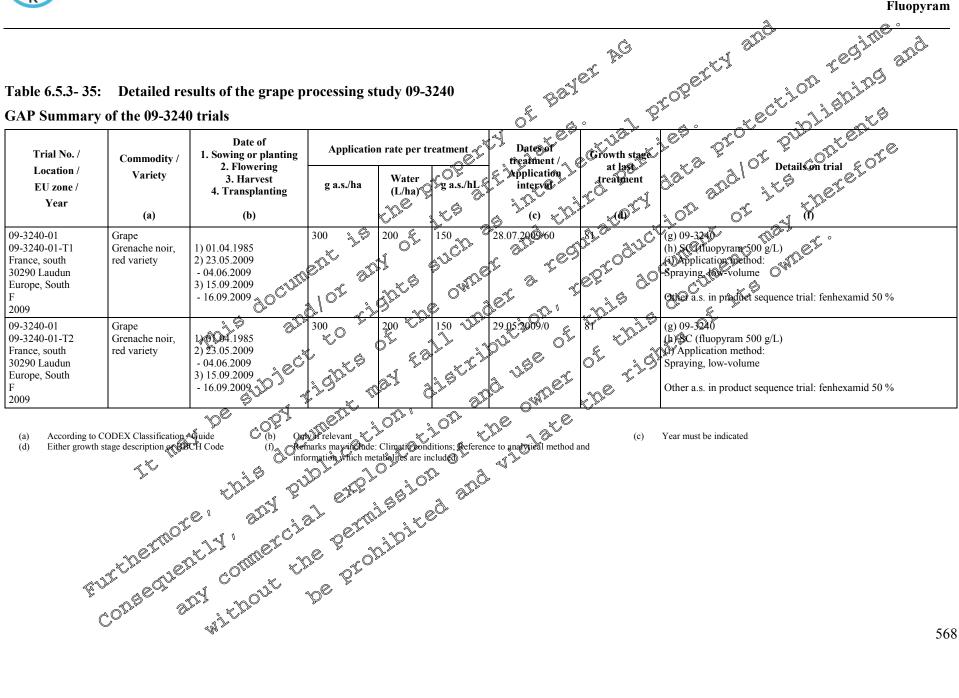


Trial	09-3240	-01-T1	09-3240	-01-T2	Proposed	
Sample material	Residues (mg/kg)	PF	Residues (mg/kg)	PF	PF (mean if applicable)	
Pomace, grape	0.01	1.0	< 0.01	n.c	1.0	S' . '0'
Wine at bottling	< 0.01	<1.0	< 0.01	n.c	<1.0 <1.0 <1.0	
Wine at 1 st taste test	< 0.01	<1.0	< 0.01	n.c	<1.0 0°	
Fluopyram-pyridyl-ace	tic-acid*				A	
Bunch of grapes (RAC)	< 0.01		< 0.01	õa	Ĩ	
Must	< 0.01	n.c	<0.01	n.c	@n.c	
Pomace, grape	< 0.01	n.c	< 0.01	n.c	or n.c	
Wine at bottling	< 0.01	n.c	<0.0	n.c	n.c	
Wine at 1 st taste test	< 0.01	n.c		n.c	P gn.c P	
expressed as parent compou	nd		Qn .	\sim		

I write at 1 a site test <u>10.01</u> n.c <u>10.43</u> n.c <u>10.65</u> and <u>10.05</u> and <u>10.0</u> PF (processing factor) = residue concentration in processed commodity (mg/g) / residue concentration in the RAC (mg/g)

BAYER

Page 568 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram



BAYER

Page 569 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram 4

										2		@ °
							.16	sr BG		erti anos	regji	19 July
Trial No. / Location / EU zone /	Commodity /Variety	Portion analyzed	Growth stage at sampling	fluopyram as	FLU-	sidues (mg/kg)	BOS .		(days)	orotect		çů e
Year	(a)		(d)	fluopyram	benzamide as fluopyram	arboxylic-acid fluopyram	as ace	tic acid as	¢ [™] (e)	12 × 102	COM St	
09-3240-01 09-3240-01-T1	Grape Grenache noir,	bunch of grapes	89	0.16	<0.01	0.01	0.01	rê ^y	490-00-	(g) 09 3240	2 ~~~~	
France, south 30290 Laudun	red variety	must	89		Q.01 . K	\$0.01 J.**	6807	" tot	49,0	(1) Method Validation	E Pr	
Europe, South F 2009		pomace, grape	89	0.46 D	<001	1000 a.B. O.D.C.		J. or Oli	C49	(m) Storage: (m) Gene at first taste test: wine at bothing: 756 d		
		wine at bottling wine at first	89 RECULTURE	0.05 J.D.	<0.01 9 9 9001 0		<0.01 <0.01	e ^{qt} i		pomere, grape: 800 da must: 818 days bunch of grapes: 478 d	ys	
			J. OF Jun					this .	~	- 4		
09-3240-01 09-3240-01-T2 France, south	Grape Grenache noir, red variety	bunch of grapes must	89 July 89		<0.0¥ <0.0¢ @	<0,01 5 5 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6	<0201	4 10		(g) 09-3240 (j) Analytical method: (k) LOQ: 0.01 mg/kg		
30290 Laudun Europe, South F		pomace, grape Ø		GI2 TU	10.01 0 2 C	-0.01 -0.01	60.01	N.C JA	49	(l) Method Validation (m) Storage: wine at first taste test:	580 days	
2009		wine at bottling	8994 .0994	OCAT 1	0 ¹⁰⁰¹ 101		<0.01	C.p.	49	wine at bottling: 756 d pomace, grape: 805 da must: 818 days	ys	
	TT.	whene at first taste test		<0.01	<0.01	£ ^{0.0}	<0.01		49	bunch of grapes: 478 d	ays	
(a) According to 0(b) Only if relevant	CODEX Classificatio	n / Guide	Days attendast a Remarks may in	application abel nclude Elimatic co	pre-havest interva	al Pft underline)	(h) H (i) A	Formulation typ Application met		Method validation) Storage (max)		
 (c) Year must be i (d) Either growth Code G greenhouse 	CODEX Classification ndicated stage description of the the the finance of the	BCH (g)	Study ration to Study rate and prior to fast trea	th metabolic Sand	no data a	vailable	(k) I	Method inform LOQ residue in contro	Pro	nch of grapes: between deep occessed commodities: betwe		
E	JIT VE GUE	ant com	o ^{ut} y	e Pr								
(W. L.										569



Data Point:	KCA 6.5.3/14
Report Author:	
Report Year:	2014
Report Title:	Determination of the residues of AE C656948 and fenhexation in/on grap and the processed fractions (champagne) after praying of fluopy and SC 500 and fenhexamid WG 50 in the field in France (north)
Report No:	09-3242
Document No:	<u>M-485016-01-1</u> (2) (2) (2) (2) (2) (2) (2) (2) (2) (2)
Guideline(s) followed in	EU-Ref: Council Directive 91/41 EEC of July 5, 1991,
study:	Annex II, part A, section 6 and Annex III, parOA, section 8 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
	Residues in or on Treated Products, Food and Feed
Deviations from current test guideline:	none (2)
Previous evaluation:	yes, evaluated and accepted Yes, conducted and a CP/Officially recognised testing facilities
GLP/Officially recognised	Yes, conducted and er GDP/Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes Q Q Q Q Q Q Q

I. Materials and Methods

The study included two supervised residue trial with grape, conducted in the field in northern Europe (northern France) in the 2009 season. The purpose of this study was to determine the magnitude of the residues of fluopyram and its metabolites fluopyram benzamide (AE F448815, alias FLU-benzamide), fluopyram-pyridyl-acetic acid (BCS-AA10139, abras FLU-PAA) and fluopyram-pyridyl-carboxylic acid (AE C657188, alias FLU-PCA) in on grape (bunch of grapes) and its processed fractions of champagne (after botting and after maturation).

<u>Field part</u>

In field trial 09-2242-04-T1, the treated plot was sprayed once at BBCH growth stage 67 (70% of flowerhoods fallen) with fenhexamid WG 50, a water-dispersible granules formulation and 63 days later once at BBCH 81 (beginning of ripening: berries begin to develop variety-specific colour) with fluopyram SC 500 a suspension concentrate (SC) formulation containing 500 g/L fluopyram. In field trial 09-2240-01-92, the treated plot was sprayed once at BBCH growth stage 67 with fluopyram SC 500 at BBCH 81 (beginning of ripening). The treated plot was sprayed once at BBCH growth stage 67 with fluopyram. In field trial 09-2240-01-92, the treated plot was sprayed once at BBCH growth stage 67 with fluopyram SC 500 and 63 days later on the treated plot was sprayed once at BBCH growth stage 67 with fluopyram SC 500 and 63 days later on the treated plot was sprayed once at BBCH growth stage 67 with fluopyram SC 500 and 63 days later on the treated plot was sprayed once at BBCH growth stage 67 with fluopyram SC 500 and 63 days later on the treated plot was sprayed once at BBCH growth stage 67 with fluopyram SC 500 and 63 days later on the treated plot was sprayed once at BBCH growth stage 67 with fluopyram SC 500 and 63 days later on the treated plot was sprayed once at BBCH growth stage 67 with fluopyram SC 500 and 63 days later on the treated plot was sprayed once at BBCH growth stage 67 with fluopyram SC 500 and 63 days later on the treated plot was sprayed once at BBCH growth stage 67 with fluopyram SC 500 and 63 days later on the treated plot was sprayed once at BBCH growth stage 67 with fluopyram SC 500 and 63 days later on the treated plot was sprayed once at BBCH growth stage 67 with fluopyram sc 500 growth stage 67 with

Bunch of grape samples were taken 28 days after the last treatment at BBCH 89 (last treatment was done with fluopyram on trial -T1 and with fenhavamid on trial -T2).

Samples for processing were transported to processing laboratory in fresh conditions.

After processing, the processed samples of champagne after bottling were shipped to laboratory logistics in Lyon (France) and then transported at ambient temperature to the laboratory for preparation of the examination samples. The aboratory samples were stored in a freezer at -18°C until preparation of the examination samples.

Processing procedu

The processing study simulated industrial practice at a laboratory scale. The white grape specimens were processed into champagne according to the standard operating procedures in use in the processing laboratory.



The bunches of grapes were pressed to extract "cuvee" and "taille" (must). The obtained must was filled into a steel tank of 50L. After sulfiting with 6 g/hL, the must was racked for 12-16 hours and the cafter a clarified.

Alcoholic Fermentation (AF):

The clarified must was vinified in 30L glass carboys with chaptalization of RCM and addition of yeast (Saccharomyces cerevisiae, Trade name: LSA Levuline CHP; 10 g LSA / hL must). Alcoholic fermentation was carried out at 16-18°C for approx. a month under monthoring density and temperature measurements over time.

Malolactic Fermentation (MLF):

At the end of alcoholic fermentation, the wines were racked into 20-L carboys and immediately inoculated with malolactic bacteria (*Oenococcus Geni*, Trade name: Inobacter). At the end of MLF, the wines were racked and 20 mg/L of SO2 was fill between the bacteria (*Denococcus Geni*, Trade name: Inobacter). wines were racked and 20 mg/L of SO2 was added to each lor, after sampling for senological analysis Ś and degustation test.

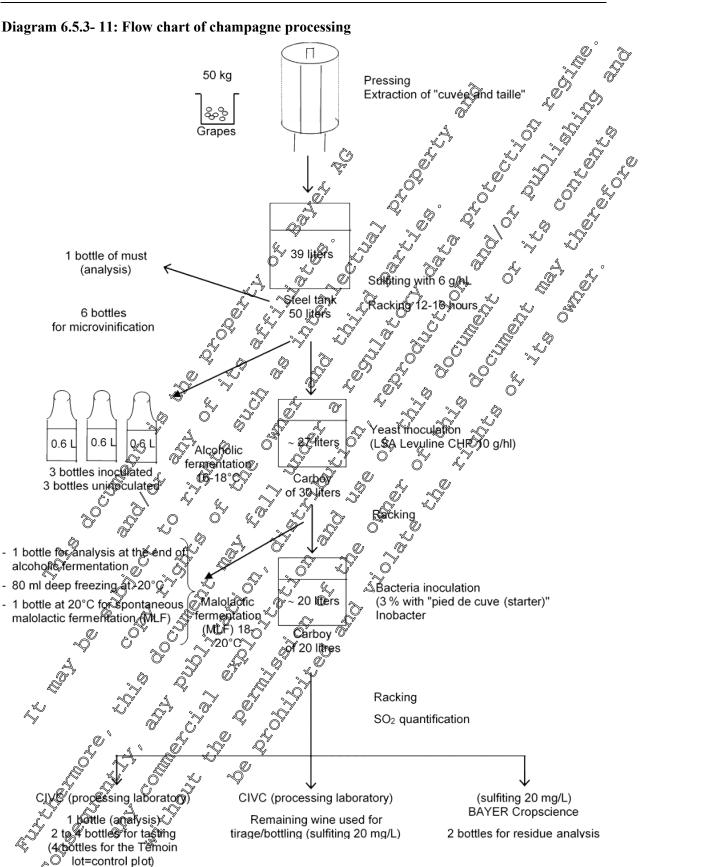
The remaining wine was bottled for residue analys after champagne, bottling) used for Ø Of the second se "champagnization".

Processing to Champagne:

The processing to champagne was carried out after MLF by racking of wines in 10L carboys and addition of 20 mg/L SO2. The wine in carboys was stored at -4°C for 0 days. The Ot was filtrated through 1.2 µm membrane filter. After filtration, the wine was bottled, Girage With 20 g/Lougar to form of RCM (natural alcoholic content at the end of AF 12% vol.), 60 mL/hL of riddling adjuvant and 4% of yeast (strain Levuline CHP). L.Q

Second fermentation (formation of carbon dioxide; bubbles) was done at 18-20° Cander monitoring and Second termentation (formation of carbon dioxide: bibbles) was done at \$\$20°C ander monitoring and analysis at the end of termentation. Enrally, the wines were stored in a vine cellar at 14°C for 12 months. Then riddling, discorring and terms were carried out, yielding in samples for residue analysis (champagne, after maturation). The processes are illustrated in Diagram 65.3-16. analysis at the end of fermentation. Finally, the wines were stored in a wine cellar at 14°C for 12 months.







Residue analysis

Residues of fluopyram in/on plant material were determined by HPLC-MS/MS according to BCS method 01207 based on the QuEChERS multi-residue method (S., 11/12/2013, M-424756) 02-1, see section MCA 4.1.2).

Analytical method BCS 01207 is based on the QuEChERS multi-residue method. Extraction of residues was done with acetonitrile/water (4/1, v/v) by shaking. The residues of fluoryram, FLU-benzamide and FLU-PCA were extracted together but separately to FLU-PAA.

An aliquot of the extracts was taken, and stable-labelled internal standards were added excepted for FLU-PAA where the stable-labelled internal standard was added at the beginning of the extraction procedure. The final extracts were subjected to LC-MS/MS. The quantification was performed by internal standardization using stable-labelled internal standards in pure solvent for flugbyram FLU-benzanade and FLU-PCA. The quantification was performed with matrix matched standards with internal standard for FLU-PAA.

The Limit of Quantification (LOQ) was 0.01 mg/kg for flyopyran and its metabolites all calculated as parent equivalents and for all matrices.

During the course of this study, the method performance was checked by concurrent recoveries. Details on concurrent recovery data are shown in Table 6.5.3-36. No average recovery or RSD value can be calculated. The overall average recoveries (n=2) were within the acceptable range of 70 - 110%.

The levels of residues of fluopyram and its periabolites in the processed samples are summarized in Table 6.5.3-38. No residues above the LOG were found of the control samples. The results were not corrected for concurrent recoveries

The residue level of fluoryram in bunch of grape (RAC for the calculation of the processing factors) ranged from 0.03 mg/kg (trial 09-2242-01-T2) to 0.22 mg/kg (trial 09-2242-01-T1). Residues values of fluopyram ranged from <0.01 to 0.04 mg/kg in processed commodities.

For all metabolites residues levels were always 501 mg/kg in the RAC and in all processed commodities.

The processing factors (PF) were calculated based on the residue level in the treated processed commodity and residue level in the RAC specimens (bunch of grape). When residues in the RAC and in the processed fractions were both 0.01 mg/kg a processing factor could not be calculated. The proposed processing factors are commanised below in Table 6.5.3-3%.

The analyses over done after a maximum trozen storage period of 520 days for bunch of grapes and 278 days for processed commodities



Two residue trials were conducted in borthern Europe in 2009. Grapes were treated once with fluopyram SC 500 at a growth stage BBCH 6% or BBCH 81 with a dose rate at 1 x 300 g a.s./ha. All applications were at the required rates \sim

Bunch of grape camples from white grape varieties were processed in order to obtain champagne. The samples (RAC and processed fraction) were analysed for the residues of fluopyram parent compound and is metabolites FLU-benzamide, FLU-PAA and FLU-PCA. The processing study was conducted according to GLP.

The results of the study indicate that residues of fluopyram can decreased from bunch of grape with processing procedures resulting in very low residues in champagne (PF < 0.24 after botting and < 0.26 after maturation).



Assessment and conclusion by applicant:

Table 6.5.3- 36:

The study i	s acceptable.										,
able 6.5.3	- 36: Recove into ch	ry res ampa	sults for fluop gne Fortification level* (mg/kg)	yram and	l its met	abolite	in pro	cesse	d corps	odiție	S S S S S S S S S S S S S S S S S S S
Study	Portion analysed	n	Fortification level* (mg/kg)		V Iual reco	Rector	ery (% Min	o) Mart	Magn	RSD	
09-3242	Fluopyram			- Å	~						5
	Grape / champagne (after bottling)	1 1 2	0.01 0.10 Overall	¥_03	88 78 0		88 48 78 78	88 70 88	0 - 45 - 7 - 7 - 7		¢ ¢
	Fluopyram-be	enzam	ide 🗸		V A	A	- Â	7	<u>s</u>		P
	Grape / champagne (after bottling)	1 1 2			72 ~78 ~78	Ŏ,	73 78 73	7678 78 78 78	\$ 0- 76-4		
	Fluopyram- p	yridyl	-acetic acid		5	- Ag	8	. 0	0		
	Grape / champagne (after bottling)	2 2	\$9.01 \$ 0.100 Overill				104 86 Ø	004 86 164	- - 95	-	
	Fluopyram-p	yridyl	-carlogxylic mi	d 🔊	() [·]		· ·	65			ĺ
	Grape / A champene (after)		Ovæill → carløyylic @i		×81 ×83 ×83 ×83		81 (83	81 83 83	-	-	
. fortification	bot(ing)	24	Qverall ~				81	83	82	-	

FL: fortification less RSD - delative condard (Diviation Final determination as: fluopram Residues calculated as: fluopram Table 6, 5, 7-37: Summary of residues in grape and proposed processing factors for fluopyram and its metabolities for grape Tested GAP, 9× 300 g a.s./ha at BBCH 67 (-T2) or 81

		Oʻ 🟑		A'	C 27
Trial	509-32 32 -	O í	09-32 0 2-	01-T2	Proposed PF (mean if applicable)
Sample material	Residues (19g/kg)	PF Q	Residues (nug/kg)	PF	
Fluopyram	õ.		° Z		ni.
Bunch of grapes (RAC)	0.2%		0 0 03	(1 444)	
Champagne after bottling	<u>₀0.03</u>	0.14	< 0.01	< 0.33	< 0.24
Champagne after maturation	CA 04	V 0 1(Q)	< 0.01	< 0.33	<0.26
Fluopyram-bertamide*		X			-
Bunch of grapes (RAC)	2 <0.04 2 <0.94	a, *-	< 0.01		
Bunch of grapes (RAC) Champagne after bottling S Champagne after maturation	\$9.01	n.c	< 0.01	n.c	n.c
Champa de after maturation	o [₹] 0.01	n.c	< 0.01	n.c	n.c
Fluopyram-pyridyl-carboxy	ic-acid*				
Bunch of gropes (RAC)	< 0.01		< 0.01		
Bunch of groves (RAC)	< 0.01	n.c	< 0.01	n.c	n.c
Champagne after maturation	< 0.01	n.c	< 0.01	n.c	n.c
Fluopyram-pyridyl-acetic-ac	cid*				
Bunch of grapes (RAC)	< 0.01		< 0.01		
Champagne after bottling	< 0.01	n.c	< 0.01	n.c	n.c



Trial	09-3242-	-01-T1	09-3242-	01-T2	Proposed PF (mean if applicable)	
Sample material	Residues (mg/kg)	PF	Residues (mg/kg)	PF	~	
Champagne after maturation	< 0.01	n.c	< 0.01	n.c	ADric .	
*expressed as parent compound					- OF	

*expressed as parent compound

 Simple material
 (mg/kg)
 PF
 (mg/kg)
 PF

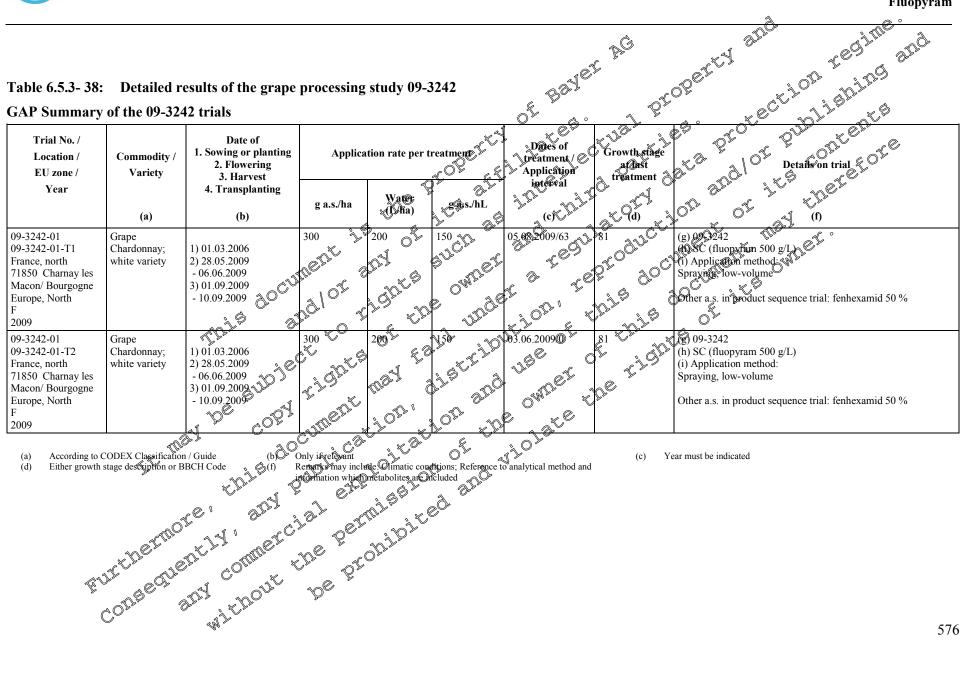
 champage after maturation
 0.01
 n.c
 0.00
 0.00

 Perpressed sparent compound
 Option
 0.00
 0.00
 0.00
 0.00

 recorressing factor be residue concentration in processed composity (mg/kg) / residue calculated (site)
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0.00
 0



Page 576 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram



BAYER

Page 577 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

										i iuopyi	
								4 C L	4 J	erty and regime.	>
Trial No. / Location / EU zone / Year	Commodity / Variety (a)	Portion analyzed	Growth stage at sampling (d)	AE C656948 as AE C656948	AE C656948- benzamide as AE C656048	lues (mg/kg)	ABC6569 ABC6569 Dyridyl-ac acid-as		P(days) (e)	OPERITY OPE	
09-3242-01 09-3242-01-T1 France, north 71850 Charnay les Macon/ Bourgogne Europe, North F 2009	Grape Chardonnay; white variety	bunch of grapes champagne after bottling champagne after maturation	89 89 89	0.22 0.03 0.04 0.04 0.04 0.04		CO.01		5 ¹² 20 28 28	900 9770	(g) 0=3242 (a) Analytical method: 01207 (k) LOQ 0-01 mg/kg (l) Method Validation Data: 01207 (c) Storage champage after bottling and after maturation): 278 days bunch 0# grapes: 520 days	
09-3242-01 09-3242-01-T2 France, north 71850 Charnay les Macon/ Bourgogne Europe, North F 2009	Grape Chardonnay; white variety	bunch of grapes champagne after bottling champagne after maturation		0.03 2 2 2 ~001 ~0.01 6 JA ⁺ 10 ⁶	<0.01 50.01 <0.02 2.2. 21 31 31 31 31	0 ° 00 <0.00 00 <0.00 00 <0.00 00 <0.00 00 <0.00 00 00 00 00 00 00 00 00 00 00 00 00 0	~0.00 ~0.00 ~0.00 J.F OWE	28 5 5 7 7 7 7 8 7 8 7 8 7 8 7 8 7 8 7 8	hì ^{\$} rì ⁹⁰	(g) 09-32(2 (i) Analytical method: 01207 (k) OQ: 0.01 mg/kg (i) Method Validation Data: 01207 (m) Storage: champagne (after bottling and after maturation): 278 days bunch of grapes: 520 days	
 (a) According to C Guide (b) Only if relevant 	CODEX Classificati	or (e) Day (f) Re method an	ys after la Cappli parks may inclui	cation (Beel pre	-harvest merval	l, PHI, underline) e lo analytica K		ormulation typ	e (l) hod (m)) Storage (max)	
 (c) Year must be i (d) Either growth Code G greenhouse 	ndicated stage description or F UC+DeCU	bunch of grapes champagne after bottling champagne after maturation (e) Day (f) Re method after BBCH (g) Sta (C) DU (C) D	ormation of the formation of the formati		nordate av	Gibbe ailable	(j) M informatic (k) L0 ** re	ethod m DQ sidue in contro	Bu and Pro ol and	nch of grapes: between deep-freezing (in the field) I date of last extraction bocessed commodities: between their deep-freezing I date of last extraction	
		Also .									577



Data Point:	KCA 6.5.3/15
Report Author:	
Report Year:	2016
Report Title:	Amendment no.1 to final report BCS-0497 - Determination of residues of
	fluopyram in wine processed from grapes treated with two applications of Luna
	Privilege 500 SC at rates of 7.5 or 15 g a.i./100 L
Report No:	BCS-0497
Document No:	<u>M-558007-02-1</u> (3) (3) (3) (3) (3) (3) (3) (3) (3) (3)
Guideline(s) followed in	APVMA Residue Guideline No. 1
study:	US EPA OCSPP Guideline Number: 860.SUPO 🗸 🖉 🖉
Deviations from current	none
test guideline:	
Previous evaluation:	yes, evaluated and accepted
GLP/Officially recognised	Yes, conducted under GLP Officially recognised testing facilities A
testing facilities:	
Acceptability/Reliability:	Yes $\frac{2}{\sqrt{2}}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$

ecials and Methods

The study included 13 supervised residue fral with grap@ conducted in the field in Asistralia in the 2014 season. The purpose of this study was to determine the magnitude of the residues of fluopyram in/on grape (berries) and wine.

Field part

Two residue studies BC \$60481 and BC \$-0482 were conducted in wine stapes in 2014 in Australia to assess residues of fluopyram at six test sites following a number of different treatments of Luna Privilege 500 SC. To earble the transfer of residues from grapes to wine to be assessed, two replicate samples were taken One was used to determine fluopy am residues in wine grapes and the other was used to process to wine and analyse for fluopyram as part of this story BCS-0497.

Field and application data are peported in reports BCS-0481 and BCS-0482.

For study BCS-0486, residue trials were conducted by Bayer CropScience in wine grapes at two test sites: B481-1 at Yering and B482-2 at Wahgunyah, both in Wictoria (Australia).

For study BCS-0482, residue fials were conducted by Eurofins Agrisearch in wine grapes at four test sites: A482-1 at Barossa in South Australia (Medot wine grapes), A482-2 at Southern Vales in South Australia (Shiraz wine gopes) A482 S at Reverland in South Australia (Cabernet Sauvignon wine grapes) and A482-4 at Orange in New South Wales (Sauvignon Blanc wine grapes).

Two applications of Lona Privilege 500 SC a surpension concentrate (SC) formulation containing 500 g/L fluopyram were made at various timbers at rates of 7.5 or 15 g/hL fluopyram corresponding to 48-72 or 48-173 g/ha fluopytam, respectively and using a spray volume of 323-971 L/ha.

Treated plot were sprayed twice from 15 days before growth stage BBCH 57 (12 leaves separated, inflorescence well developed, single flowers separated) to growth stage BBCH 61 (10% cap fall). The interval between applications was 5-21 days and the pre-harvest interval was 87-126 days. All treatments were made at the scheduled rates.

Frozen/samples of wine grapes were received at the processing laboratory and were stored frozen prior to commencement of the processing phase.

All samples of wine were transported to the analytical test site at ambient temperature.



Processing into wine:

Grape study samples were analysed as whole commodity without caps and stems. Samples were partially defrosted and prepared. An approximately 800 g subsample of grapes was separated for vinification. These samples were processed. Vinification subsamples were thawed overnight then manually crusted and the must added to a one litre glass fermentation vessel to which approximately 50 mg/L situphur dioxide, as potassium metabisulphite, and 200 mg/L diammonium phosphate solution, was added. The must was then inoculated with rehydrated active dried wine yeast, and fermented on skins at 25°C, with daily mixing of the skins and liquid. After seven days, the ferment was pressed twice, each time at approximately 19 Nm for two minutes, with mixing of the pomace between pressings. The wine was returned to the original vessel and allowed to ferment to dryness (C1 g/L residual sugar) at 25°C. Once fermentation was established as complete using *Climitis* steps a dirther 100 mg/L potassium metabisulphite solution was added and the wines stored at approximately 4°C to cold settle and clarify. After approximately seven days the wines were tacked from the gross lees and 2 x 155 mL subsamples were taken and transported to the analytical text site.

Residue analysis

The samples were analysed for fluor ram using multi-residue analytical method ATAF-003&04 (Bayer CropScience Australia, 2011) which was validated on stape, althoud (Fernel Hull and shell), tomato and banana.

Analytical method ATM-0038-04 was developed for the quantitative determination of fluopyram, tebuconazole, triadimenol grifloxystrobin and tradoxystrobin acid restrices in or on plant matrices from the high protein, high starth, high oil, high water and high acid raw agricultural commodity groups by LC MS/MS.

Extraction of residues was done with acetonitrile water (5/1, v/y) followed by high-speed blending. After filtration, dilution and addition of internal standard, final extracts were subjected to LC-MS/MS. The quantification for fluopyram was performed by internal standard tration using a stable-labelled internal standard in pure solvent.

The Limit @Quantification (LQ9) was 0.01 mg/kg for fluopyram and for all matrices.

This method was locally developed and validated in Australia. As analyses during a processing study are performed to calculate transfer factor and not absolute residue levels this method is considered as fit for purpose. The results are fully comparable and the processing factors for wine are in the same range than the other processing studies conducted on grapes.



During the course of this study, the method performance was validated by concurrent recoveries. Details on concurrent recovery data are shown in Table 6.5.3- 39. The average recoveries were within the acceptable range of 70 - 110%. The RSD values were below 20%.

The levels of fesidues of floopyram in the processed samples are summarized in Table 6.5.3-41. No residues above the LOQ were found in the control samples. The results were not corrected for concurrent recoveries

The residue level of fluopyrum in berry (RAC for the calculation of the processing factors) ranged from <0.01 to 0.12 mg/kg Residues values of fluopyrum ranged from <0.01 to 0.05 mg/kg in wine.

The processing factors (PF) were calculated based on the residue level in the treated processed commonly and residue level in the RAC specimens (berry). When residues in the RAC and in the processed fractions were both <0.01 mg/kg a processing factor could not be calculated. The proposed processing factor is summarised below in Table 6.5.3-40.



The analyses were done after a maximum frozen storage period of 75 days for berries and 203 days for wine.

III. Conclusions

vram Thirteen residue trials were conducted in Australia in 2014. Grapes were treated twice with fluor SC 500 (Luna Privilege) at a growth stage 15 days before BBCH 57 to BBCH 61 with a cose rate at 7.5 or 15 g/hL fluopyram. All applications were at the required rates.

Berries samples from grape varieties (red and white) were processed in order to obtail wine The samples (RAC and processed fraction) were analysed for the desidues of floopyram. The processing study conducted according to GLP.

The results of the study indicate that residues of fluopyram can decreased from berries with processing procedure resulting in low residues in wine (PF ≤ 2.0). The results are fully comparable and the processing factors for wine are in the same range than the other processing studies conducted on grapes.

			×A .*		
The study is acceptable.		4 . G	29 ~ °		
		, , &	, 2		
Table 6.5.3- 39: Recover	ry Fesults for fly	o S	where Ô	Î, D	2 ⁰ %

BCS-0497 Grapo wine 3 0.0 5 8659,90 80 90 88 2.4 Grapo wine 3 6.1 90 100, 600 799 600 100 0.5	Study	Portion &	n	(mg/kg)	Orecoveries	Reg			Mean	RSD
	BCS-0497	Û,	3		\$ 863,89,90	, in the second	\$ @		1933	2.4
		Grapo winco	3	y by s	, \$ 9 ,100, \$9 0	Ő	∲99	G00	100	0.58
$ \begin{bmatrix} 0 & 0^{2} & 6^{2} \\ 0 & 0^{2} & 0^{2} \end{bmatrix} $			6	Overall			86%	100	94	6.8

RSD = Relative Stan and Destation

*Fortified and calculated as fluop cam

Ľ Table 6.5.3-40: Sommary of residues w grape and proposed processing factor for grape for Huopyram

Tested GAP: 2 x 7.5 or 2x 15 shL fluopyram from 15 days before BBCH 57 to BBCH 61

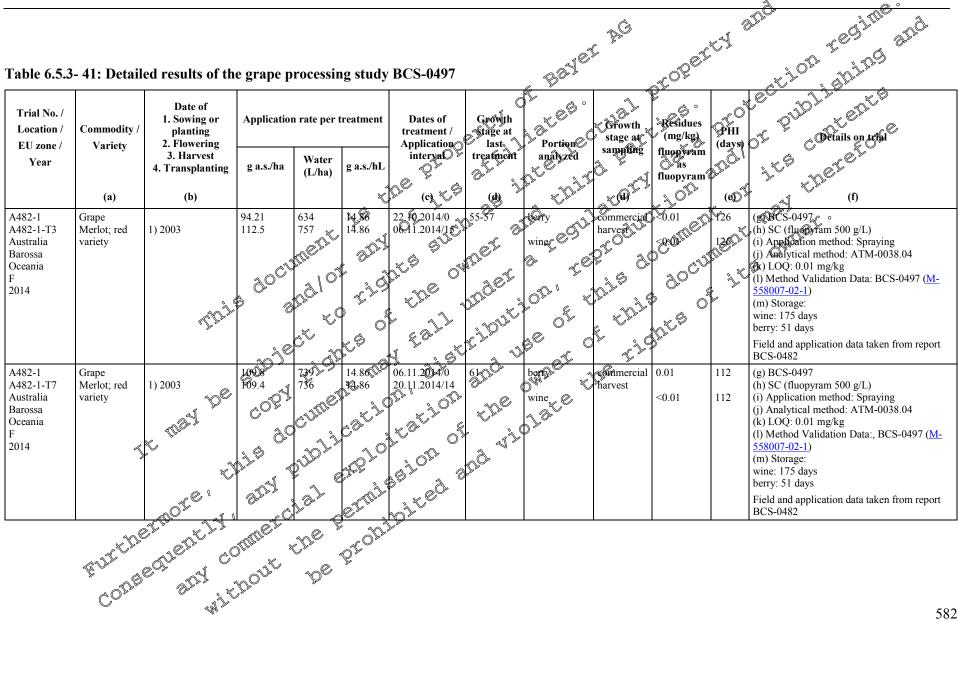
Samplematerial	Berry	VENIC		
Trial G	Residuces (mg/kg)	Residues *(mg/kg)	PF	Mean PF
Fluopyram 🔗 🔬				
A482-1-T3	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	< 0.01	n.c	
A48/-1-1/	£ 0,01 £	< 0.01	<1.0	
A482-2-12	Ø ~ \$0.02 ~ \$	< 0.01	< 0.50	
A482-2-T3 0 5	0.05	0.01	0.20	
A482-2-T2 A482-2-T3 A482-2-T6 A482-2-T6 A482-2-T6 A482-2-T6	\$ 0.08 0 0.05 0 02	0.01	0.33	
AAX/=deta/	0 0.05	0.03	0.60	0.37
A48234T6 67 7	0.02	< 0.01	< 0.50	0.57
A483-3-T7	0.03	< 0.01	< 0.33	
A482-4-70	0.02	< 0.01	< 0.50	
A482-4-916	0.07	0.02	0.29	
A482-4-T7	0.12	0.05	0.42	
B481-1-T7	< 0.01	< 0.01	n.c	



Sample material Berry Wine (mg/kg) PF Mean PF 1481-277 -0.01 -0.01 n.c residue (mg/kg) n.c -0.01 -0.01 -0.01 residue (ng/kg) n.c -0.01 -0.01 -0.01 PF (processing factor) = residue concentration in processed commodity (mg/kg) n.c -0.01 -0.01 a.c processing factor and excluding (residue set O) (in RAC and in processed commodity). The mean value is calculated for residue >0.01 mg/kg in wine sample? a.d b.d b.d b.d b.d b.d b.d c.d b.d c.d b.d c.d c.d d.d <lid.d< li=""> d.d <lid.d< li=""> <</lid.d<></lid.d<>	Sample material	Berry	Wine			
B4812-217 0.01 n.c 0.01 n.c F (processing factor) = residue concentration in processed commodity (ma/kg) / residue conceptention in the RAC (mg/kg) / residue conceptentin in the RAC (mg/	Trial	Residues (mg/kg)	Residues	PF	Mean PF	¢ í
Torcessing factor) = residue concentration in processed commodity (mg/kg) residue concentration in processed commodity (mg/kg) residue concentration in the RAC mg/kg) residue concentration in the RAC mg/kg in value in ease the residue level in the RAC = 2.0 Dut residues in the processed commodity (mg/kg) residue concentration in the RAC mg/kg in value in ease the residue level in the RAC = 2.0 Dut residues in the processed commodity (mg/kg) residue concentration in the RAC mg/kg in value in ease the residue level in the RAC = 2.0 Dut residues in the processed commodity (mg/kg) residue concentration in the RAC mg/kg in value in ease the residue level in the PAC = 2.0 Dut residues in the processed commodity (mg/kg) residue concentration in the RAC mg/kg in value in ease the residue level in the processed commodity (mg/kg) residue concentration in the RAC mg/kg in value in ease the processed commodity (mg/kg) residue concentration in the RAC mg/kg in value in ease the processed commodity (mg/kg) residue concentration in the RAC mg/kg in value in ease the processed commodity (mg/kg) residue concentration in the RAC mg/kg in value is calculated for residues >0.01 mg/kg in value and the processed commodity (mg/kg) residue concentration in the RAC mg/kg in value is calculated for residues >0.01 mg/kg in value and the processed commodity (mg/kg in value in the RAC mg/kg in value is calculated for residues >0.01 mg/kg in value and the processed commodity (mg/kg in value in the RAC mg/kg in value in the RAC mg/	B481-2-T7	<0.01	(шg/кg) <0.01	ne		ý S
e: no processing factor can be calculated (residues <loq and="" commodify)<br="" in="" processed="" rac="">value: in case the residue level in the RAC is ≥ LOQ but residues in the processed commodify. The mean value is calculated for residues >0.01 mg/kg in wine sample is estimated with the LOQ as residue level in the processed commodify.</loq>	F (processing factor) = residue co	ncentration in processed of	commodity (m	g/kg) / resid	lue concentration in the RACI	ng/kgôn
581	the processing factor can be call value: in case the residue level in actor is estimated with the LOQ as he mean value is calculated for re	culated (residues <loq but="" in="" is="" loq="" of="" processed="" rac="" residues="" respectively="" the="" ≥="">0.01 mg/kg in with the processed of the residues >0.01 mg/kg in with the processed of the residues >0.01 mg/kg in with the processed of the residues >0.01 mg/kg in with the processed of the residues >0.01 mg/kg in with the processed of the residues >0.01 mg/kg in with the processed of the residues >0.01 mg/kg in with the processed of the residue in the processed of the residues >0.01 mg/kg in with the processed of the residues >0.01 mg/</loq>	A C and in esidues in the pessed commod ne samples	processed concessed conces	and concentration in the recent commodify) ommodify are < LOQ, the proce	



Page 582 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram





Page 583 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

									P.G		* A	regine and
Trial No. / Location / EU zone /	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering	Application	n rate per t	treatment	Dates of treatment / Application	Growth stage at last ()	BONE .	stage at [®]	Residues (mg/kg)	PHI (days)	ection public and
Year	(a)	3. Harvest 4. Transplanting (b)	g a.s./ha	Water (L/ha)	g a.s./hL	interval	treatedent	analezed			1000 /	(g) BCS-0497 (h) SC (fluowram 500 g/L) (i) Application method: Spraying
A482-2 A482-2-T2 Australia Southern Vales Dceania 7 2014	Grape Shiraz; red variety	1) 1985	48.0 54.2	ent	1 201	22,10,2614/0 0611.2014/15 05 05 05 05 05 05 05 05 05 05	ner	elt wine this pole tegui de tegui	erodul		K _/	(g) DČS-0497 (h) SC (fluoyofam 500 g/L) (i) Application method: Spraying (i) Application method: ATM-0038 04
A482-2 A482-2-T3 Australia Southern Vales Dceania 2014	Grape Shiraz; red variety	1) 1985 De	96.44 110.7		14.86 14.86 14.86 14.86	122.10.2014/0 06.11.2014/15	rilDut	wine $\beta^{(1)} = \beta^{(1)} =$		0.05 O	102 102	(g) BCS-0497 (h) SC (fluopyram 500 g/L) (i) Application method: Spraying (j) Analytical method: ATM-0038.04 (k) LOQ: 0.01 mg/kg (l) Method Validation Data: BCS-0497 (<u>M-558007-02-1</u>) (m) Storage: wine: 199 days berry: 75 days
A482-2 A482-2-T6 Australia Southern Vales Oceania 2 2014	Grape Shiraz; red S variety	ETTROTE 1 ETTROTE 1 ETTROT	55.6 OC 62.45 ALL S ALL	748 830 200 200 200 200 200 200 200 200 200 2	7.43 7.43 6.2 6.2 7.43 0 7.4 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	00:11.2014/00 21.11.2014/15 9 1 2 1.11.2014/15	61 JE	berry wine	commercial harvest	0.03 0.01	87 87	(g) BCS-0497 (h) SC (fluopyram 500 g/L) (i) Application method: Spraying (j) Analytical method: ATM-0038.04 (k) LOQ: 0.01 mg/kg (l) Method Validation Data: BCS-0497 (<u>M-558007-02-1</u>) (m) Storage: wine: 199 days berry: 75 days
	Colfe	e du c	hone	Y ^e	<u>15</u>	1	1	1	1	1	1	5



Page 584 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

												â
									₽Ĝ		*1	And regine on and
Trial No. / Location /	Commodity /	Date of 1. Sowing or planting 2. Flowering	Application	n rate per t	treatment	Dates of treatment / Application	Growth stage at last 《	BONE .	stage at [®]	Besidues (mg/kg)	PHI	ection personal and the second
EU zone / Year	Variety (a)	3. Harvest 4. Transplanting (b)	g a.s./ha	Water (L/ha)	g a.s./hL	interval	treatment	analyzed		fluoreram	e)	(g) BCS-0497 (i) Application method: Spraying
A482-2 A482-2-T7 Australia Southern Vales Oceania F 2014	Grape Shiraz; red variety	1) 1985	112.0 104.3	ent	2 0 0 1 0 0 1 0 1 0 1	06.11.2014/0 p.F.11.2014/15 0F 50C 50C	A CLEI		Commercial harvest	0.05 Parona Cumen docu	K./	(g) BCS-0497 (h) SC (flux yram 500 g/L) (i) Application method: Spraying (i) Application method: ATM-0038 04
A482-3 A482-3-T6 Australia Riverland Oceania F 2014	Grape Cabernet Sauvignon; red variety	1) 1990 👘 🖓	86.0 0 72.2			97.11.2014/14 E 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	rildui and u	wine O ^T		0.02 O	102 102	(g) BCS-0497 (h) SC (fluopyram 500 g/L) (i) Application method: Spraying (j) Analytical method: ATM-0038.04 (k) LOQ: 0.01 mg/kg (l) Method Validation Data: BCS-0497 (<u>M-558007-02-1</u>) (m) Storage: wine: 198 days berry: 74 days
A482-3 A482-3-T7 Australia Riverland Oceania F 2014	Grape Cabernet Sauvignon; red variety	Equentity is and the set of the s	134.6 OC 1423 ALAN ALAN ALAN ALAN ALAN ALAN		14.86 14.86 260 260 260 200	24:10.2014/00 07.11.2014/10 9 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	61 J	berry wine	commercial harvest	0.03 <0.01	102 102	(g) BCS-0497 (h) SC (fluopyram 500 g/L) (i) Application method: Spraying (j) Analytical method: ATM-0038.04 (k) LOQ: 0.01 mg/kg (l) Method Validation Data: BCS-0497 (M- <u>558007-02-1</u>) (m) Storage: wine: 198 days berry: 74 days
	COLLE	eor crit	hour	N.	<u>N</u>	1	1	1	1	1	<u>I</u>	58



Page 585 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

									A.C		*1	regine and
Trial No. / Location / EU zone /	Commodity /	Date of 1. Sowing or planting 2. Flowering	Application	n rate per t	reatment	Dates of treatment / Application	Growth stage at last ()	BONE Portion .	stage at [«]	Besidues (mg/kg)	PHI	(g)BCS-0497 C ² (h) SC (flux)pyram 500 g/L)
EU zone / Year	Variety (a)	3. Harvest 4. Transplanting (b)	g a.s./ha	Water (L/ha)	g a.s./hL	interval	treatedent	analezed			Carysh D ^{TO}	(g) BCS-0497 (h) SC (fluggram 500 g/L) (i) Application method: Spraying
A482-4 A482-4-T3 Australia 2800 Orange Oceania F 2014	Grape Sauvignon blanc; white	1) 2003	74.30 117.7	ent	J.	05 11.2014/0 20 11.2014/25 0 5 6 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	r det		erodu	0.02 <0.00 X.I CUINER	*/ 0*	(i) Application method: Spraying
A482-4 A482-4-T6 Australia 2800 Orange Oceania F 2014		1) 2003 The	39.4 60.0	**************************************	t The	96.12.2014/10 E 2 4/10	TilDut and v	Wine OF		0.07 Ö	87	(g) BCS-0497 (h) SC (fluopyram 500 g/L) (i) Application method: Spraying (j) Analytical method: ATM-0038.04 (k) LOQ: 0.01 mg/kg (l) Method Validation Data: BCS-0497 (M- <u>558007-02-1</u>) (m) Storage: wine: 184 days berry: 60 days
A482-4 A482-4-T7 Australia 2800 Orange Oceania F 2014	Grape Sauvignon blanc; white variety	PAN Providence Provide	118.9 OC 1203 AL ALAY ALAY		14.86 14.86 14.86 25 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	26.11.2014/00 06.12.2014/10 5 5 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	61 J	berry wine	commercial harvest	0.12 0.05	87 87	(g) BCS-0497 (h) SC (fluopyram 500 g/L) (i) Application method: Spraying (j) Analytical method: ATM-0038.04 (k) LOQ: 0.01 mg/kg (l) Method Validation Data: BCS-0497 (M- <u>558007-02-1</u>) (m) Storage: wine: 184 days berry: 60 days
	Corre	Soft of the soft	hout	De.	<u></u>	1	1	1	1	1	L	58



Page 586 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

												*
									₽ ^Ĝ		*1	ARD REGITICE .
Trial No. / Location / EU zone /	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering	Application	n rate per t	reatment	Dates of treatment / Application	Growth stage at last 《	Portion •	stage at	Besidues (mg/kg)	PHI (days)	C ^t iO ^{fb} jDietails on striat
Year	(a)	3. Harvest 4. Transplanting (b)	g a.s./ha	Water (L/ha)	g a.s./hL	interval	treatedent	analezed	sampling	fluoreram as fluopyram		C ^{CS} 2 ^{Lb} C ^{CL} 0 ^{Lb} ghilt ^C Details on strift 0 ^L C ^{OLL} 0 ^{LC} 0 ^L C ^{OLL} 0 ^{LC}
B481-1 B481-1-T7 Australia 3770 Yering Oceania F 2014	Grape Cabernet Sauvignon	1) 1999	126.6 173.7	852 1169	j.9 829 1		Der Ber	wine that wine that the the the the the	12	2001 2000 2000 2000 2000 2000 2000 2000	2110 1100 5	(g) DCS-0497 (h) SC (fluoperam 500 g/L) (i) Application method: Spraying (i) Charlytical method: ATM-0038.04 (k) LOQ: 0.01 mg/kg (l) Method: Alidation Data: BCS-0497 (M- <u>558(0) 402-1</u>) (m) Storage: wine: 170 days berry: 6 days
B481-2 B481-2-T7 Australia 3687 Wahgunyah Oceania F 2014		1) 1960's Chil	10 ³⁰	323 386 °C C ^{°C} T ^{°I} O ^{II} C ^{°UII} O ^{II}	K ^{\$}	31.10.2014) E 2 4 H 2 5	rijout Zijout	wine O	89 - D.	<0.01 O	104 104	(g) BCS-0497 (h) SC (fluopyram 500 g/L) (i) Application method: Spraying (j) Analytical method: ATM-0038.04 (k) LOQ: 0.01 mg/kg (l) Method Validation Data: BCS-0497 (<u>M- 558007-02-1</u>) (m) Storage: wine: 203 days berry: 13 days
Guide (b) Only if (c) Year m	ling to CODEX Classical control of the second state of the second	billion or BBCC 1 (1) Billion or BBCC 1 (2) (2) (3) (4) (5) (5) (5) (6) (7) (7) (7) (8) (9) (9) (9) (9) (9) (9) (1) (1) (1) (1) (2) (2) (2) (2) (2) (3) (4) (5) (4) (5) (5) (5) (5) (5) (5) (5) (5	Days after Romaks n thought information Fror to las	ence C	Climatic com Ontes are in Ontes are in	e-harvest interval, 19 Intions: Responde to related no data availa	Gunderline) analytical ble	 (h) Formul (i) Applic: (j) Method information (k) LOQ ** residue 	lation type ation method d : in control	(m) StorageBerries: betwee analysed	n deep-fre	eezing (in the field) and date of analysis (last samples between their deep-freezing and date of analysis (last
		A.										586



Overall summary of calculated processing factors in grape commodities for all submitted studies.

Sample material	Trial nb	Mean PF	Studies		Sample material	Overall trial no	Overall mean PF
uice	4	0.02		3	Juice	\$ \$	× 01 ×
omace, dried	4	6.4			Pomace, Gried	Å.	9 6.4
omace, wet	4	3.2	A.		Pomaçe, wet	× 6 0	33 (1)
Berry, washed	4	0.6	KCA		Pomaçe, grape		03.4
omace, grape	4	3.4	6.5 <i>3</i> 01-01		Berry, washed		© 0.60
Iust	4	0.2	- 1			<u>≫.</u> 10 ×	0.00 0.%
vine at 1st taste test	4	0.2	k o°		Mees (1.19
	4	0.2		Č	Wine at 1 st aste	- 11	0.4 °
Vine (wine 1)	-	0.2.		Ŭ	Wine at 1 st beste	8 8 V	
Raisin	4	3.7	~KCA ~		Wine C	≪15 ,	
laisin waste	4	1.24	§ 6.5.3.1 93	0	Raisin	5 C	3 .4
aisins	1	<u>8</u> .4 §		Ĉ	Raigin waste	- 40°	<u>a</u> 11.4
Trape juice	1	V 0.5 0	KČA	ŕ	Letty O C		0.1
ruit, washed	1	0.80	63.3.1-04			Ô. 'n	-
elly	JØ	~ <u>0</u> .1	The state of the s	, C		Ş <u>.</u>	_
omace wet	×2	32 ~		al y		<u> </u>	_
ees /		1.95	Í ÁČA O	-		Q -	_
nust 📎	A0 ()	0.9	65.3.1-40	ſ	<u>, v. , v</u> .	2-	_
Vine bottled		Ø.7	8 & X	Ô	<u> </u>	Š -	_
vine at 1st taste test 🔊	02	₩0.8 _@ ,		¥	O X X	-	_
lust a	2 8	1.90	N 2			-	_
omace, grape 🔊 🐧	2^{\sim}	3.4	× KCA	8		-	_
Wine at bottling	2	Ø.34 (6.5,3.1-12	~	\$ -\$	-	_
Vine at 1st taste test 🖇 ,	O_2	© _{0.34} %		2	Ö.U	-	-
Aust 🗞	2,0	1,0	No.		×-	-	-
omace grape	ALY .	Q.5	KCA	S C	~~-	-	-
Vine & Bottling	ÔŽ	0.41	§ 6.5.30Î-13 ¥	ľ	<u> </u>	-	-
Vine at 1st taste test		J<0.30	KCA 6.5.01-13 *		A -	-	_
		<0.24		~	"	-	_
Champagne after		©0.26	KCA	ĴÇ,	r	-	_
Champagne after softling	õ,	0.26 C	[∞] 6.5.5¥-14 (F	-		
	\mathbf{p}		OKCA O			-	-
Vine O		0.5%	%CA %		-		
rocessing factor calc	ulatQd	according	🕼 tồ y the	;	following equation	on:	
rocessing factor calc Residue concentration in the	processed	product [i "Ş				
Residue concentration	vin the RAC	$\left[\frac{mg}{kg}\right]$	~~				
imated values " <xxx" are="" cons<="" not="" td=""><td>sidere (Cin o</td><td>verall mean</td><td>calculation</td><td></td><td></td><td></td><td></td></xxx">	sidere (Cin o	verall mean	calculation				
Å 1 [\]	Û j	, Çi k	Ş″				
	Ç"						
	× L	~Q~					
rocessing factor calc Residue concentration in the Residue concentration in the residue concentration imated values " <xxx" are="" con-<br="" not="">the set of the set of t</xxx">	Ĩ						
N & A	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~						
	S) 1						



Data Point:	KCA 6.5.3/16
Report Author:	
Report Year:	2007
Report Title:	Determination of the residues of AE C656948 in/on apple that and the processed
	fractions (fruit, washed; raw sauce; sauce; washings; strain rest; juice; pornace,
	wet; pomace, dried; raw juice; fruit, dried, peel rest; fruit, peeled) afters
Report No:	RA-3605/06
Document No:	<u>M-295672-01-1</u> & A X X
Guideline(s) followed in	EU-Ref: Council Directive 91/414/EEC of July 5, 1991, Anne II, par A, section
study:	
	Residues in or on Treated Products, Food and Feed Pre-Registration:
	SANCO/3029/99 Rev. 4, 2000-07-11
Deviations from current	none a rational statement of the rational st
test guideline:	
Previous evaluation:	yes, evaluated and accepted a contract of the second s
GLP/Officially recognised	Yes, conducted ander GIP/Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q
Data Point:	KCA 6,53/17 0 0 0 0
Report Author:	
Report Year:	
Report Title:	Depermination of the residues of AE C650948 in on apple fruit and the processed
· Ø	fractions (fruit, washed, raw sauce; save; washings; strain rest; juice; pomace,
	Divet; pomace, dried; faw juice, fruit, dried, per rest, druit, peeled)
Report No:	RA-3606/06
Document No 🏷 🔗	<u>MQ29571Q01-1</u> % & & @
Guideline(s) followed in	EU-Ret Council Directive 91/914/EEC of July 15, 1991, Annex II, part A, section
study:	6 and Annex off, part A, section 8
Ê ^V	Reodues in or on Treated Broducts, Food and Feed Pre-Registration:
	\$ANCO3029/98 Rev. 4, 2000,07-11
Deviations from current	none \mathcal{O}^{*} \mathcal{O}^{*} \mathcal{O}^{*}
test guideline:	<u> </u>
Previous evaluation:	yes evaluated an acceptor
Y Y	
GLP/Officially recognised	Yes, conducted and coll P/Officially recognised testing facilities
Acceptability/Reliability.	
· "	
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
Cast System	

Test System Balance studies of processing of apple ato juice, sauce and dried fruit were conducted to determine the transfer of fluopyram (AE C656948) and its metabolites fluopyram-benzamide (AE F148815, FLUbenzamide), the pyram-pyricyl-carboxylic-acid (AE C657188, FLU-PCA), fluopyram-pyridyl-aceticacid (BCS-&A 10139, FLU-PAA), from apple fruits into processed fractions. Trials summary is presented of Table 6.5.3–49.

Juice, sauce and fruit dried were produced from apples obtained from 4 different trials located in Southern and Northern Europe. The processing of apple fruits into fruit (washed), raw sauce, sauce,

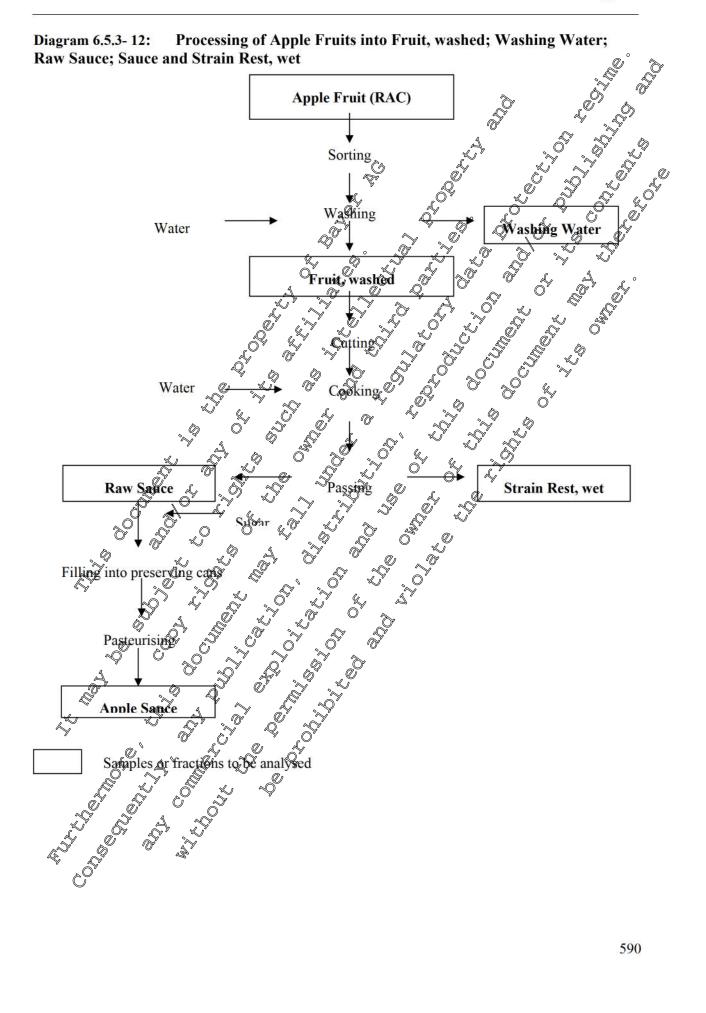


washings, strain rest, juice, pomace (wet and dried), raw juice, fruit (dried), peel rest and fruit (peeled) was performed in the Food Processing Laboratory (FPL) of BCS-D-ROCS in Monheim. The washing of apples simulated household processing whereas the apple preparation of juice, sauce, and fruit aried simulated the industrial practice at a laboratory scale.

Sauce production: The apples were washed in lukewarm standing water. The washed apple were out with a knife into small pieces and were heated after addition of water to 98 aloo°C for 40 min, After blanching the apple pulp was passed through a strainer to separate raw sance and strain set. The raw sauce was mixed with sugar, filled in preserving cans and afterwards pasteurized in an autoclave. Juice production: The deep-frozen apples were washed in lukewarm standing water The washed faits were crushed into mash in a cutter and afterwards warmed up to 40° G for 30 - 40 mm. The warm apple mash was then pressed in a high-pressure press into raw juice and pomace, wet The web pomace was dried in a fan-assisted oven at about 100°C. The raw juice shortly was heated to 80 4 90°C and then cooled down to 45-50°C. The sample was enzymated by adding the enzymes Pectinex XXL and Amyrase AG300L. After 20 h cooled storage, the sample was sentrifuged and the supernational was cleared by ultra-filtration. Thereupon, the filtrated juice was passeurised in a plate heat-exchanger **Dried fruit production:** Ø

The lightly defrosted apples were peeled with a krife and the apple cores were removed. Subsequently The processes are described in detail in Diagram 6.5.3-12 to Diagram 65.3-14. the fruits were cut into 5 to 7 mm slice To prevent enzymatic reactions, exidation and to save the vitamins a treatment with sulphite solution (w = 0.00) and citric acid solution (w = 0.00) followed. The treated apple slices were thoroughly washed in standing lukewarm water and the washed apple slices







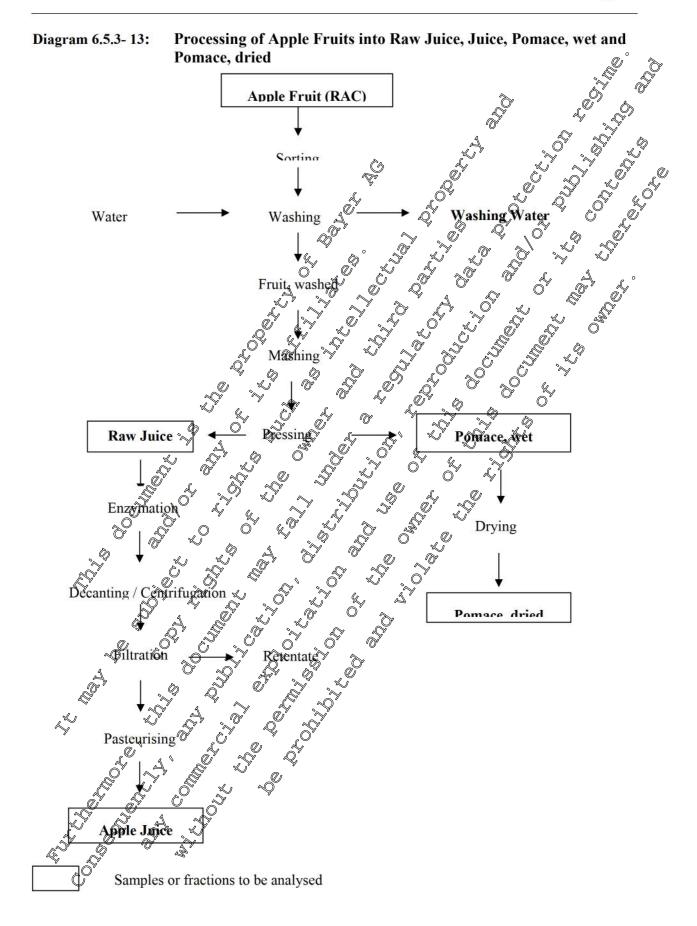
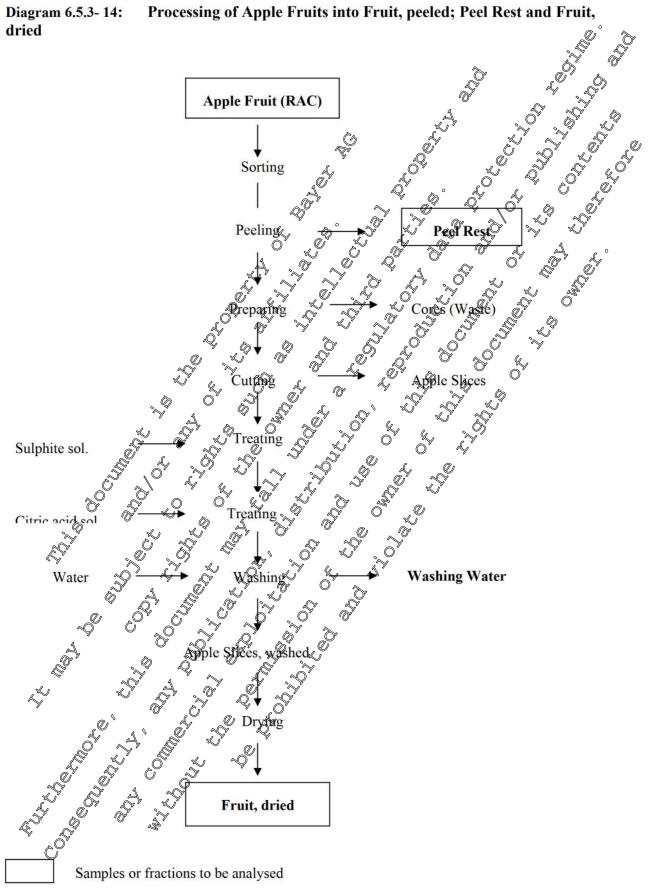




Diagram 6.5.3-14: Processing of Apple Fruits into Fruit, peeled; Peel Rest and Fruit, dried





## **Residue analysis**

Residues of fluopyram and its metabolites were determined by LC-MS/MS according to method , 2007, M-295145-03-1, see MCA section 4.1.2). Full details and acceptable 00984/M001 ( validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues were extracted from 10 g of sample material by wo successive extractions using of ghigh blender with a mixture of acetonitrile:water (4:1; v:v)

Subsequently, the raw extracts were diluted 10-fold by adding internal standard solutions:

- One dilution and an additional clean-up step were performed under acidic conditions L) determination of FLU-PCA Another dilution was performed under basic conditions for determination of fluopyram, FLUdetermination of FLU-PCA
- benzamide and FLU-PAA Ő Ø

Residues were quantified by reversed-phase chromatography coupled with and mass spectrometry (MS/MS) with electrospray ionisation@One mjectiof in positive electrospray ionisation allowed the determination of fluopyram, FLU-benzamide and FLU-PACA. Another infection in negative electrospray ionisation allowed the determination of FLO-PCA under different conditions

The quantitation was carried out by internal standard ation using stable abelled internal standards in pure solvent. Ŵ Ň 0

The Limit of Quantification (LOQK was QOI mg/kg for Buopyram and its metabolites, all calculated as parent equivalents and for all matrices.

O NO Recovery findings in apple fruits and in processed commodities were within guideline requirements (70-

Recovery findings in apple fruits and in processed commodities were we 110%, RSD <20%). Betails of the ecovery results are summarised in the covery results are



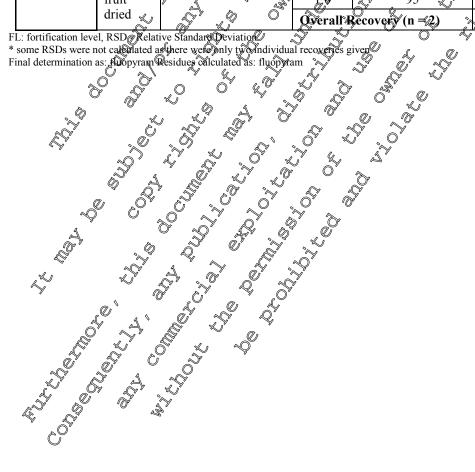
A CONSTRUCTION OF THE OWNER OF

ected in amples rank of the second of the se Table 6.5.3- 43 to Table 6.5.3- 46. No residues above the LOQ of 0.01 mg/kg could be detected in any of the corresponding control samples. The storage period of deep frozen processed samples ranged



Table 6.5.3- 43:	Recovery results for fluopyram in apple fruits and processed commoditie	es of
apple sauce, apple	juice and fruit dried production	a

Report No.	Sample Material	Matrices covered	FL	Single Values	Mean ≪Yalue	RSD %	S LOG
Report 10.	Material		[mg/kg]	[%]	© [%]	[%]	[nog/kg]
Analyte: fluo	pyram (AE	C656948)			r		× ×
			0.01	102; 95; 117; 177	108 🧞	©10.3 Ø	
	apple	apple fruit apple fruit, washed	0.10	103; 96	100		
	fruit	apple fruit, washed	1.0	93:85	2°	St.	
			Overall R	ecovery (n = 8)	<b>Q</b> 02	ح‱9.8	
	,	apple raw sauce apple sauce	0.01	~ ¹ 130°	°, , 0°	Ô	Ĩ
	apple sauce		[♥] 0.10 °	29 29 LT	ð		0.01
RA-2605/06			Overall R	ecovery $(n = 2)$	À 06 🔍	- 4	¢
RA-2606/06	apple juice	apple washings	0.01	<u>♀101</u>	, - ^{O'}		Ó
RA-3605/06			¥ 1,0, ¥	LO3 103 3	<u> </u>	k) - L	0.01
RA-3606/06	Juice	apple raw juice	Overall R	ecovery $(n = 20)$	<b>102</b>	× - 0	
		apple straun rest	°≫0.01 ₩	N 1090 6	¥ .5	. L	
	pomace, dried	apple pomace wet appl@pomace/dried @	1.0	27 AQ3 2	a 0- <i>(</i> ,	- ~	0.01
	anea	apple peel rest	Overall R	ecovers (n = 2)	⁰ 105 0	-	
	apple		° 0.01	1157 ~	Ĵ. Ĉ	-	
	fruit 🕅	apple fruit, drigd		5 5 J	- -	-	0.01
	dried 🔬	y providence of the standard Deviation	Qverall R	ecovery (n = 2)	105	-	



~



Table 6.5.3- 44:	Recovery results for fluopyram-pyridyl-acetic acid in apple fruits and
processed commoditie	s of apple sauce, apple juice and fruit dried production

Report No.	Sample Material	Matrices covered	FL	Single Values	Mean Value	RSD	STOO
			[mg/kg]	[%]	<b>@</b> [%]	[%]	[mg/kg]
Analyte: fluo	pyram-pyr	idyl-acetic acid (BCS A	A10139)	Ő	<u>y</u>	~	
			0.01	82; 83; 99; 98	91	Õ10.2 🖉	
	apple	apple fruit	0.10	94; 90	92 🔬		
	fruit	apple fruit, washed apple fruit, peeled	1.0 🕅	90; 80	85	. <del>S</del>	
		upple fluit, peeled	Overall R	ecovery (n = 8)	. 90	<b>8.1</b>	(0.01)
	_		0.01	×84 @	ð Á	-	Å.
RA-2605/06	apple sauce	apple raw sauce apple sauce	0.10	0 ⁷ 8 ⁴ 7 m	×.	¢.	0.01
101 2005/00	sauce	apple sauce	Overall R	covery (n = 2)	84	× - 4	9
RA-2606/06	_	apple washings A	0.01	Q 86 0	<u> </u>	Į Į	a second
RA-3605/06	apple juice	apple juice	7 1.0	_~~~ 8 <i>2</i> → O	×		\$ \$ 0.01
	Juice	apple raw jui		eçovery $(n = 2)$	85	Ç - Ö	
RA-3606/06		apple straiprest	\$0.01	~ 116 J	\$ - Q	<u>D</u>	
	pomace, dried	apple pomace, wet apple pomace, dried	1.00	\$° \$0 0		°~-	0.01
	dified	apple poinace, aned	Overall R	ecovery(n = 2)	8100 %	- 1	
	apple		£ 0.01	× 112 . ¢		-	
	fruit 🔩	apple froit, dried	1.0	20 20 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		-	0.01
	dried		Overall R	$\frac{1}{2} \frac{1}{2} \frac{1}$	\$101	_	

FL: fortification level, RSD - Relative Sundard Deviation * some RSDs were not calculated as there were only two individual recoveries given. Final determination as: FFC PAA Residues calculated as: fluopyram



Table 6.5.3- 45:	Recovery results for fluopyram-benzamide in apple fruits and	processed
commodities of apple	sauce, apple juice and fruit dried production	<i>a</i> [°]

	Sample	Matrices covered	FL	Single Values	Mean	RSD ≽	
Report No.	Material	Matrices covered	[mg/kg]	[%]	Value	[%]	[ <b>pg</b> /kg]
Analyte: fluo	pyram-ben	zamide (AE F148815)		Ő	ř	a a	
			0.01	94; 82; 97; 95	93 🧞	© 8.2 Ø	\$2
	apple	apple fruit	0.10	89; 89	89 🖑	2	. Ôn
	fruit	apple fruit, washed apple fruit, peeled	1.0	100687	2ª	ų,	
			Overall R	ecovery(n = 8)	<u></u>	[≈] 6.9°	
			00.01	~~ ⁹ 90 °°	°, °, °,	Ô	Ő
RA-2605/06	apple sauce	apple raw sauce apple sauce	[♥] 0.10 °	S & v	ð	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.01
	sauce		Overall R	ecovery (n = 2)	89		e °
RA-2606/06		apple washings	~0.01~°	/ ^Q 100 <u>S</u>	, - O.	ų.	Ő
RA-3605/06	apple juice	apple juice	1.0		Z.E	U	0.01
	Juice	apple raw junce	Overall R	ecovery $(n = 20)$	<b>6</b> 99 0	* - «	
RA-3606/06		apple straun rest 🔊	≫ _{0.01} ∞	<i>₽</i> 968 8	Ú.	Ľ,	
	pomace, dried	apple pomace wet appl@pomace/dried @	1,0	\$ <b>\$</b> \$	»O- /»	-	0.01
	uneu	apple peel rest	Overall R	x cover $x$ (n = 2)	° 96 0	-	
	apple		¢ 0.01 V	⁵ 97, ⁵	ţ.	-	
	fruit 🔌	apple fruit, dræd	1.0	<u></u>	~~-	-	0.01
	dried 🔬	ye Standar@Deviation	Qverall'R	ecovery (n =<2)	95	-	

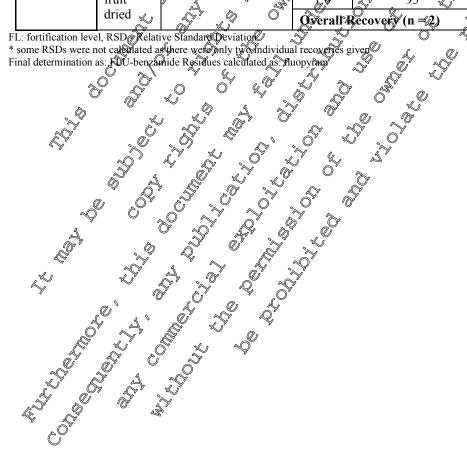




Table 6.5.3-46:	Recovery results for fluopyram-pyridyl-carboxylic acid in apple fruits an	nd
processed commodit	ies of apple sauce, apple juice and fruit dried production	7,

Report No.	Sample Material	Matrices covered	FL	Single Values	Mean Value	RSD %	S rog
Report no.		s	[mg/kg]	[%]	Q [%]	[%]	[mg/kg]
Analyte: fluo	pyram-pyri	idyl-carboxylic acid (Al	E C657188)		ř		
	apple fruit	apple fruit apple fruit, washed apple fruit, peeled		89; 81; 92; 12 100; 10 92: 0 Recovery n = 8)	93 102 2 2 95	013.6 ¢ 	20.01 x 2 2 2 2 2 2 3 2 3 0.01
RA-2605/06	apple sauce	apple raw sauce apple sauce	0.01 0.10 ° Overall R	$\frac{99}{3}$	€ - 0° © °96 ,(	- 4	0
RA-2606/06 RA-3605/06	apple juice	apple washings	0.01 19 Overall R	$\frac{94}{163}$			\$ 0.01
RA-3606/06	pomace, dried	apple juice apple raw junce apple strain rest apple pomace, swet apple pomace, dried apple peel rest	Vo.01 1 Overall R	→ 106 C	-35 -0- -0- -0- -0- -0- -0- -0- -0- -0- -0	-	0.01
	apple * fruit & dried \$	apple fruit dried		$\begin{array}{c} & & & & \\ & & & & \\ & & & & \\ & & & & $	92	-	0.01

FL: fortification level, RSQ - Relative Standard Deviation * some RSDs were not chculated as there fore only two individual recoveries given Final determination as TLU-PCA Residues calculated as: theopyram ×,

#### Findings:

Ś In apple this used for processing, residues of fluopyram were between 0.08 and 0.21 mg/kg. A mean of 34 % of the absolute resided was recovered in the washing water. A major part counting for 69 % of the initial absolute osidue temained in the washed fruit

Ò

During apple sauge production 20% of the absolute residue estained in the strain rest whereas 55 % were transferred into raw sauce, leading to values between 0.05 mg/kg and 0.05 mg/kg in the final product O V V apple sauce. Õ

With apple juice production a mean of \$1 % and 5 % of the absolute residue was recovered in wet pomace and dried pomace respectively. A minor part counting for only 16 % of the initial absolute residue Sould be found in raw fuice, leading to valoes below the LOQ of 0.01 mg/kg in the final product juice. O

During apple dried fruit production a mean  $\rho D67$  % of the absolute residue was recovered in the peel rest whereas 20% of the initial absorbte regidue remained in the peeled fruit leading to values between 0.07 mg/kg and 0.13 mg/kg in the final product dried apple fruit.

# Conclusion

Residue values of flugpyrant in apple fruits and processed commodities of juice, sauce and dried fruit production are summarized in Table 6.5.3-47. Ò ŝ

#### Assessment and conclusion by applicant:

The study is acceptable.



Table 6.5.3- 47:	Residues of fluopyram and metabolites in apple fruits and processed
commodities of apple	sauce, apple juice and fruit dried production

Country	Crop		Residues (mg/kg) expressed as fluopyram equivalents					
	<b>.</b>	DALT		••• •				
Study No. Trial No.	Portion analysed	DALT (days)	fluopyram	pyridyl-acetic acid	benzamide	x pyrdyl- carboxylic acid		
Belgium	fruit	(uays) 3	0.11	< 0.01	< 0.01			
RA-3605/06	fruit, washed	3	0.06	< 0.01 (0.01)	< 0.01 0			
R 2006 0396/7	raw sauce	3	0.06	< 0.01	< 0.01	$-\frac{1}{3}$ $-\frac{1}{6}$		
R 2000 0370/7				d( ))				
	sauce	3	0.04	< 0.00%				
	washings	3	0.00	< 0.01				
	strain rest	3	02.0	< 0.01	$Q^{<0.019}$	< 0.901		
	juice	3	≪∕0.01		~~~ <u>~</u> ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	\$0.01		
	pomace, wet	3	& 0.19¢	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	∛ 01.01 کړ	∞€ 0.01		
	pomace, dried	3	0.69		@0.01			
	raw juice	3		~~0.01	Q < 0.0₽	<0.01		
	fruit, dried	3	$\sim 0.07 \sim$	0.01	$\bigcirc$ < $\bigcirc$ 0.01	\$0.01		
	peel rest	30'	× 0.60	× <0001 ×	0:01	0.01		
	fruit, peeled	_O¥ {	<u>v 0.02</u>	r 60.01 0	0.01	< 0.01		
United	fruit	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.21	× 0.01	~ < 0,69r	× 0.01		
Kingdom	fruit, washed	× 3 Ø	ې 0.09	< 0,04 ~~		< 0.01		
RA-3605/06	raw sauce	~ <i>3</i>	0.08° ,	$\sim \sim 0.01$	≈0.01 %	< 0.01		
R 2006 0413/0	sauce 🔊	<u>3</u>	¢ 0.05 °	0.01	o = 0.01 (C)	< 0.01		
	washings	° 3 5	0.04	< 0.01	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	< 0.01		
	strain rest		<ul> <li>√ 1.0√</li> <li>&lt; 0√</li> <li>&lt; 0√1</li> <li>&lt; 0√1</li> </ul>		v <b>X0</b> .01	< 0.01		
	juice 🏑 🔊	C)	O <195,191 . ⊌		0.01 🔊	< 0.01		
	pomace, wet O		Q.26 🔬	Q 0.0 b	× 0.01	< 0.01		
	poppace, dried		1.2	Q < 0.01	< 0.01	< 0.01		
	raw juice	3	0.03	s <@,01 ∧S	< 0.01	< 0.01		
~		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	€ ¹ € ¹ 3 ~	<b>€</b> 0.01 [™]	< 0.01	< 0.01		
C	peel jest	° 3 ° ≫	<u></u>	$\bigcirc < 0.0 $	< 0.01	< 0.01		
<u> </u>	fruit, peeled		\$1.6 \$70.05\$	< 0,01	< 0.01	< 0.01		
Southern	fruit 🖉 🔊	<u></u>	0.08	\$ \$9.01	< 0.01	< 0.01		
France	fruit, washed	3	× • 0.11	0.01 کچ	0.03	< 0.01		
RA-3606/06	raw Sauce 🗸 🖌	3.0	<i>‱</i> 0.07 <i>∽</i>	ً≪ 0.01	0.02	< 0.01		
R 2006 0399/1	sauce	ί 🔊	0.05	<ul><li>&lt; 0.01</li></ul>	0.02	< 0.01		
(	washing 5	63	> <0,01	× < 0.01	< 0.01	< 0.01		
~Õ	straincrest	× 3 ~	\$\$ <b>0</b> .75	< 0.01	0.03	< 0.01		
.1	juice 🕉 👡		~~ 0.04°	< 0.01	0.01	< 0.01		
E C	pomace wet	Ò,	× 0.33	< 0.01	0.02	< 0.01		
	pomače, dried 💙	<u>∼</u> 3 ∠	° <b>∯</b> 95	< 0.01	0.09	< 0.01		
s the	raw juice	@" 3 _O"	×××0.03	< 0.01	0.02	< 0.01		
" <b>\</b>	fruit, dried	3″≫∕	0.07	< 0.01	0.02	< 0.01		
6	geel rest		<b>6</b> ∕ 0.64	< 0.01	0.09	< 0.01		
~	fruit, peèled	<u>الم</u>	♥ 0.02	< 0.01	0.01	< 0.01		
	fruit, washed raw sauce washings strain rest juice pomace wet pomace dried raw juice fruit, dried peel rest fruit, Aceled	, ~Ç						



Country	Crop		Residues (	(mg/kg) expresse	d as fluopyram	equivalents
Study No. Trial No.	Portion analysed	DALT (days)	fluopyram	pyridyl-acetic acid	benzamide	poridyl- carboxylicarcid
Italy	fruit	3	0.11	< 0.01	0.01	<0_Q1
RA-3606/06	fruit, washed	3	0.04	< 0.01	× 0.01	≪ <b>0</b> ?:01
R 2006 0414/9	raw sauce	3	0.05	< 0.01	< 0.01	0.01
	sauce	3	0.04	< 0.01	<0.01 °, ^{O°}	$2^{3} < 0.01^{3}$
	washings	3	0.03 🖉	< 0.01	< 0.01	$\sim$ < $0.91$
	strain rest	3	0.75 🚿	< 0.0.0	< 0,01 🌋	9 ×0.01 ×
	juice	3	< 0.0	< 0,0	< 9.01 .	Ø.0≰
	pomace, wet	3	0.2	< <b>Q</b> 01 ~ °	\$0.01 ×	Č < 0, Ø2
	pomace, dried	3	0084	~~ 0.01 °	Q 0.Q10	© < \$01
	raw juice	3	0.03 °		⊘~ < <b>Q.0</b> 1	<u>کې چ</u> 0.01
	fruit, dried	3	× 0.10	$\sqrt{2} < \alpha 01$	v ≪00.01 ×	< 0.01
	peel rest	3	0:63	ž <b>20</b> .01 🔊	⁰⁰ 0.01	→ 0,01°
	fruit, peeled	3	> ~ 0.03	<u>~</u> ≪0.0 <u>1</u>	\$ < 0.0 ×	<b>2 2 0</b> .01
DALT = days af	ter last application	<u>j</u>				

Average factors of 0.1, 0.43 and 0.75 were calculated for the transfer of duopyram from apple fruits into juice, sauce and dried fruit respectively. The transfer factors of fluop ram from apple ray agricultural commodity into juice, sauce, dried fruit and the processed by products are summarised in Table 6.5.3-Ŵ 48.  $\bigcirc$ Ô

Transfer factors for the residue of fluopyram in processed commodities of Table 6.5.3-48: Ő apple juice, sauce and dried fruit production Ň 6 **&** .

Sample material RA-3605/06 R2006 0396/7 Regium Ra-3605/06 R 2006 0443/0 R 2006 0 R 2006 0								
	<b>R</b> 2006 0396/7	605/06 R 2006 0443/0	<b>R</b> 2006 (\$999/1	606/06 R 2006 0414/9	Mean			
		United Kingdom		Italy				
fruit, washed	<u> </u>		01.5	0.4	0.70			
washing water	0.20 2		<u>∼</u> 0.1	0.2	0.15			
raw sauce 🥎		0.4	0,9	0.4	0.55			
sauce	×0.4 ×		<b>∀ 0</b> .7	0.3	0.43			
strain rest, wet	6.7	× 48	<b>O</b> 10	6.6	7.03			
raw juice		×0.1	0.4 x	0.2	0.23			
juice 🔊 🕻	) <u>6</u> .1* ~~		0.1*	0.1*	0.10			
pomace, wet	0~1.7 _{~0} ~	Le la o	4.3	2.3	2.38			
pomace, pied		0 25/4	13	7.4	7.78			
fruit peeted	Q.2 ~~~	\$\$0.2 ~ V	0.3	0.2	0.23			
peel rest 🔬	× ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	0 7.4 Y	8.6	5.5	6.70			
fruit, dried	<del>ک</del> 0.7 ک	~~× ,006°	0.9	0.8	0.75			

 Irun, aned
 0.70°
 * (16)
 0.9
 0.8
 0.75

 Mean values calculated based on counded results
 *
 For calculation of the cansfer factor the residue in the processed product was set at the LOQ (0.01 mg/kg)
 *
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •
 •

BAYER

Page 601 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No. / Location / EU zone / Year	49: Resu Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest				Dates of treatment or no. of treatments and last date	Growth	Portion analyzed	Growth Stage at sampline	~ ¥	CG ° Residues	0 ⁵⁰	PUD CUD	PP() Glays)	Details on trial
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL 🛛		ð Ør	j.n.c.		fluoryfam Os AE C656948	FLU- benzamide as AE C656948	PCX as AE C656948	PAA as AE @656948	(d)	(f)
2 2006 0396/7 0396-06 Belgium 3-6220 Fleurus Hainaut) Europe, North 7 20006	C	1) 01.03.1991 2) 25.04.2006 - 30.05.2006 3) 01.09.2006 - 30.09.2006	125.0	9279/1 7.1900	(12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50 12.50	2006/7 ( * ¹ ) ^(C)	WREL		80 80 89 89 89 89 89 89 89 89 89 89 89 89 89	0.09 EDD	<0.01 JT ^{III} <0.0C 9.01 <0.01	<0.01 ₩	<0.01 0.01 <0.01 <0.01 <0.01 <0.01	1 <u>3</u> 7	(g) RA-2605/06 (h) SC 500 (i) Application method: Spraying (j) Analytical method 00984/M001 (k) LOQ:0.01 mg/kg (m) Storage:
	Ţ	t may be armore i armore i armore i armore i with	BUD COP	econ Y T ⁱ Nocom			tra and tra	whole fruit, washer raosauce sauce washangs stain rest juice	2 89 E 2 89 E 8 89 89 89 89 89 89	0.06 0.06 0.04 0.01 0.76 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	$\frac{3}{3}$ $\frac{3}{3}$ $\frac{3}{3}$	whole fruit, washed 249 days washings: 249 days strain rest: 249 days raw sauce: 249 days raw sauce: 249 days pomace, wet: 249 days pomace, dried: 249 days
	~	ermore'	1 OLOY	y c ^j d ^j	Permi	ssired	Orpe	pomace, wet pomace, dried raw juice	89 89 89	0.19 0.60 0.02	<0.01 0.01 <0.01	<0.01 <0.01 0.01	<0.01 <0.01 0.01	<u>3</u> <u>3</u> <u>3</u>	peel rest: 249 days juice: 249 days fruit, peeled: 249 day fruit, dried: 249 day fruit: 247 days
	EUICTLA EUICTLA	equeir c	thout	Ltr Ltr	, P ^T			fruit, dried peel rest	89 89	0.07 0.60	<0.01 0.01	<0.01 <0.01	<0.01 <0.01	<u>3</u> <u>3</u>	

Page 602 of 801 2021-02-26



Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest	Applicati	on rate per	treatment	Dates of treatment or no. of treatments and last date	Growth stage at last treatment	anadyzed	Growth Ostage at	AG	Residues (	gi ^{ls} mg/kg) ∢O ^t €	JJD:	PHÍC (Hays)	Details on trial
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	(c) 0 P		, at C	1ect	C656948	FLU- benzamide as AE C656948	FLU- PCA as AE C656948	FLU- PAA as GoE C656948	Jr.	f)
								fruit	\$2-89	CO2	5004×	692	0.01	<u>3</u>	
R 2006 0413/0 0413-06 United Kingdom GB-SG8 8SS Royston (Herefordshire) Europe, North F, 2006	Apple Jonathon	1) 01.12.1994 2) 05.04.2006 - 30.04.2006 3) 01.10.2006 - 25.10.2006 - 25.10.2006 - 25.10.2006	125.0 125.0 125.0 125.0 25.0 200 200 200 200 200 200 200 200 200 2			F Eall	UIDU ETIDU BIDD	treat	87 87 87 87 87 87 87 87 87 87 87 87 87 8	0.09 0.24 0.21 0.13 0.01 0.09 0.09 0.08 0.05 0.04 1.0	<0.01 <0.01 <0.01 0.01 0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 0.01 0.01 0.01 0.01 0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01 <0.01	$^{\circ} 0^{*}$ $^{\circ} 0^{*}$	(g) RA-2605/06 (h) SC 500 (i) Application method: Spraying (j) Analytical method: 00984/M001 (k) LOQ:0.01 mg/kg (m) Storage: whole fruit, washed: 215 days strain rest: 215 days straw sauce: 215 days raw sauce: 215 days raw juice: 215 days pomace, wet: 215 days pomace, dried:
	2	*	M ¹ P	PULO.	CXP 1	55 ^{10¹}	9.Dg	juice pomace, wet	87 87	<0.01 0.26	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<u>3</u> <u>3</u>	215 days peel rest: 215 days juice: 215 days fruit, peeled: 215 days
		ant of the st	I W	Clor	OCLU	10 ^{1^t}		pomace, dried	87	1.2	< 0.01	< 0.01	< 0.01	<u>3</u>	fruit, dried: 215 days fruit: 213 days
		T. OF LI	MARIE	me	10 m	J.		raw juice	87	0.03	< 0.01	< 0.01	< 0.01	<u>3</u>	-
	EULE	edner.		rt». 1 pe	P ^{II -}			fruit, dried peel rest	87 87	0.13 1.6	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<u>3</u> <u>3</u>	

Page 603 of 801 2021-02-26



Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

															°
										PC.	~*	A O _{IN}		a e	JITT ADO
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest	Applicatio	on rate per	treatment	Dates of treatment or no. of treatments and last date	Growth stage at last treatment	analyzed	er .	Jail .	Residues (	mg/kg)	- JUO	PHI) (days)	Details on trial
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	(c) Ő	perty aft		Ject	fluonveam ASAE C656948	FLL- benzamide as AE C656948	FLU- PCA as OAE C656948	FLU- PAA as SeE C656948	0»°	F ^{OT} (f)
						LL it	p D	fruit peeled	\$2.87	K ⁰³⁵	<0042 x	< 602	<0.01 ×	<u>3</u>	
R 2006 0399/1 0399-06 France, south F-82370 Reyniès (Midi- Pyrenees) Europe, South F 2006	Apple Granny	1) 01.01.2003 2) 01.04.2006 - 25.04.2006 3) 05.10.2006 - 10.10.2006 - 10.10.2006 - 10.10.2006	125.0 125.0 125.0 125.0 125.0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	STROL !		E LAC	JILOU JILOU	E and a c	L LL	this	<0.01 Jilli 0.01 0.01	<0.01 <0.01 <0.01	<ul> <li>&lt;0.01</li> <li></li></ul>		(g) RA-2605/06 (h) SC 500 (i) Application method: Spraying (j) Analytical method: 00984/M001 (k) LOQ:0.01 mg/kg (m) Storage: whole fruit, washed: 214 days washings: 214 days strain rest: 214 days raw sauce: 214 days raw sauce: 214 days raw juice: 214 days pomace, wet: 214 days pomace, dried: 214 days peel rest: 214 days
		ao ^{re 1}	ardy	Cil Ql	eser hi	\$9°°ed	e Ore	wet pomace, dried	89	0.95	0.09	< 0.01	<0.01	<u>3</u>	juice: 214 days fruit, peeled: 214 days fruit, dried: 214 days fruit: 258 days
	A THE	CIT CIT		the the	Y TON			fruit, dried	89 89	0.03 0.07	0.02 0.02	<0.01 <0.01	<0.01 <0.01	<u>3</u> <u>3</u>	nan. 250 days
	CODE	equi ant	thout	, De				peel rest	89	0.64	0.09	<0.01	<0.01	<u>3</u>	603

Page 604 of 801 2021-02-26

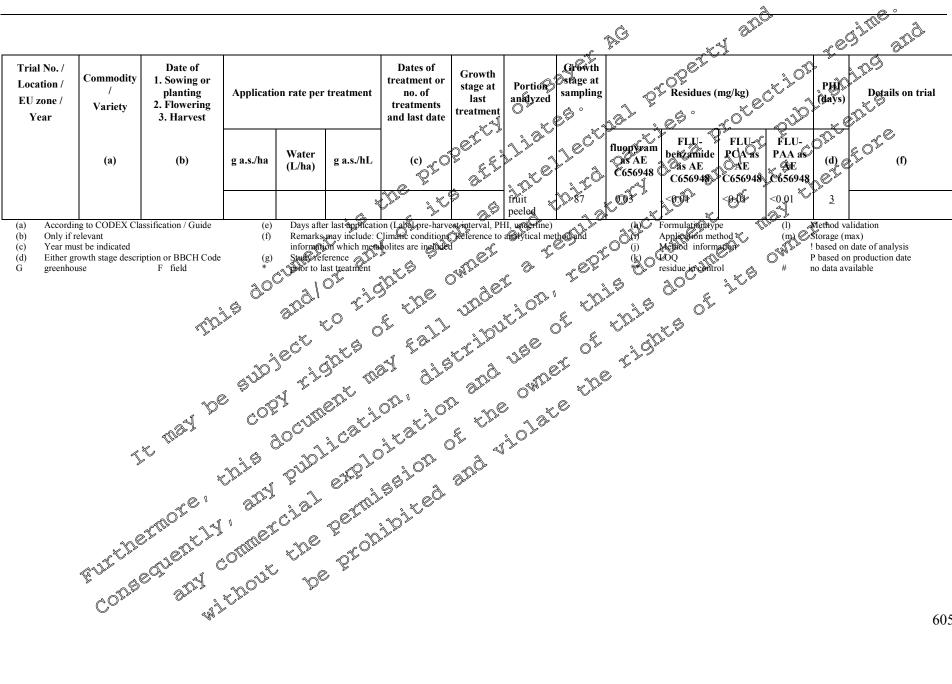


Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

													<b>`</b>		ruopyrum
										P.C	~	V. OID	<u>}</u>	, C	J ^{1 Me} and
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest	Applicati	on rate per	treatment	Dates of treatment or no. of treatments and last date	Growth stage at last treatment	Portion analyzed	sampling	Dal P	Residues (	mg/kg)	a Ulo	PHI (Mays)	Details on trial
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	(c) 0	perti aft		Ject i To	fluorypam Or AE C656948	FLU- benzamide as AE C656948	FLU- PCA as OAE C656948	FLU-	OLL	f (f)
					*	in it		fruit peeled	\$2.89	KOZ "	LOF F	< <del>6</del> 02	<0.01	<u>3</u>	
R 2006 0414/9 0414-06 Italy I-37059 Zevio (Veneto) Europe, South F, 2006	Apple Golden Rainders	1) 1998 2) 11.04.2006 - 25.04.2006 3) 10.09.2006 - 30.09.2006 - 30.09.2006 - 30.09.2006	125.0 125.0 125.0 125.0 125.0			t De	UIIde UIIde UIIde	7 027 C 9 2	t Di	0.05 0.04	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	<0.01 <0.01 0.01 <0.01 <0.01 <0.01 <0.01 <0.01	$\frac{3}{7}$ $\frac{3}{10}$ $\frac{3}{2}$ $\frac{3}{2}$	(g) RA-2605/06 (h) SC 500 (i) Application method: Spraying (j) Analytical method: 00984/M001 (k) LOQ:0.01 mg/kg (m) Storage: whole fruit, washed: 246 days strain rest: 246 days straw sauce: 246 days raw sauce: 246 days
		TO T	c ^{os}	OCULL OCULL			E EDE	washings strain rest	87 87 87	0.03 0.75 <0.01	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	<u>3</u> <u>3</u> <u>3</u>	raw juice: 246 days pomace, wet: 246 days
	5	₽Ç [®]	n ^{jĝ}		1010			pomace, wet	87	0.27	<0.01	< 0.01	<0.01	<u>3</u>	pomace, dried: 246 days peel rest: 246 days
		@. 1		P. 7	et-r	GG ^{'J} OJ	Organ	pomace, dried	87	0.84	0.01	< 0.01	<0.01	<u>3</u>	juice: 246 days fruit, peeled: 246 days
		COLOT 13	1 02	CÌÓI	PETTU	DÌT		raw juice fruit,	87 87	0.03 0.10	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<u>3</u> <u>3</u>	fruit, dried: 246 days fruit: 290 days
	a the	L LERE L	ORDE	f.De	-oror			dried peel rest	87	0.63	0.01	0.01	<0.01	3	
	Colle	eor and	F DOUL	, de	») /			-							604

BAYER

Page 605 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram



605



ź

Data Point:	KCA 6.5.3/18
Report Author:	
Report Year:	2007
Report Title:	AE C656948 500 SC - Magnitude of the residue on apple processed commodities
Report No:	RAGMP033
Document No:	<u>M-299547-01-1</u>
Guideline(s) followed in	EPA Ref.: OPPTS 860.1520;
study:	PMRA Ref.: DACO 7.4.5 🕉 🖉 🖉
Deviations from current	none
test guideline:	
Previous evaluation:	yes, evaluated and accepted
GLP/Officially recognised	Yes, conducted under GEP/Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes O C O A A co

#### Material and Methods

An apple processing trial was conducted to measure the magnitude of fluopyram [N [2]3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)benzanide] residue in apples and apple processed commodities following exaggerated rate applications of AE C656948 500 SC to tomatoes. The test substance, fluoipyram 500 SC, is a suspension concentrate formulation containing 500 g ai/L.

Information on the trial site and the actual use pattern is provided in Fuble 653-50. Two airblast applications were made to apple trees in the treated plot using equipment customarily used to apply pesticides in this manner to apples. The first application was made to the apples at the beginning of ripening (BBCH & ), with a 6-day interval between the two applications. The test substance applications were applied at a target rate of 1.115 lb ai/x/application (1250 g ai/ha application) in a target spray volume of 35 (GPA) (327-655 L/10). The achieved total seasonal rate was 2.24 lb ai/A (2511 g ai/ha). This rate is equivalent to five times (5X) the foral maximum proposed label rate for a single growing season.

Table 6.5.3- 50:	Study Use	Pattern for AE C65	5948 ø	§ Apples.	•			
		XY O O	<b>S</b> pp	lication				
a degion			me 🧳	a)	(days)	Volume L/ha)	Rate A /ha)	Mix ⁄ant
Location: City, Stat NAKTA I NAKTA I Trial No.	Year's Endel	Sth Str	Plot Name	Rate lb ai/A (kg ai/ha	RTI ^b (d	Spray V GPA (L	Total Rat lb ai/A (kg ai/ha)	Tank Mix Adjuvant
North Rose,		Beginning of Fibl		1.125 (1.261)	0	65.3 (610)		
North Rose, New York GM04 Region 1 0-06P		ast C	TRT 5X				2.24 (2.511)	None
^a Trabing = Arst Appli		Airbl Advanced ast Ripening		1.115 (1.250)	6	65.2 (610)		



One control bulk apple sample and one treated bulk apple sample were collected at a 5-day pre-harvest interval (PHI) and shipped via overnight carrier to the processing facility. Prior to processing, random sub-samples of the control and treated bulk apple samples were collected for analysis, and the remainder of the apple samples were used to generate the required processed commodities of apple wet pomace and juice. In addition, samples of washed fruit, peeled fruit, applesauce, and dred fruit were generated for use in the dietary risk assessment for fluopyram. Processing was performed using procedures which simulated commercial processing practices. The resultant apple samples and processed commodities were analyzed to determine fluopyram residue.

The residue data for grape raw agricultural commodity and grape processed commodities were obtained using the analytical method for determining the fluopyram residue in that 00984 (M=283301-01-1), see MCA section 4.1.2) with modifications (M=207568-01-2)

Briefly, a 5-g aliquot of the crop matrix was extracted by blending fivice, each time with a mixture of acetonitrile/water (4/1; v/v). Each extract was filtered, the filtrates were combined, and an isotopically labelled internal standard was added. An aliquot of the mixture was loaded on a small &-18 solid phase extraction (SPE) cartridge and eluted into an HPLC vial with 0.1 % (aq.) asetic acid for analyse by LC/MS/MS.

The quantitation was carried out using sotopically labelled internal standards. The Limit of Quantitation (LOQ), defined as the lowest validated forthication level, was 0.01 mg/kg in all tester matrices.

Recovery of fluopyram from apples and apple processed commodities was measured concurrently with the set of samples to verify method performance. The validation and concurrent recovery data for fluopyram residue are summarized in Table 6.5.3-51. The data demonstrate acceptable method performance during sample analysis.

Recoveries	Mean Recovery ± Standard Deviation
<i>⊈</i> 95, 98, 104, 87, 92, 91, 93	94 ± 5
110, 108, 106	$108 \pm 2$
92, 90, 82, 78	$86 \pm 7$
96, 99, 97	97 ± 2
95, 92, 89	92 ± 3
107, 110, 108	$108 \pm 2$
99, 99, 94, 79, 77	$90 \pm 11$
95, 98, 74, 70	$84 \pm 14$
90, 87, 91	89 ± 2
103, 92, 101	$99 \pm 6$
93, 82, 88	$88 \pm 6$
87, 90, 94	$90 \pm 4$
	Recoveries           995, 98, 104, 87, 92, 91, 93           995, 98, 104, 87, 92, 91, 93           90, 99, 97           96, 99, 97           96, 99, 97           95, 92, 89           107, 110, 108           99, 99, 94, 79, 77           95, 98, 74, 70           90, 87, 91           103, 92, 101           93, 82, 88

 Table 6.5.3- 51:
 Summary of concurrent recoveries of Quopyram from apple fresh fruit and apple processed commodities

 apple processed commodities
 Summary of concurrent recoveries of Quopyram from apple fresh fruit and apple processed commodities

Final determination as: fluopyram Residues calculated as: fluopyram

The apple fresh fruit and the apple processed commodities analyzed in this study were held in frozen



storage for a maximum of 11 months prior to extraction, see Table 6.5.3-52.

T	able 6.5.3- 52:	Summary of Storage (	Conditions for apple	RAC and Apple Pro	ocessed 🖉	<i>A</i>
C	ommodities					O,

<u> </u>	ommountes				
	Residue Component(s)	Matrix (RAC)	Storage Temperature (°C)ª	Actual Study Duration (days) ^b	Limit of Demonstrated Storage Stability (days) ^c
	AE C656948	Apple Fruit	<-15°C	× 245	See Section IIA Point
	AE C656948	Processed Commodities	<-15°C	232-234 232-234	See Section IIA Point $G^{*}$

^a Temperature is the sample storage temperature from sample receipt at the analytical facility through the last extraction..

Actual storage duration = number of days between the vest and first extract date for RAC sample of number of days between processing and first extract date for processed commodity.

^c Demonstrated freezer stability in diverse crops is representative of the freezer stability of AE C656948 residues to be expected for the apple and apple processed commodities from this study

#### **Findings**

All control interferences were tess that the LOQ (<0.01 mg/kg) for apple fresh fruit and all the apple processed commodities.

The fluopyram residue data for apple fresh fresh and the apple processed common the solution of apple wet pomace, juice, washed fluit, preled truit, and dried fruit are summarized in Table 6.5.3-53.

Table 6.5.3- 53: Struct and apple processed commodifies residue data from the processing study with Quopyram.

	Commodity	Total Rate	fluopyram Residue (mg/kg)	Processing Factor ^a
Apple	NA ^b S		0.95 0.92 0.92 Avg: 0.93	NA
	Wet Popnace		2.22 2.11 2.09 Avg: 2.14	2.3 X
	Jance ()		0.43 0.37 0.44 Avg: 0.41	<1.0 (0.4X)
	Wasted Fruit		0.69 0.63 0.62 Avg: 0.65	< 1.0 (0.7X)
	Peeled Fruit		0.03 0.02 0.03 Avg: 0.03	<1.0 (0.03X)



RAC	Processed Commodity	Total Rate lb ai/A (kg ai/ha)	fluopyram Residue (mg/kg)	Processing Factor ^a
	Applesauce		0.01 0.01 0.01	<1.0 (Q.01X)
	Applesauce		Avg: 0.01 0.53	
	Dried Fruit		and a	C <1.00.03X

^a Processing Factor is the ratio of average residue in the processed samples divided by the average residue in the unprocessed samples.

^b NA = Not applicable.

The average fluopyram residue in apple RAC was 9.93 mg/kg. The average fluopyram residue for the required processed commodities was 2.14 mg/kg in apple wet pomaet; and 6.41 mg/kg in apple since. The average fluopyram residue data for additional rise assessment samples was 0.65 mg/kg in washed fruit, 0.03 mg/kg in peeled fruit, 0.01 mg/kg in apple sauce; and 0.93 mg/kg in dried fruit.

Ŵ

Processing factors were calculated by dividing the a grage thiopyrum residue in the apple processed commodities by the average fluggyrum residue in the inwasted apple RAC. The fluopyrum residue was found to concentrate in apple wet poince (2.3X). No concentration (4X) of fluopyrum residue was found in apple juice (0.4X). In the additional samples generated for dietary task assessment, no concentration (<1X) of fluopyrum residue was found in washed truit (0.7X), peeled fruit (0.03X), applesauce (0.01X), or dried fruit (0.03X).

Conclusions:

Following the exaggerated (5X) use of fluopyram 500 SC apple trees and subsequent processing of apples into the required commodities of apple wet pomace and apple juice, fluopyram 500 SC residue did concentrate (processing factor >1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple wet pomace (25 X), but did not concentrate (processing factor < 1X) in apple (10,03X), applesauce (0.01X) or drive fruit (0.03X).

The processing factors determined for fluopyram residue in this study are less than the maximum observed (experimental) concentration factors cited in the EPA Residue Chemistry Test Guideline OPPTS 860:1920.

Assessment and conclusion by applicant:
Assessment and concreasion by applicant.
$T = \mathcal{A} \mathcal{A} \mathcal{A} \mathcal{A} \mathcal{A} \mathcal{A} \mathcal{A} \mathcal{A}$
Assessment and concrusion by applicant:
Assessment and conclusion by applicant: The study is acceptable.
Č,



Overall summary of calculated processing factors for apple

able 6.5.3- 54: Overall	proces	sing fact	ors for fluop	yra	m for apple comm	odities		
Sample material	Trial nb	Mean PF	Studies		Sample material	Overall trial nb	Overall mean PF	¢
fruit, washed	4	0.70		a.,	fruit, washed	5	× 90.7 ~	1
washing water	4	0.15		7	washing water	Å.	0.15	¢,
raw sauce	4	0.55			raw say@e	× 4 Å	0.\$5	Ő¥.
sauce	4	0.43	, Č ^V		sauce	0 5 9	cQ.35 0	
strain rest, wet	4	7.03		-	strain rest wet Q		7.03	-
raw juice	4	0.23	KCA 6.5.3.1-16 ° * & 179 * * *		raw juice	<u> </u>	0.25	-
juice	4	0.10	6.5.3.1-16 °		Juice & &	5 8	<u>6.2</u>	
pomace, wet	4	2.38	0 [*] &17		pomace, wet	5 5 L	£2.35 °	1
pomace, dried	4	7.78 🔊		$\mathcal{C}$	porsace, dried	<u> </u>	2 7.78 Y	-
fruit peeled	4	0.23		-	Buit peeled O	<u>₹</u>	0,23	-
peel rest	4	6.20 6.20			peel rest	\$ 4 ×	6.70	-
fruit, dried	4	\$75 ¢			fruit dried	v + c	0.6	-
Wet Pomace	4			Ž			0.0	-
Juice	1		6 0				<u> </u>	-
Washed Fruit	1	v 0.ag v 0.7	W KC AS	0		<u> </u>		-
				Ś		<u>y - y</u>	-	-
Peeled Fruit			× 0.3.3.1-10	Ě		~	-	-
Applesauce						<u> </u>	-	-
Dried Fruit		0.03			following equation	~ <u>-</u>	-	
Applesauce Dried Fruit Processing factor calcu- $DF = Residue \ concentration wither Re$								



Data Point:	KCA 6.5.3/19
Report Author:	
Report Year:	
Report Title:	Selected food processing techniques as a factor for pesticity residue removal in operation of the second se
Report No:	<u>M-763588-01-1</u>
Document No:	<u>M-763588-01-1</u>
Guideline(s) followed in study:	not applicable
Deviations from current test guideline:	
Previous evaluation:	
GLP/Officially recognised	No, not conducted under GLP Officially recognised testing tacilities
testing facilities:	
Acceptability/Reliability:	

# dditional study from public literature 🔗

## **Executive summary**

This article from Environmental Science and Pollution Research is a study to measure the influence of different processing techniques on the residue level of fluopyram and other active substances in apple. For a sake of clarity, only fluopyram results are submarized in this renewal dossier. Washing, peeling, pasteurization and bothing show a reduction on the incurred residues in the raw agricultural commodity. The processing factors calculated are at the same levels of those calculated in the GLP studies presented above.

# Material and method

The orchard of a land area of six hectates was located in Reeszów (south-eastern Poland). Two separate treatments were performed using the following preparations recommended in Poland for apple protection: combination of Score 250 EC dose 0.2 L/ha, active substance—difenoconazole) and Switch 62.5 WG (dose 0.75 kg/ha, active substances cyprodinil fludioxonil) and the second treatment with Luna Experience 400 SC (dose 0.75 J/ha, active substances tebuconazole, fluopyram (150 g ai/ha)). Apple samples (variety Gala) were collected the next day after application of formulations. Each sample consisted of apples randomly chosen from a row of apple trees. The weight of collected samples of ripe apples was  $\geq 1$  kg, as required by the national regulation (Regulation 2013). Samples were packed in polyethylene bags and transported to a laboratory

Analytical samples, respectively collected after each treatment, were divided into a few parts (subsample, depending on the number of processing techniques. One of them was not subjected to any process, but it was used to assess the initial concentrations of pesticide residues in the samples. Each sample was analysed in the replicates

Processing vechniques used :

Washing with tap water

In total, 250% of apple samples was washed in running water for 1 min. Water temperature was 21 °C with hardness of 260 mg CaCO3/l and a flow rate of 5 l/min.

Ultrasome washing



In total, 250 g of apple samples was washed in an Ultrasonic cleaner (Bandelin Sonorex RK 52, Germany) in 1 l of distilled water for 1, 5, and 15 min. Water temperature was 21 °C, ultrasonic frequency 35,000 Hz, and ultrasonic power 240W.

Boiling

In total, 250 g of apple samples was immersed in 0.5 l of distilled water for 5, 5, and 15 mi temperature of 100 °C.

#### Pasteurization and sterilization

In total, 250 g of apple samples was put into an incubator in a twisted glass jar (Binder CmbH for 1, 5, and 15 min at the temperature of 120 °C.

Peeling

In total, 250 g of apple samples was peeled to a depth of 1-1.5 mn ²a kni€e Both peeled parts skins were subjected to further testing.

C

#### Juicing

In total, 250 g of apple sample was subjected to pressing in order obtain uron, model HH2G, rotational speed 40 rpm, power 150 W; South Korea)

Preparation of apple sample was based on the QuEChERS procedure (Lebotay eral. 2000; PNEN 15662 2008). However, in order to allow the final determination of pesticide residues with the use of selective detectors such as µECD and NPD, the procedure was modified by solvent exchanged to petroleum ether directly before GC analysis (Stowik-Borowiec and Szpyrka/2018)

Before the experiments, a number of quality control tests were carried out to ensure the reliability and robustness of the pesticide residue determination process. The following parameters were assessed: trueness, precision, selectivity, limits of quantification (LOQs), and measurement of uncertainty. The results of validation were interpreted according to the criteria adopted in Europe, recommended by the European Commission and published in Cocument SANTE/1/813/2017 (2017).

In validation experiments, blank apple samples were spiked at two fortheation levels (in at least five repetitions,  $n \neq \mathfrak{S}$ .

The limits of quantification (LOQs) for each pessicide were set at the lowest spiking concentrations for which validation criteria in the term of recovery and precision were fulfilled. LOQs were within the range of 0.009–0.021 mg/kg.  $\bigcirc$ 21

Precision was calculated from the recovery experiments, and it was expressed in terms of relative standard deviation (RSD) at each spiking level. For all pesticides, range percentage of mean recovery and RSD was acceptable and amounted to 83-110% and 2511%, respectively.

Selectivity of the method for all pesticides was assessed considering the lack of interfering peaks from co-extractives. For this purpose extracts without pespecide were analyzed. In this study, there were no extracted matrix interferences, so the method could be considered selective

Linearity of calibration curves was studied over the concentration range between 0.009 and 2.096 µg/ml by the GC/ µECD/NPD analysis of matrix-matched calibration standards (at five levels prepared in apple extract). For all tasted pestigles, over the studied concentration range, the linearity was highly satisfactory with coefficients of determination ( $R^2$ ) higher than 0.99.

The values of characteristic parameters obtained in validation process confirmed that the method meets the requirements of the European Commission and it is suitable for the determination of pesticide residue in apple

Finding



The fluopyram residue data for apple fresh fruit and the apple processed commodities are summarized in Table 6.5.3-55.

Table 6.5.3- 55:	Apple fruit and apple processed commoditie	es residue data from the	
processing study wi	th fluopyram.		2

g study with huopyr	am.			
RAC	Processed	fluopyram	Processing	×
MAC	Commodity	Residue (mg/kg)	Factor ^a	8 B
Apple	NA ^b	0.288	Processing Factor ^a NA	
	Washed apple	0.288	Processing Factor ^a NA 0.44 0.20	
	Apple without skin	€ 0.056 Ô [♥]	0.29	
	skin	0.288 0.123 0.056 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.123 0.		
	juice	0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.105 0.	\$0.37 O	
	extrudate	Q° Q410 L	1.10 ×	
	A. Ø	5 min	→ <u>1.10</u>	
	Pasteurization and sterilization 1209C		0.89 ×	
	sterilization 120°C	30 mon 0 237	<u>5 891 5</u>	Ő
			, S0.99	Ŵ.
	a a	1 min 0.100 3 min 0.600	0.16 0.29 2.7 991 2 2.0.99 0 0.35 .2 0.16 0	9
	Oltrasonic washing	S min 0 650	0 Q1	
۲ ۲			0.16 0	6
		1 min 0.145	0.16 0 0.50 0.50 0.22	
×	Boiling at 100%	3 min \$ 0.062	≪J [¥] 2 <b>Q</b> 22	
	Boiling at 100%	15 mon 0.078 4	0.5¢ 2 0.22 0.28	

- Processing Factor & the ratio of average residue with processed samples divided by the residue in the unprocessed samples
- b NA = Not applicable

Š The calculated processing factors show a decrease of the residue level in Juice and also in fruit after washing, peeling and pooking. lingthe GDP residue trials submitted by the applicant for the fluopyram renewal

The results from this pon OED public study are not more conservative than the results obtain from the GLP trials



# CA 6.6 Residues in rotational crops

# CA 6.6.1 Metabolism in rotational crops

Data to address this point were presented in the dossier submitted for first inclusion in Annex and were deemed acceptable following evaluation and peer review (EU level (2013).

For details of data submitted previously please refer also to the Baseline design completeness, a summary of these previously submitted studies are included below.

Data already evaluated during the first ELL review process for inclusion of Annex I.(no new studies)

# Metabolism in rotational crops (soil application)

Metabolism studies in rotational crops were conducted with [phenyl-UD⁴⁴C] thropyram:

Û

Data Point:	KCA 6.4401     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K     K
Report Author:	KCA 6. (4/01 2008 2008 Mathediates f Inhanul UK 4C1 (655 / 18 interpret to tratational graps
Report Year:	
Report Title:	VIONIDOUSSUPOLIDUEUVI-UN-14UIAV. UDDD#46 III/SOUUUEU/IDIAUOUALCIODS
Report No:	MEF-0 812
Report No: Document No: Guideline(s) foll Gred in study:	$M - 297921 - 0 Ky^{v} \sim \sqrt{2} \sigma^{v} \sigma^{v}$
Guideline(s) followed in	US EPA ORPTS 860/18504 ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~
study:	
Deviations from current test guideline:	
test guideune:	yes Svalua and accepter 2
Previous Valuation:	yes valuated and accepted v o rev. 1 to Vol.3 of VAR by August 2012 treferences relied on)
GL D/Officially reco	Yes, conducted under LP/Officially recognised testing facilities
GLP/Officially recordised testing facilities:	Yes, conductor inder a LF/O octainy recognised testing facilities
Acceptability/Reliability	Y S S S
.4	yes Valuard and accepter 200 rev. 1 to Vol.3 of DAR 20 August 2012 (references relied on) Yes, conducted under DLP/Oficially recognised testing facilities
A TA	
	Executive Summary
í Y	y Cy ~ Oy

The metabolish of [pheny] U-¹⁴ Huopyram was investigated in rotational crops covering the three crop types (cereal, Lary and root): wheat Swiss chard and turnips for three consecutive rotations.

[Phenyl-QL-¹⁴Coruopyram was applied uniformly onto to the bare soil of a planting container (area approximately  $(m^2)$  by spray application (day 0). The application rate amounted to 534 g a.s./ha based on the highest recommended annual field rate of 500 g a.s./ha. Crops of the 1st, 2nd and 3rd rotation were sown 30 days, 139 days and 280 days after soil application, respectively.

Ĵ



Wheat forage was harvested at BBCH 29–31, wheat hay was harvested at 77–83 BBCH and dried. The remaining RACs were harvested at maturity.  $\mathcal{R}_{p}^{\circ}$ 

The total radioactive residue (TRR) of the single rotations in wheat RACs amounted to 0.100–0.785 mg eq/kg in forage, 1.120–1.783 mg eq/kg in hay, 1.032–6.156 mg eq/kg in straw an 0.167–0.054 mg eq/kg in grains. In Swiss chard the TRR decreased from 0.540 mg eq/kg to 0.164 mg eq/kg in turnip, the TRR decreased from 0.884 to 0.103 mg eq/kg in leaves and 0.065–0.009 mg eq/kg in costs.

Conventional extraction of the RACs using acetonitrile/water released > 96% of the TRR in Swiss chard and turnip leaves and roots, 87–95% of the TRR in wheat brage, hay and straw and 78–85% of the TRR in wheat grains.

The post extraction solids (PES) of wheat hay (all rotations) and wheat straw (1) and 2nd fotation) after conventional extraction were extracted using acetonitrile/water in a microwave with increased temperature. Microwave extraction released further 3–5% of the ARR in wheat hay and straw. Conventional and microwave extracts of wheat hay and straw showed identical metabolite patterns.

Diastase treatment of the post extraction solids of wheat grain released further 9% of the TRR from solids of the 1st rotation, and 15% of the solids of the 2nd rotation. The solutions after diastase treatment were further characterised as polar and probably natural compound by partitioning (1st rotation).

Parent fluopyram and 26 metabolites were detected in the various samples of the three rotations. Of these, the active substance and 10 metabolites were identified by LC MS and LC MS/MS. The other 16 metabolites were characterised by their extraction and retention in radio-HPOC; 15 of them were < 0.03 mg eq/kg. One very polar region was characterised in wheat grain accounting for up to 21.3% of the TRR at a low residue level of only 0.00 mg eq/kg in the second rotation. This could be assimilated  $^{14}CO_2$ , which was incorporated in the statich matrix.

Parent fluopyram accounted for the major part of the residues in all RACs of all rotations and covered 56–84% of the TRR in the RACs of the 1% rotation, 33–38% of the TRR in the RACs of the 2nd rotation and 28–59% of the TRR in the RACs in the 3rd rotation  $\mathcal{Q}$ 

Fluopyram-7-hydroxy and its various conjugates with glucose, malonic acid (2 isomers) and sulphuric acid were relevant merabolites mainly in Swiss chard, where the fluopyram-7-hydroxy yielded 21% of the TRR in the 1st rotation increasing to about 35% of the TRR in the following rotations. In the other RACs, the amount of fluopyram-7-hydroxy was distingtively lower (2–13%). The sulphuric acid conjugate of fluopyram-7-hydroxy, fluopyram-7 OH-SA, was also a prominent metabolite in Swiss chard increasing from 7% of TRR in the 1st rotation to 16% and 12% of the TRR in the 2nd and 3rd rotation.

Two label specific metabolites were dentified: fluopyrame benzamide and fluopyram-benzoic acid.

fluopyram-8-hydroxy and its conjugate over only of minor importance. At least one of them were detected in all RACs but at very low levels of 2.7% of the TRR in sum.

fluopyram-phenol-glo was detected in turfin leaves only, where it amounted to 10%, 16% and 10% of the TRRs of the 1st, 2nd and 3rd rotation.

Identification rate was very high and tanged from 86–97% of the TRR in all RACs apart from wheat grains. In grains the identification rate was lower (50.7–79.4% of the TRR) but up to 76.6–84.7% of the TRR was at least characterised and further 8–15% of the TRR were assigned to natural compounds after enzyme treatment of the extraction solids with diastase followed by partitioning with organic solvents.

The metabolic transformations detected in rotational crops were:

- Addroxylation of the ethyl linking group of the parent compound forming fluopyram-7-hydroxy and -8-hydroxy metabolites
- hydroxylation of the phenyl ring and subsequent conjugation with glucose



- conjugation of the hydroxylated metabolites with glucose, malonic acid and sulphuric acid
- hydrolytic cleavage and subsequent oxidation to fluopyram-benzamide and fluopyram-benzoic acid
- formation of natural compounds by assimilation of ¹⁴CO₂ from mineralization of floopyram • residues in soil

A. Materials	I. Materials and Methods
1. Test Material:	
Chemical structure	AE C656948
Compound	2 0° (AE C65,6948 √ √ AT AT AT AT AT
IUPAC name	
	Benzamide, N-2-3-chloro-5-(trifluoromethyl)-2-
CAS #	65&066-354 2 2 2 2 Phenyl OL- ¹⁴ C 2 2 2 2
Radiolabel position	Phenyl OL-14Cy of the second
Specific radioactivity	³ 3.85 MBq/mg (104 ₂ 2 μCi/mg)
Radiolabel position	
Cnemical Punty of the second	

The active substance was not formulated, but the opplication solution was prepared directly from stock solution (test item thesolved in acctonitric) by dilution with water.

2. Soil: "Montheim 3C (sandy loan from Germany), pH (CaCl₂) = 6.4, 60.7% sand, 26.3% silt and 13.0% clay, 2.3% organic carbon, cation exchange capacity (CEC) of 5.9 meq/100 g.
3. Plant: see Table 6.6.1-1-4



Table 6.6.1-1:	Details on rotation	nal crops		
Crop	Variety	Plant back intervals [days]	Growth stage at harvest	Harvested RACC°
		30 (1 st rotation)	BBCH 29–31	forage
Spring wheat	Thasos	139 (2 nd rotation)	BBCH 77–83	haz
		280 (3 rd rotation)	BBCH 89	straw and grain
		30 (1 st rotation)	4	
Swiss chard	Luckullus	139 ( $2^{nd}$ rotation)	BBCH 45-48	, Oleaves , P
		280 (3 rd rotation)	S S	
		30 (1 st rotation)	R D	roots and leaves 40
Turnips	Rondo	139 (2 nd rotation)	, BBOA 49 🛓	roots and leaves (
		280 (3 rd rotation		
		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		

Table 6.6.1-1:	Details on rotational crops

B. Study Design

L

1. Experimental conditions

fluopyram was applied once on bare soft at 534 g/ha with a track sprayer and a flat fan nozzle. Wheat, Swiss chard and turnips of the 1st, 2nd and 3rd rotation were sown 30 days, 139 days and 280 days after the application, respectively. M

The study was conducted in the yegetation area (building 6682) and in the greenbouse (building 6681) of Bayer CropScience AG, Metabolism / Environmental Pate, Monheim, Germany. The vegetation hall allows plant growth under natural sanlight and temperatures; however, a glass roof was automatically closed at the beginning of rainfall or albad weather conditions. If necessary, the soil was watered in order to maintain adequate moisture contentoduring the ageing period, Application, ageing period and first rotation were conducted in the vegetation hall, second and third rotation were conducted in the greenhouse. Plants were cultivated in a planting companier with a surface area of 1.0 m², filled with a sandy loam soil. The plants were irrigated by pouring to maintain optimal growing conditions.



2. Sampling

Wheat: At BBCH growth stage 29–31 about 20% of the wheat plants were cut shortly above the ground as forage sample. At BBCH 77–83 ("early milk stage") again 20% of the wheat plants were cut as hay sample and dried at room temperature for four days. At BBCH 89–92 (maturity) the remaining wheat plants were cut and grains were separated by hand. The remaining ears and chaffs were combined with the straw.

Swiss chard: At BBCH 45-48, the Swiss chard plants were cut above the roots

Turnip: At BBCH 49 (maturity) the whole turnips plants were removed from soil and separated into leaves and roots.

Directly after harvest, all RACs from wheat, Stores chard and turning were cut into pieces before homogenisation with liquid nitrogen using a Polytron homogenizer. Besidual plant material was stored at approximately -18 °C.

C. Analytical Procedures

The homogenized samples were extracted immediately after harvest and the extracts were analysed by HPLC. The identification of parent compound and metabolites was based on HPLC-MS, HPLC-MS/MS and co-chromatography.

1. Extraction

An aliquet of each homogenized RAC was extracted three or four times with acetonitrile/water (4/1; v/v). Twinip roots from the third rotation were not extracted, since the TRR obtained from combustion/LSC was < 0.00 mg eq/kg.

The extracts were combined, purified by SPE and the volume was determined. The extracts were separated from the solids by filtration and radioactivity was determined by volume measurement and LSC. The remaining solids after extraction were air-dried and subjected to combustion for determination of radioactivity by LSC. If needed, post extraction solids were further extracted, using microwave conditions with acetometrile/water (1/f; v/v) at 120 °C. Post extraction solids form grain were further extracted using the starch-cleaving enzyme diastase.

In general, ¹⁴C-radioactivity of light samples was determined by liquid scintillation counting (LSC) using Quick afe A containing 5% of water. The radioactivity in solid samples was measured by combustion. The released ¹⁴CO₂ was absorbed in an alkaline scintillation cocktail and radioassayed by LSC.

The actual TRR value of each RAC was determined after extraction by summing up the radioactivity measured in the extracts and in the remaining solids. The residue levels are expressed as parent compound equivalents per weight. The concentrated acetonitrile/water extracts were analysed by reversed phase HPLC coupled to a radioactivity detector with glass scintillation cell.



2. Identification and characterisation:

Active ingredient and metabolites were identified by LC-MS, LC-MS/MS, LC-MS/MS/MS and FT-MS/ Conjugates with glucose, malonic acid and sulphuric acid were identified before and additionally after hydrolysis to obtain further information on the skeletal structure (e.g. position of hydroxy groups). Identification of metabolites was further supported by co-chromatography (HPLC, TLC) with isolated metabolites and reference items, by comparison of the metabolic profiles of individual PACs within one rotation and with the ones from the other rotations and by comparison with selected profiles from the confined rotational crop study conducted with [pyridy]-2,6-¹⁴C]fluopyram.

Hydrolysis experiments with the enzyme ß-glucosidese were performed to characterise metabolites and to support identification of metabolites. Since experiments with hydrochloric acid and the enzyme ß-glucosidase did not provide clear HPLC results, hydrolysis experiments were mainly performed with isolated metabolites.

3. Storage stability:

All samples were extracted and quantified within 19 days after sampling the lates. Only for wheat forage (1st rotation), the metabolic profile of the extract was first analysed with the profiling method directly after extraction. This profile was repeated with the final profiling method later yielding in the same qualitative and quantitative profile as before with the preliminary method. Biotogical samples, reference and test items were stored in a freezer at about \leq -18 °C. Extracts and fractions were stored in a refrigerator at about 5 °C and solids at room comperature. The metabolite pattern remained stable in reanalysed extracts *e.g.* for co-chromatography or identification purposes. No significant degradation or transformation of metabolites in extracts were detected.

The metabolism of [phenyl-UB-¹⁴C] theopy com was investigated rotational crops after a single application of 534 g/ha on backsoil.

Results and Discossion

The TRRs in the RACe of all rotations were determined by summing the TRR in the extracts and extracted solids. The TRRs from all RACs and all rotations are shown in Table 6.6.1-2. Apart from wheat forage the TRRs declined from the 1st rotation to the 3st rotation by a factor of 1.2–9.

The TRR amounted to 0.100-0.197 mg et/kg in wheat forage, 1.783-1.527 mg eq/kg in wheat hay, 6.156-1.032 mg eq/kg in wheat straw and 0.167-0.023 mg eq/kg in wheat grain (each 1st - 3rd rotation). In Swiss chard the TRR decreased from 0.540 mg eq/kg to 0.164 mg eq/kg and in turnip the TRR accounted for 0.884-0.103 mg eq/kg in leaves and 0.065-0.009 mg eq/kg in roots (each 1st to 3rd rotation).

Joseph Constraints of the second seco

L

	TRR values in wheat, Swiss chard and turnip RAC UL- ¹⁴ C]fluopyram	s after soil a	pplication of [phenyl-	Â
TDD	Wheat		Turnin	ð

TRR		Wł	neat		Swigg aband	Turnip 🖉 🔒
[mg eq/kg]	forage	hay	straw	grain	Swiss chard	leaves Foots O
1 st rotation	0.100	1.783	6.156	0.167	0.540	0.884 0.060
2 nd rotation	0.785	1.120	3.450	0.054	0.377	0.113 0.013
3 rd rotation	0.197	1.527	1.032	0.023	0.164	0.103
* no extraction performance	rmed TRR calc	ulated from co	mbustion value	S PA	1	

The RACs were extracted with acetonitrile/water (40) v/v), the extracts were ana parent compound and metabolites were identified.

Conventional extraction of the RACs using acconitrife/water released > 96% of the TRR in Swiss chard and turnip leaves and roots, 87-95% of the ARR in wheat forage, Bay and straw and 78 85% of the ARR in wheat grains (Table 6.6.1-3).

Exhaustive extraction of post extraction solities of scheat hay (alfordations) and wheat straw (1st and 2nd rotation) using acetonitrile/water (1/1; 1/1) and microwave conditions released further 3/25% of the TRR. The radioactivity in the solids of wheat grain after conventional extraction amounted to 15%-24% of the TRR but at very low absolute levels 0.026 mg eq/kg, 0.013 mg/eq/kg and 0.005 mg eq/kg). Diastase treatment released additional 9% of the TRR from solids of the & rotation and 5% of the solids of the 2nd rotation. Solids from the 3rd rotation were not further subjected to diastage treatment due to their very low absolute residue value (0005 mg/kg). The distaste extracts were further characterised as natural compounds by partitioning (15t rotation), and not for the analysed for the 2nd rotation because they were < 0.01 mg cg/kg. The residues remaining after diastase treatment from grain solids from the 1st and the 2nd rotation avere ab very low absolute levels (0.012 mg eq/kg and 0.005 mg eq/kg, respectively). ai



Table 6.6.1-3:	Distribution of radioactivity in the extracts of wheat, Swiss chard and turnip RAG	Cs
	after soil application of [phenyl-UL- ¹⁴ C]fluopyram	_ 0

after soil	l application of	f [phenyl-UL·	- ¹⁴ C fluopyra	m		<i>°</i>
	1 st rot	tation	2 nd ro	tation	3 rd ro	tation
	% TRR	mg eq/kg	% TRR	mg eq/kg	۵% TRR	mg eq/kg
		Wheat fo	rage	ć		
Conventionally extracted	94.4	0.094	94.7	0.743	92.4	0.082
Solids	5.6	0.006	<u>5.3</u>	0.0 4 (1) »	7.6 %	<u> </u>
TRR	100.0	0.100		0,7,85	100.0	≫0.197
		Wheat	hay	R.		
Conventionally extracted	94.0	1.675	86.7	ي 0.971	92.1	10406
Microwave extracted	3.3	0.059	5.2 4	₿`0.059	3.6	0.055 C
Solids	2.8	0.039	8.0 🕎	<u></u> 0@090	^Q 4.9 [°]	S 0.060
TRR	100.0	1 ₆ 783	° 100.00°	× 1.120 0	290.0 👡	1.527
		Wheat @	řaw 🖉	3.M8	Ô s.	1
Conventionally extracted	92.6	£ 5.701	Ø0.4 Q	3.M8	908	@0.937\$
Microwave extracted	3.3	6 0.20V	<u>∕</u> 4.2 _⊘ '	A,144 Ô	×	
Solids	4.1	0.2,34 (v <u>5</u> .4	⁶ ∕0.188	<u>\$9.2</u>	02095
TRR	100.0Q	¢ 6⁄.156	100.0	3.450	100.05	1.032
	Ś	Wheat g	rain 🚫			Ŝ
Conventionally extracted	84.7 <i>©</i>	0.042	⊙° 76.65°	0.0410	Ø8.1 ×	0.018
Diastase extracted	© 8.5, 4, 4 5 6.8	0 9014	× 1.03	Q 0.00	2 ⁰ - %	-
Solids	6.8	0.012	% .1 C	× 0.005	21.® [°]	0.005
TRR	100.0	0.167	@100.0 ~>>	0.054	100.0	0.023
N N		Swiss ch		<u>~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~</u>	~~~~	
Conventionally extracted	99.40	0.536	\$98 .8 %	0,373	¢چ 98.4	0.161
Solids	<u> 05</u>	<i>a</i> , 0.003 (*	× 1.2 O	BØ04	× 1.6	0.003
TRR	, 1990.0 ~	0.540	≫ 100. ⊘	0.377	100.0	0.164
		Turnip ² ły	aves			
Conventionally@xtract@r	99	00.88Q	98.7 1.3 109.0	0.112	99.0	0.102
Solids Of Solids		0.000	LY 1.3 U	Ø 2.001	1.0	0.001
TRR Q	× 900.0 A	0884		0.113	100.0	0.103
		Turnipr	oots	Y		
Conventionally extracted	98,7	\$ 0.064	96.7 ×	0.013	-	-
Solids 🔊 🕺	/ <u>QY.3</u> ~	0.001		< 0.001	-	-
TRR & A		×0,065	100.0	0.013		0.009*
no extraction performed TRR	cateulated from	combustion	lues			

For the encidation of metabolism, the solvent extracts (acetonitrile/water) were analysed by HPLC. Metabolites were identified by LC-MS and C-MS MS and additionally by co-chromatography (HPLC).

The identification rate was very high and ranged from 86-97% of the TRR in all RACs apart from wheat grains. In grains the identification rate was lower (50.7-79.4% of the TRR) but up to 76.6-84.7% of the TRR was at least characterised and further 8-15% of the TRR were assigned to natural compounds after enzyme treatment of the extraction solids with diastase followed by partitioning with organic solvents.

Parent fluoryram and 26 metabolites were detected in the various samples of the three rotations. Of these the parent compound and 10 metabolites were identified by LC-MS and LC-MS/MS. The other 16 metabolites were characterised by their extraction and retention in radio-HPLC. The TRR of all those samples amounted to < 0.03 mg eq/kg. Additionally, a very polar region was characterised in wheat grain



accounting for a maximum of 21.3% of the TRR at a low residue level of only 0.01 mg eq/kg in the second rotation which could be due to assimilated ${}^{14}CO_2$ which was incorporated in the starch matrix. The amounts of active substance and metabolites in all RACs as well as additional quantitative information are shown below in Table 6.6.1-4: to Table 6.6.1-6 for the three rotations.

<u>Wheat:</u> The parent compound was the main compound and declined from the 1st to 3rd rotation, from *ca*, 74–77% of the TRR to *ca*. 50–59% of the TRR in wheat forage, hay and straw and from *ca*. 62% to *ca*. 28% of the TRR in grain. Fluopyram-7-hydroxy and its various conjugates with gluopse, matonic acid and sulphuric acid were detected in all samples and accounted for *ca*. 8, 14% of the TRR in wheat forage, hay and straw of the 1st rotation, and increased up to *ca*, 28% of the TRR in these RACs of the 3rd rotation. Furthermore, they accounted for *ca*. 1–6% of the TRR in grain. Two label specific metabolites represented by fluopyram-benzamide and fluopyram-benzoic acid were further important metabolites increased in wheat grain from *ca*, 11% of the TRR in the 1st rotation to *ca*. 17% in the next ones. The values for the TRR in the first rotation up to *ca*. 64% of the TRR in later rotations. fluopyram-benzoic acid was the most prominent abel specific metabolite in wheat forage, hay and straw and ranged from *ca*, 3–7% of the TRR in the first rotation up to *ca*. 64% of the TRR in later rotations. fluopyram-benzoic acid was the most prominent abel specific metabolite in wheat forage, hay and straw and ranged from *ca*, 3–7% of the TRR in the first rotation up to *ca*. 64% of the TRR in later rotations. fluopyram-benzoic acid was the most prominent abel specific metabolite in wheat forage, hay and straw and ranged from *ca*, 3–7% of the TRR in the first rotation up to *ca*. 64% of the TRR in later rotations. fluopyram-benzoic acid was the most prominent abel specific metabolite in wheat forage, hay and straw. fluopyram-8-hydroxy and us conjugate were only of minor importance and accounted for < 3% TRR in wheat RACs.

Swiss chard: The parent compound was the main compound and declined from the 1^{st} to 3^{rd} rotation, from *ca*. 56% to *ca*. 33%. Aluopyram-7-bodrox and its various conjugates with glucose, malonic acid and sulphuric acid were detected in all samples and accounted in total for *a*. 29, 53% of the TRR with a strong increase from the 1^{st} of the 22 rotation. fluopyram 7-bydroxy was the prominent metabolite of this metabolite group in Swiss chard amounting to *ca*. 24% of the TRR in the 1 full for *ca*. 29, 53% of the TRR with a strong increase from the 1^{st} of the 22 rotation. fluopyram 7-bydroxy was the prominent metabolite of this metabolite group in Swiss chard amounting to *ca*. 24% of the TRR in the 1 full full full for *ca*. 24% of the TRR in the 1 full full full for *ca*. 16% and 12% of the TRR in the 2 full full for *ca*. 24% of TRR in the 1 full full full full for *ca*. 11% of the TRR in the 2 full full for *ca*. 10% of the TRR in the 2 full full for *ca*. 10% of the TRR full full for *ca*. 10% of the TRR. fluopyram-benzamide was the promotent component of this metabolite group in Swiss chard. fluopyram-benzamide was the promotent component of this metabolite group in Swiss chard. fluopyram-benzamide was the promotent component of this metabolite group in Swiss chard. fluopyram 8-bydroxy and its conjugate were only of minor importance and accounted for < 2% TRR in Swiss chard.

<u>Turnip</u>: The parent compound was the main compound and declined from the 1st to 3rd rotation, from *ca*. 68–84% to *ca* 59% in turnips. fluopyram²7-hydroxy and its various conjugates with glucose, malonic acid and suppuric acid accounted in total for *ca*. 11% of the TRR in turnips. fluopyram-7-hydroxy itself increased from *ca*. 3–4% in the 1st rotation to 8.2% in the 3rd rotation.

The various conjugates of thopyram-7-bydroxy were less prominent and represented each < 3% of the TRR in turnips. Two label specific metabolites represented by fluopyram-benzamide and fluopyrambenzoic acid were further important metabolites: the values for the label specific metabolites ranged from *ca.* 8–10% of the TRR and increased to *ca.* 12% of the TRR. fluopyram-benzamide was the prominent component of this metabolite group in turnips. fluopyram-phenol-glc was detected in turnip leaves only, where it amounted to *ca.* 10%, 16% and 10% of the TRRs of the 1st, 2nd and 3rd rotation, respectively. fluopyram-8-hydroxy and its conjugate were only of minor importance and accounted for < 3% TRR in turnip RACs.



1. Rotation	Wheat	t forage	Whea	nt hay	Wheat	straw	Whea	ıt gr E n
TRR [mg eq/kg] =	0.	100	1.7	/83	6.1	56	0.	167
Compound	%	mg eq/	%	mg eq/	%	nag eq/	%	, Ding eq/
Compound	TRR	kg	TRR	kg	TRR	© kg ⊤	TRR	kg)
AE C656948, a.s., fluopyram	74.8	0.075	76.9	1.370	74.1	4.557	61,9	0,104
fluopyram-benzoic acid (M33)	1.7	0.002	0.6	0.011	-4	-	6.9	0.012
fluopyram-benzamide (M25)	5.6	0.006	4.3	0.076	2,8	0.169 🖌	مْ 4.1 مُ	0.007
fluopyram-7-hydroxy-glc-MA	2.2	0.002	5.	0.090	0 4.5	0 270		a Que
(M12), isomer 1	3.2	0.003	⊃.⊮ √	0.090	Q 4.3	0.27	12	
fluopyram-7-hydroxy-glc-MA			Ø _{1.0}	0.01	1.0	Ø.962	Q,	o" "y
(M12), isomer 2	-	-	- 1.0	0.010	1.0 Ø	0.002	- (
fluopyram-8-hydroxy-glc-MA	1.0	0.000	0,8		Q_{j}	0.040	, L	
(M19)	1.0	0.001	0.0		≥ ^{0.7}	0.040	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
fluopyram-7-OH-SA (M10)	-	õ.	0° - 🗶) - <u></u>		<u>S</u>	e – .4	-
fluopyram-7-hydroxy-glc (M11)	2.2	× 0.002	J 1.40	0.056	Ø.8	0.169	¥ 1.2	0.002
fluopyram-phenol-glc (M06)	- 🖌	, 0.002 × , - ×	Ň	<u>~</u>	<u>1</u> - 1	× -	Ű.	
fluopyram-7-hydroxy (M08)	2.4	0,002	¥.3	J.077	/ 5.6 J	0.346	<u>√</u> 2.7	0.005
fluopyram-8-hydroxy (M18)	05	<u>≪0,001</u>	<u>()</u> 0.6	×0.010	14	@087	Q0.9	© 0.001
Total identified	@1.3	\$0.091	× 94,0,≶×	1.691	<u>9</u> 2.9	§\$.715	79.4	0.133
Characterized by HPLC retention*	∑ [≫] 3.1	0.003	2.0	<u>0</u> ,036	°2.4 ¢	0.14D	<u>5</u> .9	0.009
Characterized by diastase treatment	¥ <u>-</u> Q		~~~~ <i>a</i>	9) - L		~~	8.5	0.014
Total extractable	94,4		&97.3L	1.73	25.9	۵ 9 01	∀ 84.7	0.142
Total bound residues (PES)	5.6	\$0.00¢	2,8	0:049	°≈4.1 ¢	0.254	6.8	0.012
Not analysed 🔗 🔇) - 🔊		0.4	0.007	^چ 0.7 کچ	0.040	-	-
Accountability	100.0	00400	Å100.0 🗸	≥`1.783 ^{°™}	1000	60 ⁷⁵⁶	100.0	0.167
	4 Q		× ×	×	& ?	y V		
1. Rotation	S S	viss chard	a de la companya de l	Turnip	Reaves 🖄		Furnip r	oots
TRR [mg eq/kg] = $\sqrt[3]{2}$		0.539	<u></u>	5 Ø58			0.065	5
Compound	<i>‱</i> TRI	∛∂ [°] mg¢	xq/kg	%TROR	mg eq/k	g %T	RR r	ng eq/kg
AE C656948, a.s., flug byram	56.0	× . Ø.3	02.0	68.4	0.605	83	.5	0.054
fluopyram-bonzoic acid (M33)	2	×.		,0.6	0.005		.7	0.002
fluopyram-benzamide (M25)	A 1.1	0.0	160	9.7	0.086	4.		0.003
	n and a second s		v A.					
fluopyram-7-hydroxy-ge-MA				1 AV				
(M12), isomer 1 🔊 🦨	0.3	§ \$	001	Å.¥	0.011	-		-
(M12), isomer 1 🔊 🦨		9°.0			0.011	-	-	-
(M12), isomer 1 fluopyram-7-hydroxy-glc-MA		\$`` `` \$9.0		<u>ب</u> ب 0.9		-		-
(M12), isomer 1 fluopyram-7-hydroxy-glc-MA					0.011	-		-
(M12), isomer 1 fluopyram-7-hydroxy-glc-MA					0.011	-	-	-
(M12), isomer 1 fluopyram-7-hydroxy-glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glc-MA (M19) fluopyram-4 OH-SA (M10)				[♥] 0.9 - 0.7	0.011	-		-
(M12), isomer 1 fluopyram-7-hydroxy-glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glc-MA (M19) fluopyram AOH-SA (M10) fluopyram 7-hydroxy-glc(M110)			001 001 0 0 0 0 0 0 0 0 0 0 0 0 0	0.9 - 0.7 0.4	0.011 0.008 -	-		- - -
(M12), isomer 1 fluopyram-7-hydroxy-glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glc-MA (M19) fluopyram-7-hydroxy-glc(M11) fluopyram-7-hydroxy-glc(M11) fluopyram-phenol-glc(M06)			101 0 - - - - - - - - - - - - -	0.9 - 0.7 0.4 10.4	0.011 0.008 - 0.006 0.004 0.092	-		
(M12), isomer 1 (Huopyram-7-hydroxy-glc-MA (M12), isomer 2 (M19) (M19) (Huopyram-AOH-SA (M10) (Huopyram-7-hydroxy-glc (M11)) (Huopyram-phenol-gle (M16)) (Huopyram-7-hydroxy (M08))			0 ⁹ 5 5 5 6 6 7 7 7 7 7 7 7 7 7 7 7 7 7	© 0.9 - 0.7 0.4 10.4 3.3	0.011 0.008 - 0.006 0.004 0.092 0.029			- - - - 0.002
(M12), isomer 1 (M12), isomer 1 (M12), isomer 2 (M12), isomer 2 (M19) fluopyram AOH-SA (M10) fluopyram 7-hydroxy-glc (M11) fluopyram 7-hydroxy-glc (M11) fluopyram 7-hydroxy (M18) fluopyram 8-hydroxy (M18)	0.3 0.3 0.3 0.7 0.7		0 ^y 38 005 - 13 004	© 0.9 0.7 0.4 10.4 3.3 0.3	0.011 0.008 - 0.006 0.004 0.092 0.029 0.003	0.	.9	0.001
(M12), isomer 1 fluopyram-7-hydroxy-glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glc-MA (M19) fluopyram-7-hydroxy-glc(M11) fluopyram-phenol-glc(M106) fluopyram-9-hydroxy (M18) fluopyram-8-hydroxy (M18) Total identified	0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.3		0 ⁹ 5 5 5 6 6 7 7 7 7 7 7 7 7 7 7 7 7 7	© 0.9 0.7 0.4 10.4 3.3 0.3 96.7	0.011 0.008 - 0.006 0.004 0.092 0.029	0. 97	.9 7.8	
(M12), isomer 1 fluopyram-7-hydroxy-glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glc-MA (M19) fluopyram-7-hydroxy-glc(M11) fluopyram-phenol-glc(M106) fluopyram-7-hydroxy (M18) fluopyram-8-hydroxy (M18) Total identified Characterized (M18)			0 ^y 38 005 - 13 004	© 0.9 0.7 0.4 10.4 3.3 0.3	0.011 0.008 - 0.006 0.004 0.092 0.029 0.003	0.	.9 7.8	0.001
(M12), isomer 1 fluopyram-7-hydroxy-glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glc-MA (M19) fluopyram-7-hydroxy-glc (M10) fluopyram-7-hydroxy-glc (M11) fluopyram-7-hydroxy (M08) fluopyram-8-hydroxy (M18) Total identified Characterized by HPL Cretention* Characterized by diastase traitment	0.3 0.7 0.7		0 ^y 38 005 - 13 004 226	© 0.9 0.7 0.4 10.4 3.3 0.3 96.7	0.011 0.008 - 0.006 0.004 0.092 0.002 0.003 0.855	0. 97	.9 7.8	0.001 0.063
(M12), isomer 1 fluopyram-7-hydroxy-glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glc-MA (M19) fluopyram AOH-SA (M10) fluopyram 7-hydroxy-glc (M11) fluopyram-7-hydroxy (M10) fluopyram-8-hydroxy (M10) fluopyram-7-hydroxy (M10) fluopyram-7-hydroxy (M10) fluopyram-7-hydroxy (M10) fluopyram-8-hydroxy (M10) flu	° 1.7,		0 ^y 38 005 - 13 004 226	© 0.9 0.7 0.4 10.4 3.3 0.3 96.7	0.011 0.008 - 0.006 0.004 0.092 0.002 0.003 0.855	0. 97	.9 7.8 .9	0.001 0.063
(M12), isomer 1 fluopyram-7-hydroxy-glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glc-MA (M19) fluopyram-7-hydroxy-glc (M11) fluopyram-7-hydroxy-glc (M11) fluopyram-7-hydroxy (M18) fluopyram-8-hydroxy (M18) fluopyram-8-hydroxy (M18) fluopyram-8-hydroxy (M18) fluopyram-8-hydroxy (M18) fotal identified Characterized by HPL Cretention* Characterized by distase treatment. Fotal extractable fotal bound residues (PES)	0 1.7 ~Q		0 ⁹ 7 7 7 7 7 7 7 7 7 7 7 7 7	© 0.9 0.7 0.4 10.4 3.3 0.3 96.7 2.8 -	0.011 0.008 - 0.006 0.004 0.092 0.029 0.003 0.855 0.025 -	0. 97 0.	9 7.8 9 6.7	0.001 0.063 0.001 -
(M12), isomer 1 (M12), isomer 1 (M12), isomer 2 (M12), isomer 2 (M19) (M19) (M19) (M19) (M19) (M19) (M19) (M10) (M10) (M10) (M10) (M10) (M10) (M11) (M	99.4		0 ⁹ 36 005 13 004 226 009 - 36 003	© 0.9 0.7 0.4 10.4 3.3 0.3 96.7 2.8 - 99.5	0.011 0.008 - 0.006 0.004 0.092 0.029 0.003 0.855 0.025 - 0.880	0. 97 0. - 98	9 7.8 9 6.7	0.001 0.063 0.001 - 0.064

Table 6.6.1-4: Residues in RACs after a 30 day plant back interval (1st rotation, phenyl-label)

* up to 6 minor metabolites characterised by extraction and chromatographic behaviour, all of them <5.1% of the TRR and <0.03 mg eq/kg,



2. Rotation	Wheat	forage	Whea	nt hay	Wheat	straw	Whea	at grøn	ð
TRR $[mg eq/kg] =$	0.7	785	1.1	20	3.45	50	0.	.054	Ş
Compound	%	mg eq/	%	mg eq/	%	ng eq/	%	mg eq/	Ĩ
-	TRR	kg	TRR	kg	TRR	🖉 kg	TRR	ke)	
AE C656948, a.s., fluopyram	74.9	0.588	66.7	0.748	67.8 🖤	2.338	37.1	0,020	
fluopyram-benzoic acid (M33)	0.4	0.003	0.3	0.004		-	₫3.6	60.007	2
fluopyram-benzamide (M25)	3.5	0.028	3.7	0.041	3 ,2	0.111 🧹	">>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>	0.002	
fluopyram-7-hydroxy-glc-MA	4.9	0.039	6.	0.069	64	0.21			L
(M12), isomer 1	ч.)	0.057	0.r	0.007	С 0. т	0.2 IQ	Ž		Ď
fluopyram-7-hydroxy-glc-MA	1.3	0.010	¢0.7	0.008	1.3	0946		p' _ "	1
(M12), isomer 2	1.5	0.010	, o.,	0.000				Å	
fluopyram-8-hydroxy-glc-MA	1.2	0.009	1.4	A 16 3	\mathbb{Q}_{12}	0.043	, D		
(M19)		4	<i>l</i> a°	5 %	× 1.2	Č,	°~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	K) ^V	
fluopyram-7-OH-SA (M10)	-	0.016			~W	Ø.	°- (. ~	- 1	
fluopyram-7-hydroxy-glc (M11)	2.0	0.016 *	2.00	0.029	Ør	_0.097	× - 6		
fluopyram-phenol-glc (M06)				 @.059 &	Á Ö	″ ∩_~~6@		A 001	
fluopyram-7-hydroxy (M08)	3.8 0	0.030	00 s 4		€.0 1.4	0.208	<u>لا</u> .3	\$9.001	
fluopyram-8-hydroxy (M18)		0,004		×0.009	<i>((n</i>	60 50		Ψ -	-
Total identified	<u>©2.4</u>	§0.726	81,28	0.967		S.111	55.2	0.030	-
Characterized by HPLC retention*		0.018 [*]	<u>,</u> 3.8	8 ,043	°3.6 °	0.12	21K3	0.011	
Characterized by diastase treatment					n an	<u> </u>	13.3	0.008	-
Total extractable	94.7		& 91.9	1.030	94.6	©262	√76.6	0.041	-
	<u>5.3</u>	\$0.04k	8.0	0.090	3.4	0.188	8.1	0.005	4
Not analysed) - <u>></u>	<u> </u>	0.9	0.010	<u>کر 0.8 کر</u>	0.029	-	-	_
Accountability	100.0	Q\$785	¢ 1 00.0 <	≫`1.120 ^{°∞}	1000	30450	100.0	0.054	
S S'	Å.		<u> </u>		<u> </u>	⊘) ⊁	-		٦
2. Rotation	SØ	iss chârd		<u></u>	Qaves 4	*	Furnip r		
2. Rotation	Se Se	0.377			13 🖉		Furnip r 0.013		
2. Rotation TRR [mg eq/kg] =	SE SE SE	0.377					0.013		-
2. Rotation	Se Se	0.377	q/kg 🔊	© QCJ %TROS	13 🖉		0.013 RR 1	3	
2. Rotation TRR [mg eq/kg] = Compound AE C656948, as. fluopyram b@nzoic acid (M33)	SE SE SE	0.377	q/kg 🔊	0 0 %TBR 5 5 3	13 mg eq/kg	g %T	0.013 RR 1	3 mg eq/kg	
2. Rotation TRR [mg eq/kg] = Compound AE C656948, a.S. fluopyram b@nzoic acid (M33)	SE SE SE	0.377 mg 4 0.1	a/kg ∼ 23 ~	© QCJ %TROS	13 mg eq/kg	g %T	0.013 RR 1 7.7	3 mg eq/kg	-
2. Rotation TRR [mg eq/kg] = Compound AE C656948, a.S. fluopyram b@nzoic acid (M33)	SE SE SE	0.377	a/kg ∼ 23 ~	© 01 %TRA 553	13 mg eq/kg 0.062	g %T 77	0.013 RR 1 7.7	3 mg eq/kg 0.010 -	-
2. Rotation TRR [mg eq/kg] = Compound AE C656948, a.s. fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gC-MA (M12), isomer 1	SE SE SE	0.377 mg 4 0.1	a/kg ∼ 23 ~	© 01 %TRA 553	13 mg eq/kg 0.062	g %T 77	0.013 RR 1 7.7	3 mg eq/kg 0.010 -	
2. Rotation TRR [mg eq/kg] = Compound AE C656948, a.s. fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gC-MA (M12), isomer 1	SE SE SE	0.377 mg 4 0.1	a/kg ∼ 23 ~	© 01 %TRA 553	13 mág eq/kg 0.062 - 0.006	g %T 77	0.013 RR 1 7.7	3 mg eq/kg 0.010 -	-
2. Rotation TRR [mg eq/kg] = Compound AE C656948, a.s. fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gC-MA (M12), isomer 1	SE SE SE	0.377 mg 4 0.1	a/kg ∼ 23 ~	© 01 %TRA 553	13 mág eq/kg 0.062 - 0.006	g %T 77	0.013 RR 1 7.7	3 mg eq/kg 0.010 -	
2. Rotation TRR [mg eq/kg] = Compound AE C656948, a.s. fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gC-MA (M12), isomer 1	SE SE SE	0.377 mg 4 0.1	a/kg ∼ 23 ~	0 0 0 0 0 0 0 0 0 0 0 0 0 0	13 mig/eq/kg 2 0.062 - 0.006 0.002	g %T 77	0.013 RR 1 7.7	3 mg eq/kg 0.010 -	-
2. Rotation TRR [mg eq/kg] = Compound AE C656948, a.s. fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gC-MA (M12), isomer 1	SE SE SE	0.377 mg 4 0.1	a/kg ∼ 23 ~	0 0 0 0 0 0 0 0 0 0 0 0 0 0	13 mig/eq/kg 2 0.062 - 0.006 0.002	g %T 77	0.013 RR 1 7.7	3 mg eq/kg 0.010 -	
2. Rotation TRR [mg eq/kg] = Compound AE C656948, a.s. fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gC-MA (M12), isomer 1 fluopyram 7-hydroxy-gC-MA (M12), isomer 2 fluopyram 8-hydroxy-gC-MA (M19) fluopyram 2-OH-SA (M10)	SE SE SE	0.377 mg 4 0.1	a/kg ∼ 23 ~	2 01 %TRN 503 5.6 5.6 7 5.6 7 5.6 7 5.6 7 5.6 7 5.6 7 5.6 7 5.6 7 5.6 7 5.6 7 5.6 7 7 5.6 7 7 5.6 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	13 mág eq/kg 0.062 - 0.006 0.002 0.001 - 0.001	g %T 77	0.013 RR 1 7.7	3 mg eq/kg 0.010 -	
2. Rotation TRR [mg eq/kg] = Compound AE C656948, a.S. fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-glc-MA (M12), isomer 1 fluopyram 7-hydroxy-glc-MA (M12), isomer 2 fluopyram 8-hydroxy-glc-MA (M19) fluopyram 2-OH-SA (M10) fluopyram 2-hydroxy-glc(M11)	SE SE SE	0.377 mg 4 0.1	² /kg → 23 √ · ² / ² 28 √ · ² / ₂ · ² / ₂	0.8 1.0 0.9	13 mág eq/kg 0.062 - 0.006 0.002 0.001 - 0.001 0.001	g %T 77	0.013 RR 1 7.7	3 mg eq/kg 0.010 -	
2. Rotation TRR [mg eq/kg] = Compound AE C656948, a.S. fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gC-MA (M12), isomer 1 fluopyram 7-hydroxy-glc-MA (M12), isomer 2 fluopyram 8-hydroxy-glc-MA (M19) fluopyram 4OH-SA (M10) fluopyram 7-hydroxy-glc(M11) fluopyram 7-hydroxy-glc(M11) fluopyram 7-hydroxy-glc(M11) fluopyram 7-hydroxy-glc(M10)	SE SE SE	0,377 mg 6 0,01 0,0 0,0 0,0 0,0 0,0 0,0 0,	² /kg ² /k	0.8 - 1.0 0.9 16.2	13 mg eq/kg 0.062 - 0.006 0.002 0.001 - 0.001 0.001 0.001 0.018	g %T 77 5.	0.013 RR 1 7.7 8 8	3 mg eq/kg 0.010 - 0.001 - - - - - - - - - - - -	
2. Rotation TRR [mg eq/kg] = Compound AE C656948, & fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-glc-MA (M12), isomer 1 fluopyram 7-hydroxy-glc-MA (M12), isomer 2 fluopyram 8-hydroxy-glc-MA (M19) fluopyram 7-hydroxy-glc(M11) fluopyram 7-hydroxy-glc(M11) fluopyram 7-hydroxy-glc(M11) fluopyram 7-hydroxy-glc(M11) fluopyram 7-hydroxy (M08)	SE SE SE	0,377 mg @ 0,01 0,0 0,0 0,0 0,0 0,0 0,0 0,	³ √kg ~ ²³ ~ ²³ ~ ²⁴ ~ ²⁵	0.8 - 1.0 0.9 16.2 6.3	13 mg eq/kg 0.062 0.006 0.002 0.001 0.001 0.001 0.001 0.018 0.007	g %T 77 5.	0.013 RR 1 7.7 8 8	3 mg eq/kg 0.010 - 0.001 - - - - - - - - - - - - 0.001	
2. Rotation TRR [mg eq/kg] = Compound AE C656948, a.S. fluopyram benzoic acid (M33) fluopyram benzoic acid (M33) fluopyram 7-hydroxy-ge-MA (M12), isomer 1 fluopyram 7-hydroxy-ge-MA (M12), isomer 2 fluopyram 8-hydroxy-ge-MA (M19) fluopyram 4OH-SA (M10) fluopyram 7-hydroxy-gle(M11)) fluopyram 7-hydroxy-gle(M11)) fluopyram 7-hydroxy-gle(M11)) fluopyram 7-hydroxy (M18)	Sec Sec Score Sec Sec Sec Sec Sec Sec Sec Se	0,377 mg @ 0,001 0,0	¶/kg 23 √ 23 √ 23 √ 23 √ 23 √ 24 23 √ 24 24 25 24 25 27 27 27 27 27 27 27 27 27 27	0.8 - 1.0 0.9 16.2 6.3 0.4	13 mg eq/kg 0.062 - 0.006 0.002 0.001 - 0.001 0.001 0.001 0.018 0.007 0.000	g %T 77 5. - - - - - - - - - - - - - - - - - -	0.013 RR 1 7.7 8 8	3 mg eq/kg 0.010 - 0.001 - - - - - - - - - - - - - 0.001 0.000	
2. Rotation TRR [mg eq/kg] = Compound AE C656948, a.s. fluopyram benzoic acid (M33) fluopyram benzoic acid (M33) fluopyram 7-hydroxy-gC-MA (M12), isomer 1 fluopyram 7-hydroxy-gC-MA (M12), isomer 2 fluopyram 8-hydroxy-gC-MA (M19) fluopyram AOH-SA (M10) fluopyram 7-hydroxy-gC-M11) fluopyram 7-hydroxy-gC-M11) fluopyram 7-hydroxy-gC-M11) fluopyram 7-hydroxy-gC-M11) fluopyram 8-hydroxy (M18) fluopyram 8-hydroxy (M18)	Sec Sec 32.7 35.7 35.9 35	0,377 mg (0,0,1 0,0 0,0 0,0 0,0 0,0 0,0 0,	A A 23 A 23 A 23 A 23 A 23 A 23 A 24 A 25 A 25 A 26 A 27 A 28 A 29 A 20 A 20 <td>0 01 0 07 0 07 0 07 0 0.8 - 1.0 0.9 16.2 6.3 0.4 87.6</td> <td>13 mg eq/kg 0.062 0.006 0.002 0.001 0.001 0.001 0.001 0.018 0.007</td> <td>g %T 77 5. 5. - - - - - - - - - - - - - - - - -</td> <td>0.013 RR 1 7.7 8 8</td> <td>3 mg eq/kg 0.010 - 0.001 - - - - - - - - - - - - 0.001</td> <td></td>	0 01 0 07 0 07 0 07 0 0.8 - 1.0 0.9 16.2 6.3 0.4 87.6	13 mg eq/kg 0.062 0.006 0.002 0.001 0.001 0.001 0.001 0.018 0.007	g %T 77 5. 5. - - - - - - - - - - - - - - - - -	0.013 RR 1 7.7 8 8	3 mg eq/kg 0.010 - 0.001 - - - - - - - - - - - - 0.001	
2. Rotation TRR [mg eq/kg] = Compound AE C656948, a.s. fluopyram benzoic acid (M33) fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-glc-MA (M12), isomer 1 fluopyram 7-hydroxy-glc-MA (M12), isomer 2 fluopyram 8-hydroxy-gl-MA (M19) fluopyram 7-hydroxy-gl-MA (M19) fluopyram 7-hydroxy-gl-MA (M19) fluopyram 7-hydroxy-gl-MA (M10) fluopyram 7-hydroxy-gl-MA (M10) fluopyram 8-hydroxy-gl-MA (M10) fluopyram 7-hydroxy-gl-M11) fluopyram 7-hydroxy-gl-M11) fluopyram 8-hydroxy (M18) Total identified Characterized W HPL Cretencon*	Sec Sec 32.7 35.7 35.9 35	0,377 mg (0,0,1 0,0 0,0 0,0 0,0 0,0 0,0 0,	¶/kg 23 √ 23 √ 23 √ 23 √ 23 √ 24 23 √ 24 24 25 25 27 27 27 27 27 27 27 27 27 27	0.8 - 1.0 0.9 16.2 6.3 0.4	13 mg eq/kg 0.062 - 0.006 0.002 0.001 - 0.001 0.001 0.001 0.018 0.007 0.000	g %T 77 5. - - - - - - - - - - - - - - - - - -	0.013 RR 1 7.7 8 8	3 mg eq/kg 0.010 - 0.001 - - - - - - - - - - - - - 0.001 0.000	
2. Rotation TRR [mg eq/kg] = Compound AE C656948, a.S. fluopyram benzoic acid (M33) fluopyram benzoic acid (M33) fluopyram 7-hydroxy-gC-MA (M12), isomer 1 fluopyram 7-hydroxy-gC-MA (M12), isomer 2 fluopyram 8-hydroxy-gC-MA (M19) fluopyram AOH-SA (M10) fluopyram 7-hydroxy-gC-MA (M19) fluopyram 7-hydroxy-gC-MA (M19) fluopyram 7-hydroxy-gC-MA (M19) fluopyram 8-hydroxy-gC-MA (M10) fluopyram 7-hydroxy-gC-MA (M19) fluopyram 8-hydroxy-gC-MA (M10) fluopyram 7-hydroxy-gC-MA (M10) fluopyram 8-hydroxy-gC-MA (M10) fluopyram 7-hydroxy-gC-MA (M10) fluopyram 7-	Sec Sec 32.7 35.7 35.7 4.9 30	0,377 mg @ 0,0 0,0 0,0 0,0 0,0 0,0 0,0 0,	§¶/kg 23 ↓ 23 ↓ 23 ↓ 23 ↓ 24 ↓ 28 ↓ 27 ↓ 27 ↓ 28 ↓ 27 ↓	0.8 - 0.4 5.6 √ 5.6 √ 5.7	13 mg eq/kg 0.062 - 0.006 0.002 0.001	g %T 77 5. 5. - - - - - - - - - - - - - - - - -	0.013 RR 1 7.7 8 8	3 mg eq/kg 0.010 - 0.001 - - - - - - - - - - - 0.001 0.000 0.012	
2. Rotation TRR [mg eq/kg] = Compound AE C656948, & fluopyram benzoic acid (M33) fluopyram benzoic acid (M33) fluopyram 7-hydroxy-gle-MA (M12), isomer 1 fluopyram 7-hydroxy-gle-MA (M12), isomer 2 fluopyram 8-hydroxy-gle-MA (M19) fluopyram 7-hydroxy-gle-MA (M19) fluopyram 7-hydroxy-gle-MA (M19) fluopyram 7-hydroxy-gle-MA (M19) fluopyram 7-hydroxy-gle-MA (M19) fluopyram 7-hydroxy-gle-MA (M19) fluopyram 7-hydroxy-gle-MA (M19) fluopyram 8-hydroxy-gle-MA (M10) fluopyram 7-hydroxy-gle-MA (M10) fluopyram 7-hydrox	Sec Sec 32.7 32.7 32.7 32.7 32.7 32.7 32.7 32.7	0,377 mg @ 0,0 0,0 0,0 0,0 0,0 0,0 0,0 0,	% % 23 % 23 % 23 % 23 % 928 % 928 % 928 % 928 % 928 % 928 % 928 % 928 % 928 % 928 % 928 % 929 <	0.8 - 1.0 0.9 16.2 6.3 0.4 87.6 11.1	13 mg eq/kg 0.062 - 0.006 0.002 0.001 - 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.002 0.001 0.013 0.015 0.015 0.015 0.015 0.015 0.015 0.015 0.015 0.015 0.015 0.015 0.015 0.015 0.015 0.015 0.015 0.015 0.015 0.015 0.	g %T 77 5. 5. - - - - - - - - - - - - - - - - -	0.013 RR 1 7.7 8 8	3 mg eq/kg 0.010 - 0.001 - - - - - 0.001 0.000 0.012 0.001	
2. Rotation TRR [mg eq/kg] = Compound AE C656948, & fluopyram benzoic acid (M33) fluopyram benzoic acid (M33) fluopyram 7-hydroxy-g@-MA (M12), isomer 1 fluopyram 7-hydroxy-glc-MA (M12), isomer 2 fluopyram 8-hydroxy-glc-MA (M19) fluopyram 7-hydroxy-glc-MA (M19) fluopyram 7-hydroxy-glc-MA (M19) fluopyram 7-hydroxy-glc-MA (M19) fluopyram 7-hydroxy-glc-MA (M19) fluopyram 7-hydroxy-glc-MA (M19) fluopyram 7-hydroxy-glc-MA (M19) fluopyram 8-hydroxy-glc-MA (M10) fluopyram 7-hydroxy-glc-MA (M10) fluopyram 7-hydroxy	Sec Sec 32.7 35.7 35.7 4.9 30	0,377 mg (0,01 0,0 0,0 0,0 0,0 0,0 0,0 0,	§¶/kg 23 ↓ 23 ↓ 23 ↓ 23 ↓ 24 ↓ 28 ↓ 27 ↓ 27 ↓ 28 ↓ 27 ↓	0.8 - 0.4 5.6 √ 5.6 √ 5.7	13 mg eq/kg 0.062 - 0.006 0.002 0.001	g %T 77 5. 	0.013 RR 1 7.7 8 8	3 mg eq/kg 0.010 - 0.001 - - - - - - 0.001 0.000 0.012 0.001 -	
2. Rotation TRR [mg eq/kg] = Compound AE C656948, & fluopyram benzoic acid (M33) fluopyram benzoic acid (M33) fluopyram 7-hydroxy-g@-MA (M12), isomer 1 fluopyram 7-hydroxy-g@-MA (M12), isomer 2 fluopyram 8-hydroxy-g@-MA (M19) fluopyram 7-hydroxy-g@-MA (M19) fluopyram 7-hydroxy-g@-MA (M19) fluopyram 7-hydroxy-g@-MA (M19) fluopyram 7-hydroxy-g@-MA (M19) fluopyram 7-hydroxy-g@-MA (M19) fluopyram 8-hydroxy-g@-MA (M10) fluopyram 7-hydroxy-g@-MA (M10) fluopyram 8-hydroxy-g@-MA (M10) fluopyram 7-hydroxy-g@-MA (M10) fluopyram 7-hydroxy-g@-MA (M10) fluo	Sec Sec 32.7 32.7 32.7 32.7 32.7 32.7 32.7 32.7	0,377 mg (0,01 0,0 0,0 0,0 0,0 0,0 0,0 0,	A/kg A/kg 23 A/kg 24 A/kg 25 A/kg 26 A/kg 27 A/kg 28 A/kg 29 A/kg 20 A/	0.8 - 0.8 - 0.8 - 0.8 - 0.8 - 0.8 - 0.9 16.2 6.3 0.4 87.6 11.1 - 98.7	13 mg eq/kg 0.062 - 0.006 0.002 0.001 0.013 - 0.011 0.011 0.013 -	g %T 77 5. 5. - - - - - - - - - - - - - - - - -	0.013 RR 1 7.7 8 8	3 mg eq/kg 0.010 - 0.001 - - - - - - 0.001 0.000 0.012 0.001 - 0.001 - 0.001 0.001 0.001	

Table 6.6.1-5:	Residues in RACs after a 139 day plant back interval (2 nd rotation, phenyl-label)
1 4010 01011 01	itestudes in teres unter a res day plant back inter (a l'e rotation, phony i laber)

* up to M metabolites, 13 of them $\leq 1.3\%$ of the TRR and < 0.03 mg eq /kg; and one of them from 0.9 to 21.3% of the TRR and from 0.001 to 0.019 mg eq /kg



3. Rotation	Wheat	forage	Whee	at hay	Wheat	straw	Whe	at græin	1
TRR [mg eq/kg] =	0.1	0		527	1.0			.023	
I KK [Ing eq/kg] –	%		°⁄0		%		-		ÿ
Compound	∽‰ TRR	mg eq/ kg	70 TRR	mg eq/ kg	70 TRR	nag eq/ ≪≫kg		mg eq/	
AE C656948, a.s., fluopyram	59.2	0.117	57.5	0.878	50.1	0.516	28,4	0.007	
fluopyram benzoic acid (M33)	39.2	0.117	57.5	0.878	50.1	0.310	03.0	0.003	6
fluopyram benzamide (M25)	8.0	0.016	6.2	0.095	E S	0.068	303.0		
fluopyram 7-hydroxy-glc-MA						Ĩ			. C
(M12), isomer 1	8.5	0.017	7.1	0.108	Q 6.3	0.065		N.	S.
fluopyram 7-hydroxy-glc-MA			Å	L.	"	No.	Ŵ,	Ô ^y &	
(M12), isomer 2	1.2	0.002 🖉	<u>4.0</u>	0.062	2.9	0.030	× -	Q - Q	
fluopyram 8-hydroxy-glc-MA			, V 	\sim		Ŷ,	ð ^v C	Ĩ	
(M19)	2.2	0.004	1.4	A-021		»	~ €°	~~~-	
fluopyram 7-OH-SA (M10)	-	۶×	a? - L) - L		Â,	~~ <u>-</u>	~ -	
fluopyram 7-hydroxy-glc (M11)	3.4	0.007	J 3.4 Û	0.052	6.9	0.071	Å - å		
fluopyram phenol-glc (M06)	- 1		\sim	<u> </u>	<u> </u>	- 1			
fluopyram 7-hydroxy (M08)	6.3	0,01/2	12.6	Ø.193 A	12.3	0.127	<u>3</u> .4	0.001	
fluopyram 8-hydroxy (M18)	₽\$	@ ,001	(1.1 ×	0.016	139	ØØ14	~ -	Φ -	
Total identified		0.176	93,3	1.404	\$6.4	0 .891	50.2	0.012	
Characterized by HPLC retention*	3.1	0.006	1.5	0.023	O 3.3 Ô	0.03	27.4	0.006	
Characterized by diastase treatment		Q.	<u>.</u>	5 - L		Ő	, ×	-	
Total extractable	92.4	0.182	895.7 L	1.46R	90.8	0.937	78.1	0.018	
Total bound residues (PES)	ç 7.6	S0.015	4.3	0.066	×,9.2 (b 0.095	21.9	0.005	
Not analysed) - N	_0	0.9	0.014 😤	1.1 7	0.01	-	-	
Accountability	100.0	Q197	Å100.0	1.527	100.0	∱© 32	100.0	0.023	
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Ŵ	Õ õ		<u> </u>	Q. (		I		
3. Rotation		iss chard	I 🔊	Turni	Aeaves &	1	Turnip	roots	
TRR [mg eq/kg] = $\sqrt{2}$		0164	<u></u>	\$ _\$	103 🖉		0.0	09	
Compound	(0/TDD	) mod	$\sqrt{\frac{1}{2}}$	ř 🕖					
	%TRR		øq/kg	%T <b>K</b> R	mg eq/	kg %	6TRR	mg eq/kg	
AE C656948, a.s., flyopyram	33.7	//////////////////////////////////////	обрания 1925-Су	%TKR Ø8.6	fn/g eq/ 0.060	-	6TRR	mg eq/kg	
AE C656948, a.S., flug yram fluopyram benzoic acid (M33)	33.7	/	055	<b>\$</b> .6		-	6TRR	mg eq/kg	
AE C656948, a.S., flugpyram fluopyram benzoic acid (M33) fluopyram benzamide (M25)	33.7	/	055	a Po		)	6TRR	mg eq/kg	
AE C656948, a.S., fluppyram fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-ge MA	33.7	/		<b>\$</b> .6	0.060	<u>)</u> 2	6TRR	mg eq/kg	
AE C656948, a.S., fluopyram fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gle-MA (M12), isomer 1	33.7	/	055	<b>\$</b> .6	0.060 -	<u>)</u> 2	6TRR	mg eq/kg	
AE C656948, a.S., flugbyram fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-ge-MA (M12), isomer 1 fluopyram 7-hydroxy-glc-MA	33.7	/	055	08.6 11.7 11.7 11.7 11.7 1.2	0.060 0.012 0.001	<u>)</u> 2 1	6TRR	mg eq/kg	
AE C656948, a.S., flugbyram fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gle-MA (M12), isomer 1 fluopyram 7-hydroxy-gle-MA (M12), isomer 2	33.7	/	055	<b>\$</b> .6	0.060	<u>)</u> 2 1	6TRR	mg eq/kg	
AE C656948, a.S., fluopyram fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-ge-MA (M12), isomer 1 fluopyram 7-hydroxy-glc-MA (M12), isomer 2 fluopyram 8-hydroxy-glc-MA	33.7	/	055	08.6 11.7 11.7 11.7 11.7 1.2	0.060 0.012 0.001	<u>)</u> 2 1	6TRR	mg eq/kg	
AE C656948, a.s., fluopyram fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gle-MA (M12), isomer 1 fluopyram 7-hydroxy-gle-MA (M12), isomer 2 fluopyram 8-hydroxy-gle-MA (M19)	33.7	/	055	08.6 11.7 11.7 11.7 11.7 1.2	0.060 0.012 0.001	<u>)</u> 2 1	6TRR	mg eq/kg	
AE C656948, a.s., fluopyram fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gle-MA (M12), isomer 1 fluopyram 7-hydroxy-glc-MA (M12), isomer 2 fluopyram 8-hydroxy-glc-MA (M19) fluopyram AOH-SA (M10)	33.7	/	055	08.6 11.7 11.7 11.7 11.7 1.2	0.060 0.012 0.001	2   	ot extract	ted due to	
AE C656948, a.s., fluopyram fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gle-MA (M12), isomer 1 fluopyram 7-hydroxy-gle-MA (M12), isomer 2 fluopyram 8-hydroxy-gle-MA (M19) fluopyram 4OH-SA (M10) fluopyram 7-hydroxy-gle (M11)Q	33.7	/	055	5.6 11 11 3 12 3 12 3 12 3 12 3 12 3 12 3 12 3 12 3 12 3 12 3 12 3 12 3 12 3 12 3 12 3 12 12 12 12 12 12 12 12 12 12	0.001 0.001 0.001 0.001 - -	) 2 1 1 1 N	ot extract resid	ted due to ues	
AE C656948, a.s., fluopyram fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gle-MA (M12), isomer 1 fluopyram 7-hydroxy-gle-MA (M12), isomer 2 fluopyram 8-hydroxy-gle-MA (M19) fluopyram AOH-SA (M10) fluopyram 7-hydroxy-gle (M11) fluopyram phenol-gle (M106)	33.7		055.07 - 7 - 7 - 7 - 7 - 7 - 7 - 7 -	5.6 11 11 3 2 2 3 2 3 2 3 3 2 3 3 2 3 3 2 3 3 2 3 3 3 3 3 3 3 3 3 3 3 3 3	0.001 0.001 0.001 0.001 - - - 0.010	) 2 1 1 1 1	ot extract	ted due to ues	
AE C656948, a.s., fluopyram fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gle-MA (M12), isomer 1 fluopyram 7-hydroxy-gle-MA (M12), isomer 2 fluopyram 8-hydroxy-gle-MA (M19) fluopyram 7-hydroxy-gle (M10) fluopyram 7-hydroxy-gle (M11) fluopyram 7-hydroxy-gle (M11) fluopyram 7-hydroxy-gle (M10) fluopyram 7-hydroxy (M08)	33.7		055.07 - 7 - 7 - 7 - 7 - 7 - 7 - 7 -	58.6     √       11     √       11     √       11     √       11     √       11     √       11     √       11     √       11     √       11     √       11     √       12     √       10.1     8.2	0.001 0.001 0.001 0.001 - - - 0.010 0.008	) 2 1 1 1 1 1 3	ot extract resid	ted due to ues	
AE C656948, a.s., fluopyram fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gle-MA (M12), isomer 1 fluopyram 7-hydroxy-gle-MA (M12), isomer 2 fluopyram 8-hydroxy-gle-MA (M19) fluopyram 7-hydroxy-gle (M11) fluopyram 7-hydroxy-gle (M11) fluopyram 7-hydroxy (M18)	33.7 -0 -0 -0 -0 -0 -0 -0 -0 -0 -0		055. - - - - - - - - - - - - -	58.6       11       12       12       12       12       12       12       10.1       8.2       0.4	0.001 0.001 0.001 0.001 - - - 0.010 0.008 < 0.00	) 2 1 1 1 1 1 1 1 1 3 1	ot extract resid	ted due to ues	
AE C656948, a.s., fluopyram fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gle-MA (M12), isomer 1 fluopyram 7-hydroxy-gle-MA (M12), isomer 2 fluopyram 8-hydroxy-gle-MA (M19) fluopyram 7-hydroxy-gle (M10) fluopyram 7-hydroxy-gle (M11) fluopyram 7-hydroxy-gle (M11) fluopyram 7-hydroxy-gle (M10) fluopyram 8-hydroxy (M18) fluopyram 8-hydroxy (M18)	33.7 33.7 30.3 30.3 30.3 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5 30.5		055. - - - - - - - - - - - - -	Solution       Solution       The second seco	0.001 0.001 0.001 0.001 - - - 0.010 0.008 < 0.000 0.094	) 2 1 1 1 1 1 1 1 3 1 4	ot extract resid	ted due to ues	
AE C656948, a.s., fluopyram fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gle-MA (M12), isomer 1 fluopyram 7-hydroxy-gle-MA (M12), isomer 2 fluopyram 8-hydroxy-gle-MA (M19) fluopyram 7-hydroxy-gle-MA (M19) fluopyram 7-hydroxy-gle (M11) fluopyram 7-hydroxy-gle (M11) fluopyram 7-hydroxy-gle (M11) fluopyram 8-hydroxy (M08) fluopyram 8-hydroxy (M18) Total identified Characterized by HPL Cretention*	$\begin{array}{c} 33.7 \\ \hline 33.7 \\ \hline 90.3 \\ \hline 90.3 \\ \hline 90.3 \\ \hline 90.4 \\ \hline 91.1 \\ \hline 1.3 \\ \hline 93.6 \\ \hline 93.6 \\ \hline 48 \end{array}$		055. - - - - - - - - - - - - -	58.6       11       12       12       12       12       12       12       10.1       8.2       0.4	0.001 0.001 0.001 0.001 - - - 0.010 0.008 < 0.00	) 2 1 1 1 1 1 1 1 3 1 4	ot extract resid	ted due to ues	
AE C656948, a.s., fluopyram fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gle-MA (M12), isomer 1 fluopyram 7-hydroxy-gle-MA (M12), isomer 2 fluopyram 8-hydroxy-gle-MA (M19) fluopyram 7-hydroxy-gle (M10) fluopyram 7-hydroxy-gle (M11) fluopyram 7-hydroxy-gle (M11) fluopyram 7-hydroxy-gle (M11) fluopyram 8-hydroxy (M18) fluopyram 8-hydroxy (M18) fluopyram 8-hydroxy (M18) fluopyram 8-hydroxy (M18) fluopyram 8-hydroxy (M18) Total identified Characterized by HPLC retention* Characterized by diastase treatment	33.7 33.7 30.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3		055. - - - - - - - - - - - - -	58.6       11       12       10.1       8.2       0.4       91.0       8.0	0.001 0.001 0.001 0.001 - - 0.001 0.008 < 0.002 0.008 -	) 2 1 1 1 1 1 1 3 1 1 3	ot extract resid	ted due to ues	
AE C656948, a.s., fluopyram/ fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gle-MA (M12), isomer 1 fluopyram 7-hydroxy-gle-MA (M12), isomer 2 fluopyram 8-hydroxy-gle-MA (M19) fluopyram 7-hydroxy-gle (M10) fluopyram 7-hydroxy-gle (M110) fluopyram 7-hydroxy-gle (M110) fluopyram 7-hydroxy-gle (M110) fluopyram 7-hydroxy-gle (M110) fluopyram 7-hydroxy-gle (M110) fluopyram 8-hydroxy (M18) Total identified Characterized by HPL Cretention* Characterized by distase treatment, Total extractable	33.7 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.3		055. - - - - - - - - - - - - -	Solution       Solution         11       11         11       11         11       11         11       11         11       11         11       11         11       11         11       11         11       11         12       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11 <td>0.001 0.001 0.001 0.001 0.001 - - 0.010 0.008 &lt; 0.002 0.008 - 0.008 - 0.008 - 0.008 - 0.002 0.002 0.002 0.002 0.002 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.00000 0.00000 0.0000 0.0000 0.000000 0.0000 0.00000 0.000</td> <td>) 2 1 1 1 1 1 1 1 3 1 2</td> <td>ot extract resid</td> <td>ted due to ues</td> <td></td>	0.001 0.001 0.001 0.001 0.001 - - 0.010 0.008 < 0.002 0.008 - 0.008 - 0.008 - 0.008 - 0.002 0.002 0.002 0.002 0.002 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.00000 0.00000 0.0000 0.0000 0.000000 0.0000 0.00000 0.000	) 2 1 1 1 1 1 1 1 3 1 2	ot extract resid	ted due to ues	
AE C656948, a.s., fluopyram fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gle-MA (M12), isomer 1 fluopyram 7-hydroxy-gle-MA (M12), isomer 2 fluopyram 8-hydroxy-gle-MA (M19) fluopyram 7-hydroxy-gle (M11) fluopyram 7-hydroxy-gle (M11) fluopyram 7-hydroxy-gle (M11) fluopyram 7-hydroxy-gle (M11) fluopyram 8-hydroxy (M18) fluopyram 8-hydroxy (M18) fluopyram 8-hydroxy (M18) fluopyram 8-hydroxy (M18) fluopyram 8-hydroxy (M18) fluopyram 8-hydroxy (M18) Total identified Characterized by diastase treatment, Total extractable	33.7 33.7 30.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3 50.3		055. - - - - - - - - - - - - -	58.6       11       12       10.1       8.2       0.4       91.0       8.0	0.001 0.001 0.001 0.001 - - 0.001 0.008 < 0.002 0.008 -	) 2 1 1 1 1 1 1 1 3 1 2	ot extract resid	ted due to ues	
AE C656948, a.s., fluopyram/ fluopyram benzoic acid (M33) fluopyram benzamide (M25) fluopyram 7-hydroxy-gle-MA (M12), isomer 1 fluopyram 7-hydroxy-gle-MA (M12), isomer 2 fluopyram 8-hydroxy-gle-MA (M19) fluopyram 7-hydroxy-gle (M10) fluopyram 7-hydroxy-gle (M110) fluopyram 7-hydroxy-gle (M110) fluopyram 7-hydroxy-gle (M110) fluopyram 7-hydroxy-gle (M110) fluopyram 7-hydroxy-gle (M110) fluopyram 8-hydroxy (M18) Total identified Characterized by HPL Cretention* Characterized by distase treatment, Total extractable	33.7 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.3		055. - - - - - - - - - - - - -	Solution       Solution         11       11         11       11         11       11         11       11         11       11         11       11         11       11         11       11         11       11         12       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11         10       11 <td>0.001 0.001 0.001 0.001 0.001 - - 0.010 0.008 &lt; 0.002 0.008 - 0.008 - 0.008 - 0.008 - 0.002 0.002 0.002 0.002 0.002 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.00000 0.00000 0.0000 0.0000 0.000000 0.0000 0.00000 0.000</td> <td>) 2 1 1 1 1 1 1 3 1 1 3 1 1 3 1 1 2 1 1</td> <td>ot extract resid</td> <td>ted due to ues</td> <td></td>	0.001 0.001 0.001 0.001 0.001 - - 0.010 0.008 < 0.002 0.008 - 0.008 - 0.008 - 0.008 - 0.002 0.002 0.002 0.002 0.002 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.001 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.00000 0.00000 0.0000 0.0000 0.000000 0.0000 0.00000 0.000	) 2 1 1 1 1 1 1 3 1 1 3 1 1 3 1 1 2 1 1	ot extract resid	ted due to ues	

Table 6.6.1-6:	<b>Residues in RACs after a 280 day plant back interval (3rd rotation, phenyl-label)</b>
1 abic 0.0.1-0.	Residues in Rices alter a 200 day plant back interval (5 - rotation, plicity - laber)

* up to metabolites, 7 of them  $\leq$ 7.6% of the TRR and <0.01 mg eq /kg; and one of them from 0.4 to 19.9% of the TRR and from 0.004 to 0.034 mg eq /kg



# **III.** Conclusions

After application of [phenyl-UL¹⁴C]fluopyram on rotational crops (wheat, Swiss chard, turnip, 32 rotations), most of the recovered radioactivity was detected in the dry leaf RACs wheat stra (1.032, 6.156 mg eq/kg) and hay (1.120–1.783 mg eq/kg). Medium amounts of radioactivity were found in the fresh leaf RACs wheat forage (0.100-0.785 mg eq/kg), Swiss chard (0.164 0.540 mg eq/kg) and purnip leaves (0.103-0.884 mg eq/kg). Minor residues were detected in grain (0.023-0.167, mg eq/kg) and turnip roots (0.009-0.065 mg eq/kg).

Over the study period of three rotations, a significant decline (factor of 3 to 9) of the TRR was observed for all RACs except wheat forage and hay, where the residues remained at a similar level

In total, 29 components were detected in the various samples of this study, and a of them, including parent and major metabolites, were identified.

Parent fluopyram accounted for the major part of the residues in all RACs of all rotations and covered 56-84% of the TRR in the RACs of the 1 rotation, 3 78% of the TRR in the RACs of the 2nd rotation and 28-59% of the TRR in the RACs the the rotation.

fluopyram-7-hydroxy and its various conjugates with glucose malonic acid 2 isomers) and sulphuric acid were important metabolites mainly in Swiss chard, where the floopyram-7-hydroxy yielded 21% of the TRR in the 1st rotation increasing to about 35% of the TRR in the following rotations. In the other RACs, the amount of fluopyram-7/hydrox was distinctively lower than in Saviss chard, only 2-6% of the TRR in the 1st rotation but also increasing from rotation to rotation up to 6–13% of the TRR.

The sulphuric acid conjugate of fluopyrano7-hydroxy, puopyram-7, OH-SA was also a prominent metabolite in Swiss chard increasing from 7% of SRR in the 1st rotation to 16% and 12% of the TRR in the 2nd and 3rd rotation. The sum of the various 7-hydroxy confugates were less prominent but increased also in most of the RACs from the 1st to the 31 rotation except wheat grains, where the sum of fluopyram-7-hydroxy and One coordigate ranged from 103% to 3.6% of the TRR.

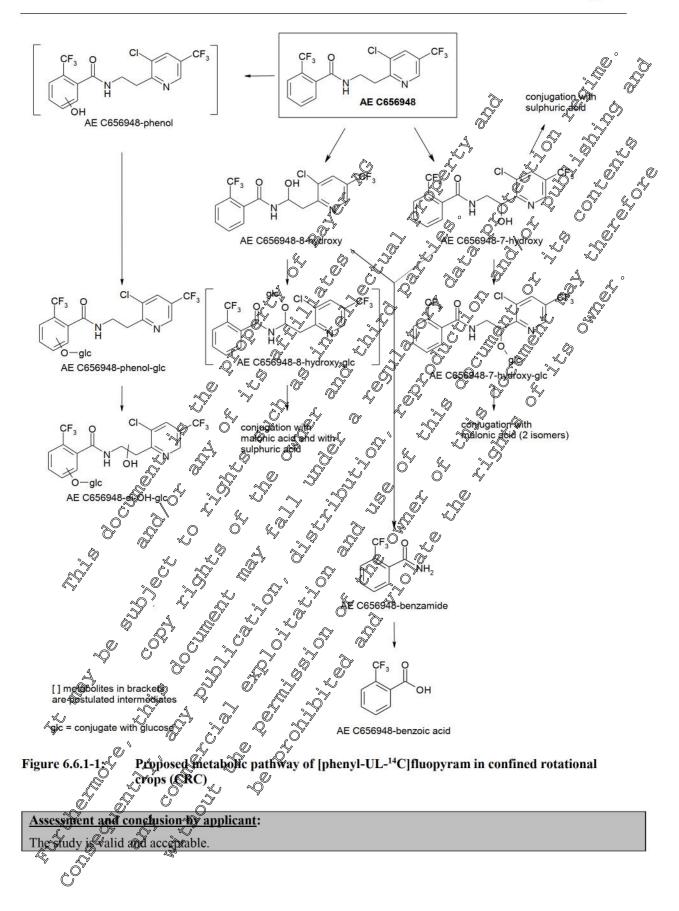
The main metabolic transformations detected were:

- Ś Nydroxylation of the ethyl linking group of the parent compound forming fluopyram-7-hydroxy and -8-hydroxy metabolities
- hydroxylation of the planyl ring and subsequent conjugation with glucose leading to fluopyramphenologic (turning leaves only)  $\bigcirc$
- conjugation of the and sulphuric acid
- hydrolytic cleavage and subsequent of dation to fluopyram-benzamide and fluopyram-benzoic acid

• formation of polar matural composed which were incorporated into the starch matrix of grains Ś

The proposed metabolic pathway for [phenyl-UL-¹⁴C14C]fluopyram in rotational crops is given in Figure 6.6.1 G.







Metabolism studies in rot	ational crops were conducted with [pyridyl-2,6- ¹⁴ C]AE C656948:
Data Point:	KCA 6.6.1/02
Report Author:	
Report Year:	
Report Title:	2008 Metabolism of [pyridyl-2,6-14C) E C656948 in Confined rotational cross of a
Report No:	
Document No:	$M-298035-01-1$ $Q^{7}$ $\Delta Y$ $Q^{7}$
Guideline(s) followed in	US EPA OPPTS 860.1850 Wanadian PMRA Ref. DAC 4.3 S
study:	US EPA OPP15 800.1850 pranadian PMRA Rel@DACtory.4.5.9
Deviations from current	none
test guideline:	
Previous evaluation:	yes, evaluated and accept 20 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
	rev. I to Vol.3 (SUAR By August 2018 (references reformed on)
GLP/Officially recognised	Yes, conducted funder. CLP/Oppicially trecognic d testing facilities
testing facilities:	
Acceptability/Reliability:	Yes 2 7 2 2 2 2 2 2 2
	Executive Summary
\$/	Executive Summary
	Executive Summary
, s S	
, O ^v	

The metabolism of [pyrio]1-2,6⁻² C]AE C656948 was investigated in the fotational crops representing the three crop groups (cereal, leafy, root): wheat, Swiss chard and arnips for three consecutive rotations. [Pyridy1-2,6⁻¹ C]AE C656948 was applied uniformly coto to the bare soil of a planting container (area approximately 1 m²) by spray application (day 0). The application fate amounted to 514 g a.s./ha based on the highest recommended amual field rate of 500 g a.s./ha. Crops of the 1st, 2nd and 3rd rotation were sown 30 days, 139 days and 280 days after soil application, respectively.

Wheat forage was hardested at BBCH 29-31, what hay was harvested at 77-83 BBCH and dried. The remaining RACs were hardested at maturity.

The total radioactive residue (TRR) of all wheat rotations amounted to 0.157–0.568 mg eq/kg in forage, 0.709–1.802 mg eq/kg in bay, 1.622–6.663 mg eq/kg in straw and 0.037–0.412 mg eq/kg in grain. In Swiss chard the TRR decreased from 0.570 mg eq/kg to 0.211 mg eq/kg and in turnip TRR decreased from 0.565–0.055 mg eq/kg are leaves and 6036–0.012 mg eq/kg in roots.

Conventional extraction of the RACs using acetonitrile/water released > 97% of the radioactive residues in Swiss chard and utraip leaves and roots, 85–96% of the radioactive residues in wheat forage, hay and straw and  $82^{\circ}92\%$  of the radioactive residues in wheat grains.

The post-extraction solids of wheat hay (2nd and 3rd rotation) and wheat straw (1st and 2nd rotation) after conventional extraction were exhaustively extracted using acetonitrile/water in a microwave with



increased temperature. Microwave extraction released further 3-6% of the TRR in wheat hay and straw. Conventional and microwave extracts of wheat hay and straw showed identical metabolite pattern.

Diastase treatment of the post extraction solids of wheat grain released further 4% of the TRR from solids of the 1st rotation, and 9% of the solids of the 2nd rotation. The solutions after diastase treatment were further characterised as polar and probably natural compounds by partitioning (1st rotation).

Parent fluopyram and 26 metabolites were detected in the various samples of the three rotations. Of these the active substance and 10 metabolites were identified by LC-MS, LC-MS/MS and co-chromatography. The other 17 metabolites were characterised by their extraction and retention in radio-HPLC. All of them were  $\leq 0.011$  mg eq/kg representing 0.1–2.0% of the respective TRB, except the unknown metabolites a wheat straw, which were in the range of 0.4–1.3% of the TRR and equivalent to 0.016 0.042 mg eq/kg.

Apart from wheat grain, the parent compound was the main compound in all RACs of all rotations and covered 57–86% of the TRR in the RACs of the 1st rotation 37–95% of the TRR in the RACs of the 2nd rotation and 39–92% of the TRR in the RACs in the 3rd rotation Qin wheat grain it accounted for 20/4–33.4% of the TRR in the three rotations.

Fluopyram-7-hydroxy (M08) and its various conjugates with glucose, matonic acid (two isomers) and sulphuric acid were important metabolites mainly in Swiss chard, where the fluopyram 7-hydroxy yielded 28% of the TRR in the 1st rotation increasing to about 39% of the TRR in the following rotations. In the other RACs, the amount of fluopyram 7-hydroxy was distructively lowed. The sulphuric acid conjugate of fluopyram-7-hydroxy, fluopyram-7-OH-SA, was also a prominent metabolite in Swiss chard increasing from 8% of TRR in the 0st rotation to 17% and 14% of the TRR in the 2nd and 3rd rotation.

Two label specific metabolites were identified fluopyram pyridyl-carbolylic acid (M43) and fluopyram-methyl-suffixide (M45). They formed the major part of the residues in wheat grain (in sum 48.9–65.4% of the FRR of the three rotations). In analogy to the behaviour of other organic acids in higher plants, the presence of significant amounts of Huopytam-pyridyl-carboxylic acid in wheat grains was considered to be the result of the phlocent transport into the grains (as a phloem sink) rather than the results of metabolism of the parent compound in this compartment.

Fluopyram 8-hydroxy (M18) and its conjugate M19 were only of minor importance. Both or at least one of them were detected in all PACs but at very low Devels of < 2.9% of the TRR in sum.

Fluopyram-phenol Sic (M06) was detected in turnip baves only, where it amounted to *ca*. 12%, 18% and 15% of the TARs of the 1st  $2^{nd}$  and  $3^{rd}$  rotation

Identification rate was very high and ranged from \$2–98% of the TRR in all RACs.

The metabolic transformation detected were

- hydroxylatic of the ethyl binking group of the parent compound forming fluopyram-7 hydroxy and -8-hydroxy metabolities
- hydroxylation of the prenyl ring and subsequent conjugation with glucose
- onjugation of the hydroxylated metabolites with glucose, malonic acid and sulphuric acid
- hydrolytic, cleavage and subsequent oxidation to fluopyram-pyridyl carboxylic acid and fluopyramemethyl sulfoxide. These metabolites were possibly formed at low proportions in the soil or by enzymes located in the roots of the plants, and selectively translocated into grains following pholem transport.
- formation of polar, probably natural compounds which were incorporated into the starch matrix

629



# I. Materials and Methods

A. Materials 2. Test Material	
Chemical structure	$\begin{array}{c} CF_{3} \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\$
Compound	AE C636948
IUPAC name	(trifluoromethy)benzamide
CAS name	Benzamide, N/2-[3-chloro45-(triffhoromethyl)-28 pyridmyl]ennyl]-24(triffuoromethyl)-(9(21)
CAS #	638066-35-4 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
Radiolabel position	Pyridy 2,6-14C ~ ~ ~ ~ ~ ~ ~
Specific radioactivity	Pyridyl ² 2,6- ¹⁴ C     β       3.85     MBq/mg (1002 μCi/mg)       299% (HPLC)
Purity	≥99% (HPLC) ~ 0 ~ ~
Chemical Purity	$ \leq 98\% \text{ (TLC)} $
The notive substance and former and	But the mulication solution Qas preserved directly from stock

The active substance was not form tated, but the application solution was prepared directly from stock solution (test item dissolved in accionitile) by dilution with water. 

2. Soil: "Monheim 30 (sandy loam from Germany), pH (CaCl₂) = 6.4,60.7% sand, 26.3% silt and 13.0% clay, 2.3% organic carbon, cation exchange capacity (CEC) of 5.9 freq/100 g



Crop	Variety	Plant back intervals	Growth stage at harvest	Harvested RAC
		[days]	~	5
		30 (1 st rotation)	BBCH 29–31	forage
Spring wheat	Thasos	139 (2 nd rotation)	BBCH 77-83	Shay S
		280 (3 rd rotation)	BBCH 89	straw and grain
		30 (1 st rotation)		straw and grain 2
Swiss chard	Luckullus	139 (2 nd rotation)	BBC 45-48	Teaves T
		280 (3 rd rotation)		
		30 (1 st rotation)	2 BBCH 40	
Turnips	Rondo	139 (2 nd rotation)	6 BBCH 40 0	roots and reaves(
		280 (Frotation)		Bots and leavest,
Study Design				

Table 6.6.1-7:	Details on	rotational crops
1 able 0.0.1-7.	Details on	rotational crops

## 1. Experimental conditions

fluopyram was applied on bate soil at 534 gha with a track sprayer and a flat fan nozzle 30, 139 or 280 days prior to sowing of the first, second or third of Swiss chard, turning and wheat, respectively. O North

Plants were grown in the vegetation area (building 6682) and in the greenhouse (building 6681) of Bayer CropScience AG, Metabolism / Phyironmental Fate, Monhem, Germany, The vegetation hall allows plant growth under natural sunlight and temperatures, however, a glass roof was automatically closed at the beginning Prainf or at bad weather Conditions. A metal set construction around the facility kept animals and birds on? If necessary, the soil was watered in order to maintain adequate moisture contents during the ageing period. The plants were irrigated by pouring to maintain optimal growing conditions. Application, ageing period and first rotation were conducted in the vegetation hall, second and third rotation were conducted in the greenhouse Plants were cultivated in a planting container with a surface area of 1.0 m2, filled with a sandy loan

# 2. Sampling

Wheat: Angrowth stage BBCH 29-3 Tobout 30% of the wheat plants were cut shortly above the ground as forage sample. At BBCH 77-83 ("early milk stage") again 20% of the wheat plants were dried at room demperature for four days, At BBCH 89-92 (maturity) the remaining wheat plants were cut and grains were separated by frand. The remaining fars and chaffs were combined with the straw.

the Swiss chard plants were cut above the roots. Swiss ch

(maturity) the whole turnips plants were removed from soil and separated into Turnip leanes and Coots

Directly after harvest, the samples were cut into pieces before homogenization with liquid nitrogen using



a Polytron homogenizer. At approx. -18 °C residual plant material was stored.

## **C. Analytical Procedures**

The homogenized samples were extracted and the extracts were analysed by HPLC for metabolite profiling. The identification of parent compound and metabolites was based on HPLC MS, HPLC-MS/MS and co-chromatography.

### 1. Extraction

An aliquot of each homogenized RAC was extracted three or four times with acetonitrile/water (4/, v/v). The extracts were combined, purified by SPF and the volume was determined. The extracts were separated from the solids by filtration and radioactivity was determined by volume measurement and LSC. The remaining solids were air-dried and subjected to combustion for determination of radioactivity by LSC.

If needed post extraction of solids were further extracted exhaustively, using microwave conditions with ACN/water (1/1; v/v) at 120 °C. Grain solids ( $1^{st}$  and  $2^{sd}$  rotation) from the conventional extraction were further extracted using the starch-cleaving enzyme diastase.

The ¹⁴C-radioactivity of liquid samples was determined by LSC using Quicksafe A containing 5% of water. The radioactivity in solid samples was measured by combustion. The released ¹⁴CO₂ was absorbed in an alkaline scintillation cocktain and radio assayed by LSC.

The actual TRR value of each RAC was determined after extraction by summing up the radioactivity measured in the extracts and in the remaining softes. The residue levels are expressed as parent compound equivalents per weight. The concentrated acetonitrite/water extracts were analysed by reversed phase HPLC coupled to a radioactivity gelector with gass scintillation cell.

# 2. Identification and characterisation:

Active ingredient and metabolites were identified by HPLC-MS and HPLC-MS/MS. Conjugates with glucose, malonic acid and support acid were identified before and additionally after hydrolysis to obtain further information on the skeletal structure (e.g. position of hydroxy groups).

The identification of metabolites was ourther supported by co-chromatography (HPLC, TLC) with isolated metabolites and reference items, by comparing individual RAC metabolic profiles of one rotation with those of the other rotations, and by comparison with selected profiles from the confined rotational crop study conducted with [phayl-UL ⁴C]fluopyram.

# 3. Storage stability:

All samples were stracted and grantified within 20 days after sampling the latest. Only for wheat forage (1st rotation), the netabolic profile of the extract was first analysed with the preliminary profiling method directly after straction. This profile was repeated with the final profiling method later yielding in the same qualitative and quantitative profile as before with the preliminary method. Biological samples, reference and test items were stored in a freezer at about  $\leq$ -18°C. Extracts and fractions were stored in a refrigered at about 5°C, and solids at room temperature. The metabolite pattern remained stable in reanalysed extracts e.g. for co-chromatography or identification purposes. It was concluded that the



results of the present study were not impacted by the storage of the samples and that no further storage stability investigations are required.

### **II. Results and Discussion**

The metabolism of [pyridyl-2,6-¹⁴C]fluopyram was investigated rotational crops after a single application of 534 g/ha on bare soil.

The total radioactive residues (TRRs) in the RACs of all rotations were determined by summing the radioactive residues in the extracts and extracted solids. The TRRs from all RACs and all rotations are shown in Table 6.6.1-8. Apart from wheat forage the TRRs declined from the C rotation to the 3rd rotation by a factor of 2 to 6 and in wheat grap from to 11.

The TRR amounted to 0.157-0.568-0.167 mg oq/kg in wheat foragy (1st-2st-3rd totation). The TRR in wheat hay decreased from 1.802 mg oq/kg to 0.709 mg oq/kg in wheat 5 mg oq/kg to 1.622 mg oq/kg in wheat straw and from 0.412 mg oq/kg to 0.037 mg oq/kg in wheat 5 mg oq/kg to 3rd rotation). In Swiss chard the TRR decreased from 0.570 mg oq/kg in 0.249 mg oq/kg in turnip from 0.565 mg oq/kg to 0.095 mg oq/kg in leaves and from 0.036 mg oq/kg to 0.012 mg oq/kg in roots (each 1st to 3rd rotation).

Table 6.6.1-8:	TRR values in whe	at, Swissehardan	d turnip RAC	s after applicatio	on of [pyridyl-2,6-
	¹⁴ CHuopyram			& `~	

	- Стиоруг	am 🔬 🖇	~	. 7		•	
TRR		N V	/heat N	×	Swiss chard	Tu	rnip
[mg eq/kg]	forage	ĵ∼yhay ¥	Straw 🛛	Sgrain	Swiss citaru	leaves	roots
1 st rotation	<b>19,1</b> 57 '	1.802		0.412	0.500 0.242	0.565	0.036
2 nd rotation	\$0.568 ^O	0.991	×2.5620	12 C	343	0.103	0.010
3 rd rotation	0.167	£ 92709	1.682	00.037	0.211	0.095	0.012
<u> </u>		\$ &			, OY		

The RACs were explaced with acetonitrile/water  $(4/5 \sqrt{v})$ , the extracts were analysed by HPLC and parent compound and metabolites were identified.

Conventional extraction of the RACs using acconitrile water released > 97% of the radioactive residues in Swiss and not turne leaves and roots, 85-96% of the radioactive residues in wheat forage, hay and straw and 82-92% of the radioactive residues in wheat forage, hay and

Exhaustive extraction of post extraction solids of wheat hay ( $2^{nd}$  and  $3^{rd}$  rotation) and wheat straw ( $1^{st}$  and  $2^{nd}$  rotation) using acetonicitle/water mixtures and microwave conditions released further 3–6% of the TRR. The fadioactivity in the solids of wheat grain after conventional extraction amounted to 8%–18% of the TRR but at very low absolute levels (0.032 mg eq/kg, 0.010 mg eq/kg and 0.007 mg eq/kg). Diastase treatment released additional 4% of the TRR from solids of the 1st rotation and 9% of the solids of the 3rd rotation were not further subjected to diastase treatment due to their very low absolute residue value (0.007 mg eq/kg). The diastase extracts of grain were further characterised as natural compounds by partitioning ( $1^{st}$  rotation), and not further analysed for the 2nd rotation because they were < 0.02 mg eq/kg. The residues remaining after diastase treatment from grain solids from the 1st and the 2nd rotation were at very low absolute levels (0.015 mg eq/kg and 0.003 mg eq/kg, respectively).



	1 st rot	ridyl-2,6- ¹⁴ C tation	2 nd ro	tation	3 rd rotation					
	% TRR	mg eq/kg	% TRR	mg eq/kg	گ% TRR	mg eq/kg				
		Wheat fo	rage	Ő	Ş					
Conventionally extracted	95.7	0.151	95.2	0.540	92.4	0,035				
Solids	4.3	0.007	4.8	0.025	7.6 %	× 0:013 🖄				
TRR	100.0	0.157	<b>10</b> 0.0	0568	100.0	≫0.167¢°́				
Wheat hay S S S										
Conventionally extracted	96.7	1.742 🔬	85.3	0.829 کچ	_091.2 [©]	00646				
Microwave extracted	-	- 🔿	6.3 *	∛ 0. <b>06</b> 1	á 4.74	0.033				
Solids	3.3	0.05	8.4 🥎	<u>_0</u> 2081	∛ <b>∢</b> .Չ՛	¢ 0.02				
TRR	100.0	1«802	° 100 0	× 0.971 0	<b>0</b> 00.0 🔨	0.209				
		Wheat S	řaw 🖉 🛛		No a	4				
Conventionally extracted	93.5	<u>6.229</u>		2.241	» 91. <b>O</b> ″	Q 1.477				
Microwave extracted	2.5	© 0.169	√ 5.2°°,	0.189 0,189	×,-					
Solids	4.0	0.265	₽ 7.4	0.189 [×]	ي 9.0 ي	Q\$46				
TRR	100.0	& Ø.663	100.0	2.562	100.0	1.622				
	Å	🛷 Wheat g	rain 🗇	de la companya de la	y St.	Ŝ				
Conventionally extracted	92.3 0	0.3380	Ö 86.55	0.0620	\$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$2.2 \$	0.031				
Diastase extracted		09017 麊	× 994	$\overset{\circ}{\mathbb{Q}}^{\mathbb{Y}} 0.00 \overset{\circ}{\mathbb{P}}^{\mathbb{Y}}$	8 - 4	-				
Solids	×, J,0	~©0.015	¥.4 °	0. <b>00</b> 3	17. <b>©</b> ″	0.007				
TRR	100.0	0.4	@100.0	<b>≈</b> 072 °~	100.0	0.037				
	, Ç	Swiss ch	· · · ·							
Conventionally extracted	§ 99.80	<b>@</b> .569&	.s	0,341 .	¢¢ 98.2	0.207				
Solids S	<u> </u>	Ø, 0.004	<u>₹</u> 0.8 0	6003 L	1.8	0.004				
TRR	1000.0	» 0.570 🔬		0.343	100.0	0.211				
		, Tarnip'h	aves 🔊 👤	ũ sĩ						
Conventionally@xtracted	995 0.5	°0.562	2 ^{97.4}	0.100	98.7	0.094				
Solids 🔍 🖓 🤞		0.003	2.6 O	<b>Ø</b> .003	1.3	0.001				
TRR 🔬 🖗	× 100.0	0565	0 100,0	0.103	100.0	0.095				
		Turnip, r		Y						
Conventionally extracted	9.8,7	\$ 0.036	00.1 \$	0.010	97.8	0.011				
Solids Solids	′, ¶.3	< 0.001	98.1 (* 1.9	< 0.001	2.2	< 0.001				
TRR & A		×0/036	100.0	0.010	100.0	0.012				

For the elucidation of metabolism, the solvent extracts (acetonitrile/water) were analysed by HPLC. Metabolites were identified by DC-MS and LC-MS/MS and additionally by co-chromatography (HPLC).

The identification rate was very high and ranged from 82–98% of the TRR in all RACs. In total, 27 components were detected in the various samples of the three rotations. Of these, the active substance and 10 metabolites were identified by LC-MS, LC-MS/MS and co-chromatography. The remaining 16 metabolites were characterised by their extraction and retention in radio-HPLC. All of them were  $\leq 0.011$  mg/eq/kg representing 0.1–2.0% of the respective TRR, except the two unknown metabolites in wheat straw, which were in the range of 0.3–1.3% of the TRR and equivalent to 0.008–0.042 mg eq/kg, each. The amounts of active substance and metabolites in all RACs as well as additional quantitative information for the three rotations are shown below in Table 6.6.1-10 to Table 6.6.1-12.

 $\mathcal{S}^{\mathsf{v}}$ 

S



<u>Wheat:</u> The parent compound was the main compound and declined from the 1st to 3rd rotation, from *ca.* 72–79% to *ca.* 58–70% of the TRR in wheat forage, hay and straw. In wheat grain, the parent compound declined from *ca.* 33% of the TRR in the 1st rotation to 20.4% of the TRR in the 2nd rotation, to *ca.* 31% of the TRR in the 3rd rotation. fluopyram-7-hydroxy and its various conjugates with plucose malonic acid and sulphuric acid accounted in total for *ca.* 7–17% of the TRR in these RACs of the 3rd rotation. In grain, fluopyram-7-hydroxy and its conjugates are of little importance, since they only accounted for *ca.* 1–2% of the TRR.

Two label specific metabolites represented by fluopyram-methyl-suffoxide (M45) and fluopyrampyridyl carboxylic acid (M43) were further important metabolites.

In forage and hay, fluopyram-pyridyl carboxylic acid was a prominent metabolite, but only in the  $1^{\text{tr}}$  rotation accounting for up to *ca*. 17% of the TAR (0.026 mg eq/kg). In the following rotations, this metabolite was  $\leq 1\%$  of the TRR. Fluopyram-methyl sulfox de was detected only in the  $2^{\text{nd}}$  and  $3^{\text{rd}}$  rotation and accounted for up to *ca*. 5% of the TRR (0.046 mg eq/kg).

In wheat straw, the two label specific metabolites covered only about 1% of the TRR in all rotation CAE C656949-pyridyl-carboxylic acid was betected only in the 1st rotation at an absolute amount of 0.06 mg eq/kg. fluopyram-methyl-sulfoxide was detected only in the 2th and 2th rotation at absolute amounts of 0.031 mg eq/kg and 0.019 mg eq/kg, respectively.

In wheat grain, the amount for fluopyram-pyridyl-carboxylic acid decreased from a. 56% of the TRR (0.23 mg eq/kg) in the 1st rotation down to ca. 16% of the PRR (0.01 mg eq/kg) and 29% of the TRR (0.01 mg eq/kg) in the 2nd and 3rd rotation, respectively. The absolute value of 0.23 mg eq/kg for fluopyram-pyridyl carboxylic acid in grain of the 1st rotation was high, but very low in the 2nd and 3rd rotation (0.01 mg eq/kg). The relative high amount of fluopyram-pyridyl-carboxylic acid in wheat grains (ca. 56% of the TRR in the 1st rotation equivalent to 0.23 mg eq/kg) is not considered to be the result of metabolic conversion of the parent compound in this compartment. It is more likely that this metabolite was taken up from soil and then selectively transported into the grain.

Only *ca.* 1% of the TRR was covered by fuopyram-methyl-sulfoxide to grains of the 1st rotation and increased to about 49% of the TRR (0.035 mg eq.kg) and 20% of the TRR (0.008 mg eq.kg) in the 2nd and 3rd rotation, respectively. The absolute amounts for fluopyram-methyl-sulfoxide in grains were significantly lower than for fluopyram-pyridyl-carboxylic acid and amounted to 0.005 mg eq/kg (1st rotation), 0.035 mg eq/kg (2nd rotation) and 0.008 mg eq/kg (3rd rotation).

fluopyram-8-hydrosy and its confugate were only of minor importance and accounted for < 3% TRR in wheat RACs.

Swiss chard: The parent compound was the main compound amounting to *ca*. 57% of the TRR (0.323 ms eq/kg), *ca*. 37% of the TRR (0.128 mg eq/kg) and *ca*. 39% of the TRR (0.081 mg eq/kg) in the 1st 2rd and 3rd rotation, respectively. Bropyran-7-hydroxy and its various conjugates with glucose, malenic acid and surphurc acid accounted in total for *ca*. 37–55% of the TRR. fluopyram-7-hydroxy was the prominent metabolite of this metabolite group amounting to *ca*. 28% of the TRR in the 1st rotation and increasing to *ca*. 29% of the TRR in the following rotations. The sulphuric acid conjugate of fluopyram-7-hydroxy, thropyram-7-OE-SA, increased in Swiss chard from *ca*. 8% of TRR in the 1st rotation to *ca*. 17% and 14% of the TRR in the 2nd and 3rd rotation, respectively.

The values for the tabel specific metabolites (fluopyram-methyl-sulfoxide and fluopyram-pyridyl carboxylic acid) remained at a comparable level accounting for  $\leq 6\%$  of the TRR. fluopyram-8-hydroxy and its coppagate were only of minor importance and accounted for < 3% TRR in Swiss chard.

Ĵ



Turnip: The parent compound was the main compound in turnip roots and leaves. In turnips roots, it amounted to ca. 86% of the TRR (0.031 mg eq/kg), 95% of the TRR (0.010 mg eq/kg) and ca. 92% of the TRR (0.010 mg eq/kg) in the 1st, 2nd and 3rd rotation, respectively. In turnips leaves, the parent compound accounted for ca. 70% of the TRR (0.399 mg eq/kg), 60% of the TRR (0.061 mg eq/kg) and *ca.* 64% of the TRR (0.061 mg eq/kg) in the  $1^{st}$ ,  $2^{nd}$  and  $3^{rd}$  rotation, respectively

Besides the parent compound, fluopyram-phenol-glc was a prominent metabolite found exclusively in turnip leaves where it amounted to ca. 12% of the TRR (0.068 mg eq/kg), 18% of the TRR (0.019 mg eq/kg) and 15% of the TRR (0.014 mg eq/kg) in the 1st, 2nd and 3rd rotation, respectively.

fluopyram-7-hydroxy increased from ca. 3-4% in the 1st rotation to 6-8% in the 3rd rotation the various conjugates of fluopyram-7-hydroxy were less prominent and represented each 3% of the ORR o c turnips RACs.

The amounts of the label specific metabolites (fluopyram-methyl sulfoxide and fluopyram-pyridyl carboxylic acid) remained at a comparable level, accounting for  $\leq 6\%$  of the TRR

The amounts of the label specific metabolites (fluopyram-prethyl-mifoxice and Huopyram-prethyl-mifoxice and Huopyram-prethyl-mifoxice and Auopyram-prethyl-mifoxice and Auopyram-prethyl-mifoxice and accounter for < 0% TRF unip RACs. TR≰∕in



1. Rotation	Wheat	forage	Whe	eat hay	Wheat s	traw	Wheat	graans
TRR $[mg eq/kg] =$	0.1	.57	1.	.802	6.66	3	0.4	12 5
Compound	%	mg eq/	%	mg eq/	%	µg eq∕	%	mg eq/
•	TRR	kg	TRR	kg	TRR	kg	TRR	kg)
AE C656948, a.s., fluopyram	71.7	0.113	78.9	1.421	73.90	4.926	33.4	0.137
fluopyram-methyl-sulfoxide (M45)	-	-	-	-	A		ĴĨ.2	Ø.005 Ø
fluopyram-pyridyl-carboxylic acid (M43)	16.5	0.026	A.9	0.088	0.9	0.060 🔭	\$ 55.9~	0.230
fluopyram-7-hydroxy-glc-MA (M12),	3.3	0.005	₹4.2	0.076	5.6	0.356	$\sim$	Ű
isomer 1	5.5	0.005 مار	v T.2	0.070	5.0	≪	Ň	
fluopyram-7-hydroxy-glc-MA (M12),	_	, Č	1.2	0-021	1.1	9.072 .	°~- ∧	) - "
isomer 2		A.				' al a		Š
fluopyram-8-hydroxy-glc-MA (M19)	-	$\sqrt[n]{0}$	0.6	~0.010@	i 0.4 i i	0.028	Ŵ.	
fluopyram-7-OH-SA (M10)			· - "		40	ð.	°~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	J ⁻
fluopyram-7-hydroxy-glc (M11)	1.30*	0.062	Q.9	0.016	S.I	Q.203	· -	-
fluopyram-phenol-glc (M06)			Ø,			0.494		
fluopyram-7-hydroxy (M08)	JAN .	0.003	0.4°	0.068			r@a	0.008
fluopyram-8-hydroxy (M18)		0.149		0.006 ³		0.087	-	<u>_</u>
Total identified	9500		94,7 	<u> </u>	(C		Ŷ	0.380
Characterized by HPLC retention*	0.7°	.0.901	≪ ^{¥.8} /	Ø.032		0.074		-
Characterized by diastase treatment		· -	- 🔺	1.742	-0	6.998	¥_J° 9∕2.3	0.017
	95.7 ¢ 4.3	0.150	96.05 3.3	0,0059		0.265		0.380
Total bound residues (PES)	4.3	0.007		(0).5/			/ 3.6	0.015
Not analysed	\$00.0		<u>0.3</u>	0.004		0.076	-	-
Accountability		20.157 [°]	0°100.0	1.802	100,0	6,603	100.0	0.412
			- Ô	(Ar		ў Лаг	•	- 4 -
1. Rotation		iss Charc 6570		Turnip			urnip ro	015
$\frac{\text{TRR} [\text{mg eq/kg}]}{\sqrt{2}} = \sqrt{2}$		6 3 / U			Ŷ	0/	0.036	/
Compound	TRR	λΩg ≫ k	eq/	′% T <b>R</b> R	nong eq/ ≫Sy kg	% TR		ng eq/ kg
AE C656948, aQ., fluggyram	<i>6</i> , <b>6</b> 6.7	× 0.3		. 0.6	0.399	86.	.1 (	0.031
fluopyram-methyl-suppoxide(M45)	$\mathbb{N}$ 04	Ø 0.0	103 (	<u>)</u> 0	-	-		-
fluopyram-@yridyl-carboxylic acid (M43)-	1.8	× 000	010 _©	4.2	0.024	6.0	0 (	0.002
fluopyram 7-hydroxy-glc-MA (Q12),		~	e la companya de la compa	~ 🔍				
		¢C?	~C	alo	0.011			
isomer S	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	, de .	- D	0.9	0.011	-		-
isomer S	6 ^{9* -} «			0.9		-		-
isomer fluopyram-7-hydrox glc-MA (M12),				0.6	0.011 0.003	-		-
isomer 2 fluopyram-7-hydroxy glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glo MA (M19)				-	0.003	-		-
isomer 2 fluopyram-7-hydroxo glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glo-MA (M19) fluopyram-7-Q4-SA (M10)	07.9			_ 0.7	0.003	-		-
isomer 2 fluopyram-7-hydroxo glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glo MA (M19) fluopyram-7-Q4-SA (M10)	0 ^{7.9}		- 4 ) - 4 )	0.7 0.3	0.003	-		- - -
isomer 2 fluopyram-7-hydroxy glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glo-MA (M19) fluopyram-7-hydroxy-glc (M10) fluopyram-7-hydroxy-glc (M11) fluopyram-thenol-glc (M06)	× × × × × × × × × × × × × ×		-05	0.7 0.3 12.0	0.003 - 0.004 0.002 0.068	-		
isomer V fluopyram-7-hydroxy glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glc MA (M19) fluopyram-7-flu-SA (M10) fluopyram-7-hydroxy-glc (M1) fluopyram-7-hydroxy-glc (M06) fluopyram-7-hydroxy (M08)	07.9 0.9 0.9 0.9 0.9 0.9 0.9 0.9 0.9 0.9 0		905 - 60	0.7 0.3 12.0 3.5	0.003 0.004 0.002 0.068 0.020			-
isomet fluopyram-7-hydroxy-glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glo MA (M19) fluopyram-7-041-SA (M10) fluopyram-7-hydroxy-glc (M11) fluopyram-7-hydroxy-glc (M06) fluopyram-7-hydroxy (M08) fluopyram-8-hydroxy (M18)	0.9¢ 0.9¢ 0.9¢ 0.9¢ 0.9¢	0.1 0.1	905 - 160 905	0.7 0.3 12.0 3.5 0.3	0.003 0.004 0.002 0.068 0.020 0.002	1.:	5 (	0.001
isomer V fluopyram-7-hydroxy glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glo MA (M19) fluopyram-7-MI-SA (M10) fluopyram-7-hydroxy-glc (M11) fluopyram-7-hydroxy-glc (M06) fluopyram-7-hydroxy (M08) fluopyram-8-hydroxy (M18) Toral identified	0.90 0.90 0.90 0.90 0.90 0.90	0.1 0.0 0.0 0.5	005 	0.7 0.3 12.0 3.5 0.3 94.3	0.003 - 0.004 0.002 0.068 0.020 0.002 0.002 0.532	1.: 96.	5 ( .7 (	0.001
isomer V fluopyram-7-hydroxy-glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glo MA (M19) fluopyram-7-041-SA (M10) fluopyram-7-hydroxy-glc (M11) fluopyram-7-hydroxy-glc (M06) fluopyram-7-hydroxy (M08) fluopyram-8-hydroxy (M08) fluopyram-8-hydroxy (M18) Total identified Characterized by HPLC retention	0.90 0.90 0.90 0.90 0.90 0.90	0.1 0.0 0.0 0.5	905 - 160 905	0.7 0.3 12.0 3.5 0.3	0.003 0.004 0.002 0.068 0.020 0.002	1.:	5 ( .7 (	0.001
isomer V fluopyram-7-hydroxy-glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glc-MA (M19) fluopyram-7-hydroxy-glc (M10) fluopyram-7-hydroxy-glc (M11) fluopyram-7-hydroxy (M08) fluopyram-7-hydroxy (M08) fluopyram-8-hydroxy (M08) fluopyram-8-hydroxy (M18) Characterized by HPLC retention Characterized by diastase treatment	0.9¢ 28.0 28.0 96% 2.2 2.2 2.2	0.1 0.1 0.0 0.0	005 	0.7 0.3 12.0 3.5 0.3 94.3 5.2	0.003 0.004 0.002 0.068 0.020 0.002 0.532 0.030 -	1.: 96. 2.0	5 ( .7 ( 0 (	0.001 0.035 0.001 -
isomer 2 fluopyram-7-hydroxy-glo-MA (M12), isomer 2 fluopyram-8-hydroxy-glo-MA (M19) fluopyram-7-flu-SA (M10) fluopyram-7-hydroxy-glc (M11) fluopyram-7-hydroxy-glc (M06) fluopyram-7-hydroxy (M08) fluopyram-8-hydroxy (M08) fluopyram-8-hydroxy (M08) fluopyram-8-hydroxy (M08) fluopyram-8-hydroxy (M08) fluopyram-8-hydroxy (M08) fluopyram-8-hydroxy (M08) fluopyram-8-hydroxy (M18) Total Identified Characterized by HPLC retention Characterized by HPLC retention Characterized by HPLC retention Characterized by HPLC retention	0.9 0.9 0.9 0.9 0.9 0.9 0.9 0.9	0.1 0.1 0.1 0.1 0.1 0.1	05 60 05 551 018 - 569	0.7 0.3 12.0 3.5 0.3 94.3 5.2 - 99.5	0.003 0.004 0.002 0.068 0.020 0.002 0.532 0.030 - 0.562	1.3 96. 2.0 - 98.	5 () .7 () 0 () .7 ()	0.001 0.035 0.001 - 0.036
isomer V fluopyram-7-hydroxy-glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glc MA (M19) fluopyram-7-hydroxy-glc (M10) fluopyram-7-hydroxy-glc (M11) fluopyram-7-hydroxy (M08) fluopyram-7-hydroxy (M08) fluopyram-8-hydroxy (M08) fluopyram-8-hydroxy (M08) fluopyram-8-hydroxy (M08) fluopyram-8-hydroxy (M08) fluopyram-8-hydroxy (M08) fluopyram-7-hydroxy (M08) fluopyram-8-hydroxy (M18) fluopyram-7-hydroxy (M08) fluopyram-7-hydroxy (M18) fluopyram-7-hydroxy (M18) fluop	0.9 28.0 0.9 28.0 0.9 0.9 0.9 0.9 0.9 0.9 0.9 0	0.1 0.1 0.1 0.1 0.1 0.1	005 	0.7 0.3 12.0 3.5 0.3 94.3 5.2	0.003 0.004 0.002 0.068 0.020 0.002 0.532 0.030 -	1.: 96. 2.0	5 () .7 () 0 () .7 ()	0.001 0.035 0.001 -
isomer V fluopyram-7-hydroxy-glc-MA (M12), isomer 2 fluopyram-8-hydroxy-glc MA (M19) fluopyram-7-flydroxy-glc (M10) fluopyram-7-hydroxy-glc (M11) fluopyram-7-hydroxy (M08) fluopyram-7-hydroxy (M08) fluopyram-8-hydroxy (M08) fluopyram-8-hydroxy (M08) fluopyram-8-hydroxy (M18) Total identified Characterized by HPLC refention Characterized by HPLC ref	0.9 0.9 0.9 0.9 0.9 0.9 0.9 0.9	0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0	05 60 05 551 018 - 569	0.7 0.3 12.0 3.5 0.3 94.3 5.2 - 99.5	0.003 0.004 0.002 0.068 0.020 0.002 0.532 0.030 - 0.562	1.3 96. 2.0 - 98.	5     ()       .7     ()       0     ()       .7     ()       .7     ()       .7     ()       .7     ()       .7     ()       .7     ()       .7     ()	0.001 0.035 0.001 - 0.036

### Table 6.6.1-10:Residues in RACs after a 30 day plant back interval (1st rotation, pyridyl-label)

* up to 17 metabolites characterised by extraction and chromatographic behaviour, all of them  $\leq 2.0\%$  of the TRR and  $\leq 0.043$  mg eq/kg

ĉ



2. Rotation	Wheat	forage	Wh	neat hay	Wheat	straw	Whea	t græns
$\Gamma RR [mg eq/kg] =$	0.5	68		0.971	2.50	52	0	.072
Compound	%	mg eq/	%	mg eq/		mg eq∕	%	∮)ng eq/
1	TRR	kg	TRR	0	TRR	<u> </u>	TRR	
AE C656948, a.s., fluopyram	77.9	0.442	66.9		73.50	1.881	20.4	0.015
luopyram-methyl-sulfoxide (M45)	2.2	0.012	4.7		42	0.031	<b>@</b> ₽9.0	0.035
fluopyram-pyridyl-carboxylic acid (M43)	1.0	0.006	Q.6	0.006	<u> </u>		16.4	0.012
fluopyram-7-hydroxy-glc-MA (M12), isomer 1	5.6	0.032	₹7.0		3.5	0.089	2	
luopyram-7-hydroxy-glc-MA (M12), somer 2	0.7	0.004	1.4		2.5		^Q - (	¢ [*] - ¢
luopyram-8-hydroxy-glc-MA (M19)	1.2	<b>0</b> 007	1.4	~0.01 ⁴	0.9 🗳	0.020 [°]	Ô.	Ø
luopyram-7-OH-SA (M10)	- "	× - 🔊	o – "	Oʻ_'Y	, P			~~
luopyram-7-hydroxy-glc (M11)	1.0	0.005	245	0.024	2.3	0.059	** <u>*</u> -	
fluopyram-phenol-glc (M06)		×,	Û,	ď.	<u></u> -	° _ A	- –	° ا
luopyram-7-hydroxy (M08)	J 3 1	0.018	5.9	0.057	6.1	0.156	0.8	0.001
luopyram-8-hydroxy (M18)	¢َ 0.7 ٍ ^م	0.004	0.7			0:030	" - ·	, SY -
Fotal identified	93Q	0.530	94		<u>\$</u> 91.0	Å	86.5	0.062
Characterized by HPLC retention*	2%.9 0 <u>~</u>	.0.011	<b>Ø</b> .5	0.004	\$ ⁰ .8 ≴	0.020	- ~~	-
Characterized by diastase treatment	<u></u>	∽- 、	~ -	J - Č	r -81	Ĵ	 	0.007
Total extractable	Ø 95.2 Q	0.540	91. <b>6</b>	0.890	<u>9</u> 07	2,973	86.5	0.062
Fotal bound residues (PES)	4.8	0.027	8.4	ØØ81	9.4	0.189	4.4	0.003
Not analysed	ŝ	e -	-	×	0.9	0.022	-	-
Accountability	\$00.0	20.568	©100.	0 0.970	100.0	2,502	100.0	0.072
	Q &			<u>, k</u>		<u>~</u>		
. Rotation 🔬 🖉	(Sw	iss char	1. O	Furni	p leaves	) Й т	<b>urnip</b>	roots
$[RR [mg eq/kg] = \sqrt[6]{9}$		0.943	L)	-0:-0;	103 🎝		0.01	
	§ %	Janê Sen	ea/	0 %.	ng eq/	0	6	mg eq/
Compound	TRK	No k	g 🔊	Υ <b>ΓΙΩ</b> Ϋ́	~♡ kg	TF	RR	kg
AE C656948, a3., flugpyram	. 67.3	× × 0.1	128	\$9.9	0.061		1.6	0.010
luopyram-methyl-suffoxide (M45)	₩0.4		<b>1</b>	<u> </u>	-	-	-	_
luopyram-øyridyl-carboxylic acid @M43)₄			01	1.5	0.001	-	-	_
luopyram 7-hydroxy-gle MA (M12), Ø	, <b>y</b> - O <b>y</b>	$\sim$						
somer 🕄 . 🖉 . 🛇 💊	~ ~	, 6°	- 10 ×	<u>م</u> .%	0.003	-	-	-
luopyram-7-hydrox glc-MA (M12),	Ő ^v 4	× 4	,	SY.	0.001			
	<u>Þ</u> - ~		× 🔊	1.2	0.001	-	-	-
		$\sim$	- 🖉	-	-		-	-
luopyram-8-hydroxy-gle-MA (\$\$19) luopyram-7-081-SA (\$\$10)		).0 [°] 0.0	)58	0.7	0.001		-	-
luopyram-7-bydroxy-glc (MQ1)	1.8	× 09.	)06	1.4	0.001	-	-	-
luopyram_phenol-glc (M08)	14 <u>-</u> 6	″   <u>,</u> ©	-	18.4	0.019		-	-
luopyra@7-hydroxy (MØ8)	36.5	× 0.1	125	5.3	0.005	3	.5	< 0.001
luopyram-8-hydroxy (M18)	\$1.1.		)04	0.5	0.001		-	-
Fotal identified	Ø 94.0		323	91.7	0.094	98	3.1	0.010
Characterized by HPLC relention			)18	5.7	0.006		-	-
Characterized by the reaction of the characterized by diastase treatment	5.0°	0.0	_	-	-		_	-
Total extractable	99.2	0 3	341	97.4	0.100	98	31	0.010
			)03	2.6	0.003		.9	< 0.001
Not analysed	0.0	0.0		2.0	0.003	1.	.,	× 0.001
Accountability	100.0	0.2	- 344	100.0	0.103	10	0.0	0.010
1000 UINADIIIIVA IF A ACS	100.0	0.2	) <del>44</del>	100.0	0.103	10	0.0	0.010

### Table 6.6.1-11: Residues in RACs after a 139 day plant back interval (2nd rotation, pyridyl-label)

 $\frac{100.0 \quad 0.344 \quad 100.0 \quad 0.103 \quad 100.0 \quad 0.010}{\text{up to 14 minor metabolites characterised by extraction and chromatographic behaviour, all of them <math>\leq 1.7\%$  of the TRR and < 0.047 mg eq/log



3. Rotation	Wheat	forage	Whe	at hay	Wheat	straw	Whea	t grains	2
TRR [mg eq/kg] =	0.1	0		709	1.6			03	S
Compound	%	mg eq/	%	mg eq/	%	≽mg eq/	%	,∯mg eq/	Ø
Compound	TRR	kg	TRR	kg	TRR	≥ kg	TRR	kg)	
AE C656948, a.s. fluopyram	70.2	0.118	66.8	0.473	58.30	0.945	31.0	0.012	
fluopyram-methyl-sulfoxide (M45)	2.0	0.003	3.5	0.025	42	0.019	Â0.3	0.008	Ø
fluopyram-pyridyl-carboxylic acid (M43)	0.9	0.002	Q.5	0.004	$\mathcal{L}^{-}$	- 1	¥28.6≈	0.01	1
fluopyram-7-hydroxy-glc-MA (M12)	7.5	0.013	9.5	0.067		0.118		<u></u>	ď
fluopyram-7-hydroxy-glc-MA (M12)	1.1	0.002	♥ 1.2	0.00	4.5	0,002	Ň		Ô
fluopyram-8-hydroxy-glc-MA (M19)	1.7	0.003	1.7	0.012	1.2	6019	~~-	×٥ - ۲	
fluopyram-7-OH-SA (M10)	-		-	~~	ô°- ć	¥ - 4	, - (	-~	
fluopyram-7-hydroxy-glc (M11)	3.0	0005	3.0	<b>√</b> 0.021@	j 3.7 🕅	0.060	Ĵ.		
fluopyram-phenol-glc (M06)	- (%)		, - (1 846	0.061		@164	°~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	«J ^{×-}	
fluopyram-7-hydroxy (M08)	5.6	0.009	846° Č1	0.061	<b>1</b> 0.1	(())) (	2.3	0.001	
fluopyram-8-hydroxy (M18)	-				©°1./	0.028	<u> </u>		-
Total identified	×92.0	0.154	95.4	0.67 <u>k</u>	87.9	1.425	82,2	0.031	4
Characterized by HPLC retention*	∲ 0.4°	0.00	0.6C	0.064	25	<0,001	<i>щ</i> -	- [*]	1
Characterized by diastase treatment		×	, Š	٨. ٣	õ- a	Q`	Ş ⁷ −	Ψ -	
Total extractable	92.4	Q <b>1</b> 55	<b>\$</b> 5.9 /	0.679	91.05	1.47	82.	0.031	
Total bound residues (PES) $Q^{\nu}$	7.6	0.013	4.1	0.029	9.0	0,146	\$17.8	0.007	
Not analysed	- 7	-\$	00	0.004	0.0	<u>0</u> .016 ¢		-	
Accountability	100.0	0.167	100.0	Ø.709 (	⊳100.0	1.6220	100.0	0.037	1
		7	0°	*		Ĉo			1
3. Rotation		iss charo	1	Tươnip	leaves	<u></u>	urnip	roots	1
TRR [mg eq/kg] =	Ő	0.2	ς Ο ^γ	% 0 <u>.</u> 0		5	0.012		
Compound	0/		æq/	0% %	mg.eq	0/		mg eq/	1
	Ç TRR'		ğ O	TRR	"kģ	TF		kg	
AE C656948, a.s. 2 0 2	38.0	°~Ø.(	)81	64.Z	0.061	91	.7	0.010	
fluopyram methol-sulf@ide (M45)	0.5	S/ 10	101	<u> </u>	♥ -		-	-	
fluopyram py y y - carboxylic acid (M43)	≪ 0.2	¢] 0,	190 (	5 1.1 Ø	0.001		-	-	
fluopyram 7-hydroxy-glc-MA (2112),		1 0	- @	10	0.002		_	-	
isomer 1 y		Ç,	~	Š	0.002				
fluopyram 7-hydroxyrglc-M& (M12),	~ ~ -	<u>م</u>	- ·	≈1.9	0.002		-	-	
isomer 2	O ^v 4	j" &	1 2						
fluopyram 8-hydroxy-glc-MA (MJ)				-	-		-	-	
fluopyram 7-OH A (MG)	.13%S		)29 Maria	0.4	0.000		-	-	
fluopyram 7-OH SA (Mtb) fluopyram 7-hydroxy-go (M14) fluopyram phenol-gle (M060	01.3	0.0 °	) <b>B</b> ^y	1.6	0.001		-	-	
			»- )81	14.7 8.3	0.014		-	-	
fluopyram (M08) fluopyram 8-hydroxy (M08)	** 2000 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			8.3 0.4	0.008 0.000		.1	0.001	1
Total identified	£94.0		198	94.2			-	0.012	-
					0.090		.0	0.012	-
Characterized by HFVC retention*	₽ 4€	» 0.0	)09	4.5	0.004		-	-	
	i d		-	-	-		-	-	4
Characterized by diastase Weatment				007	0.094	07	.8	0.011	1
Total extractable	<b>Q</b> 8.2	0.2	207	98.7	0.094	71	.0	0.011	-
Total extractable Total bound cosidues (PES)	a, [×] -		-	_	-		-	_	]
Total extractable	a) -	0.0	- 004 211	<u>-</u> 1.3 100.0	0.004		-	- < 0.001 0.012	-

### Residues in RACs after a 280 day plant back interval (3rd rotation, pyridyl-label) Table 6.6.1-12:

up to 3 minor metabolites characterised by extraction and chromatographic behaviour, all of them  $\leq 1.3\%$  of the TRR and < 0.022 mg eq/kg



Q,

# III. Conclusions

After application of [pyridyl-2,6-¹⁴C]fluopyram on bare soil, most of the recovered radioactivity was detected in the dry leaf RACs wheat straw (1.622–6.663 mg eq/kg) and hay (0.709-1.802 mg eq/kg). Medium amounts of radioactivity were found in the fresh leaf RACs wheat forage (0.57-0.568 mg eq/kg), Swiss chard (0.211-0.570 mg eq/kg) and turnip leaves (0.095-0.565 mg eq/kg), but also wheat grain of the 1st rotation (0.412 mg eq/kg).

Only minor residues were detected in grain of the  $2^{nd}$  and  $3^{nd}$  rotation (9937-0.072 mg/eq/kg) and turnip roots (0.010-0.036 mg eq/kg). A significant decline (factor of 2 to 6) of the radioactive residues was observed for all RACs except wheat forage and hay where the residues remained at a similar level.

In total, 27 components were detected in the various samples of this study, and of them, including parent and major metabolites, were identified.

Apart from wheat grain, the parent compound was the main compound in albRACs of all rotations and covered 57–86% of the TRR in the RACs of the 1st rotation, 37–95% of the TRR if the BACs of the 2nd rotation and 39–92% of the TRR in the RACs in the 3rd rotation. In wheat grain, it accounted for 20.4–33.4% of the TRR in the three rotations.

In wheat grain, two label specific, metabolites represented by fluopyram-methyl-sulfoxide and fluopyram-pyridyl carboxylic acid were main metabolites. The replaces of these metabolites were in the range of 50–65% of the TRR. fluopyram-methyl-sulfoxide amounted to 1.2% 49.0%–20.3% of the TRR (1st-2nd-3rd rotation) while fluopyram-pyridyl carboxylic acid represented 58.9% 416.4%–28.6% of the TRR (1st-2nd-3rd rotation). The relative high amount of fluopyram-pyridyl-carboxylic acid in wheat grains is considered to be the result of the phloem transport into the grains (as a phloem sink) rather than the result of metabolities of the parent compound in this compartment, in analogy to the behaviour of other organic acids in higher plants.

In the other RAOs these label specific metabolites were of less importance accounting for  $\leq 6\%$  (sum of both) of the TRRs. However, fluopyram-pyridy carbosylic and was a prominent metabolite in wheat forage of the 1st rotation accounting for 17% of the TRR but decreased to < 1% of the TRR in the following rotations.

Fluopyram-7-hydroxy and its various conjugates with glucoses malonic acid (2 isomers) and sulphuric acid were important metabolites mainly in Swiss chard, where fluopyram-7-hydroxy increased from 28% to about 39% of the TRR. In the other RACs, the amount of fluopyram-7-hydroxy was distinctively lower than in wiss chard, only 2–7% of the TRR in the 1st rotation but also increasing from rotation to rotation up to 2–10%.

The sulphuric acid conjugate of fluopyram 7-hydroxy, fluopyram-7-OH-SA, was also a prominent metabolite in Swiss that increasing from 8% of PRR in the 1st rotation to 17% and 14% of the TRR in the 2nd and 3rd rotation. The sum of the four 7-hydroxy conjugates reached a maximum of fraction of the TRR of 18% in Swiss chard of the 2nd rotation. The maximum absolute amount of 0.652 mg eq/kg was reached in wheat straw in the 2nd rotation.

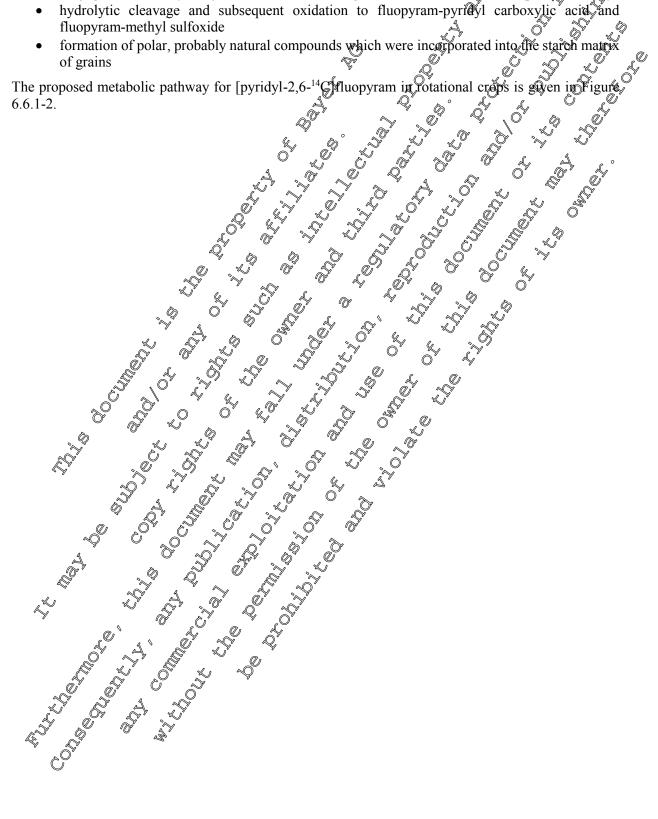
fluopyram-Shydroxy and its conjugate were only of minor importance. Both or at least one of them were detected in all RACs but a levels < 2.9% of the TRR in sum.

fluopytam-phonol-gle was detected in turnip leaves only, where it amounted to 12%, 18% and 15% of the T&R of the 1st, 2rd and 3rd rotation, respectively.

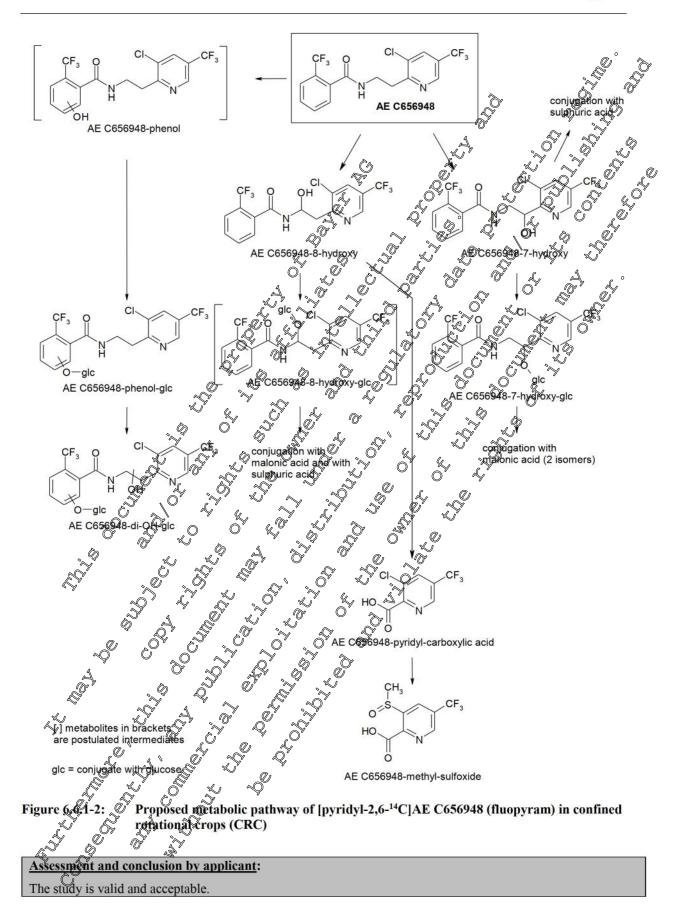
The main metabolic transformations detected were:



- hydroxylation of the ethyl linking group of the parent compound forming fluopyram-7-hydroxy • and -8-hydroxy metabolites
- hydroxylation of the phenyl ring and subsequent conjugation with glucose leading to fluop am-• phenol-glc (turnip leaves only) O
- conjugation of the hydroxylated metabolites with glucose, malonic acid and sulphuric acid ٠
- hydrolytic cleavage and subsequent oxidation to fluopyram-pyrioyl carboxylic acid and fluopyram-methyl sulfoxide Õ
- formation of polar, probably natural compounds which were incorporated into the starch matrix









# CA 6.6.2 Magnitude of residues in rotational crops

Risk assessment residue definition (EFSA Journal 2013;11(4):3052)

In food of plant origin : Sum of fluopyram and fluopyram-benzamide (M25), pressed as floopyram

Additional analytical targets in rotational field residues trials:

- Rotational crops: FLU-PCA, FLU-COH and FLU methyl-sulfaxide
- Rotational crops since 2019: FLU-PCA, FLU-7-OH, FLU-methyl-sulforide and TF

During the first submission of fluopyram in EW in 2009 (DAR, 2014), rotational crop studies were submitted and are summarized again in the present dossier (KCA 6.6.2/01 to KCA@.6.2/07).

Some trials were conducted in the USA as the dossier was a joined review (RCA 6.6.2/05 to KCA 6.6.2/07). These US studies are not summarized here as FU data are required for this renewal dossier. They are overruled by studies KCA 6.6.2-01 to KCA 6.6.2-04 and by RCA 6.6.2-08 to KCA 6.6.2-25.

According to the GAPs supported at that time, the trials were conducted at 500g af/ha following either a soil application or a primary crop application. An everyiew of these 4 RP studies (12 trials), presented in Table 6.6.2-1.

Additional trials were conducted in EU at the same dose for different crops after a plant back interval around 30 days (KCA 6.6.2/08 to KCA 6.6.2/25). An overview of these 18 studies (35 trials) is presented in Table 6.6.2-2.

Considering the whole package of residue results from the trials conducted at 500 g ai/ha, median residues values were calculated and are presented in Table 6.6.2-3. Botational crops field trials were conducted at a dose rate of application overing the max PECsoil for parent (~ 1.2N) (Germany, 2011; EFSA 2014; EFSA 2014; EFSA 2010).

As the limited crop rotational studies show residues in come of the trials and according to the OECD guidance document on residues in rotational crops ENX/JM/MONE(2018)9 from 22 May 2018, a batch of extended rotational trials stated in 2019. Studies are conducted on carrot (4 trials), leek (4 trials), wheat (4 trials), corn (4 trials) lettuce (4 trials), cabbage (4 trials) broccoli (4 trials), rape (4 trials), pea (4 trials), strawberry (4 trials), cucumber (4 trials) and potato (4 trials).

At the start of the mals, some uncertainty remained around the new PECsoil value to calculate the longterm residue accumulation plateau. Thus, an exaggerated application dose rate of 1200 g ai/ha was selected.

In addition to the fluopyram (AE C656948) and its metabolites fluopyram-benzamide (AE F148815), fluopyram-pyridyl carboxylic acid (AE C657188) fluopyram-pyridyl-acetic acid, fluopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl suffoxide (AE 1344122) the analysis of the trifluoroacetic acid (TFA) metabolite are conducted in the 2019 study package because this compound may be generated in soil.

As agreed with the RWS, an applated MCA section 06 document will be submitted in January 2022 when the final reports are available for 12 studies. The 3 remaining studies (wheat (2 trials), rape (2 trials), strawberry (2 trials)) will be made available in Q2 2022.

- ars)) w.



Page 644 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

ole 6.6.2- 1:	author	formu-	Trial	n 1st submis	dose	rot.		PBI	FLU	FR-	் FLU-PCல்	ŤLU _z 76	FLU- methyl-
reference	(report date)	lation	region plots	on	ai.ha	nb	crop	(days)	e (mg/kg)	benzamide (mg/kg)	(mg/kg)	OH Ong/kg)	sulfoxide (mg/kg)
				soil	500-	~	tettuce 5	30 - 30	0.050.04 leaf	<u>\$</u> <u>\$</u> \$ \$ 9 901	× <0.05 200.01	<u>&lt;8</u> 01 ² \$<0.01	<0.01
				(≤ 8cm)	500g	¢°°		130	28 straw		<0,001	0.1 Straw	0.09 grain 0.07 straw
A-2649/06				î	ġ,		turnip	- <u>80</u> 0-	0.Q3 leaf	C 0.01	✓ <0.01@©	°″ <0,01∘	< 0.01
296608-01-	(21/01/2008)	FLU 500SC	1 NEU 3 plots	Lefturce	500g	5 🔊	S lettuce	90	0.01 00	<0 <u>\</u> 0\1	.0.01		< 0.01
1	()		⇒0 [€]	Lettuce	Organo.	ŝ	wheat	ر ¹ 46	ŝ	0.01C ^{UI}		0.10-0.17 straw	0.05 grain
		\$	Ġ	and I	ŢĴ9	the	turanjo	3285	0.01 Deaf	\$<0.01 {	<0.01	< 0.01	< 0.01
		The P		Lettuco	500g	1	<u>lettuce</u>	×320	£ 0.01 €	<0.01	< 0.01	< 0.01	< 0.01
		"		× × /	-	£ª'	wheat	28®	0.06 straw	J 0.01	< 0.01	< 0.01	0.02 grain
			GUD	Soil Soil (< 8cm) CUIN CUIN CUIN CUIN CUIN CUIN CUIN CUIN	TRASY	ð	turnip &	30	0.06 straw 0.02 leaf % 0.02 foot	<0.01	< 0.01	< 0.01	< 0.01
		vole	d	$\frac{1}{2} (\leq 8 \operatorname{cm})^{2}$	> 500g > 0 [©]	P 1	dettuce	<u>_</u> R ^{**} ,	0.01-0.03	< 0.01	< 0.01	< 0.01	< 0.01
	-	Y Í	Ċ ^O Ľ	-CUILL	t ¹	- at i	wheat	28 0		< 0.01	< 0.01	< 0.01	0.01 grain
A-2648/06 -296625-02-		FLU		y (≤ scorpt C UT P Dettuce C D Dettuce Lectuce D D	201	, 3D	Oturnip «	216	0.04 leaf 0.02 root	< 0.01	< 0.01	< 0.01	< 0.01
<u>1</u>	(26/09/2008)	500SC*	<b>S</b> plots	Prettuce	2500g	j.	betuice	230	0.01	< 0.01	< 0.01	< 0.01	< 0.01
	×	re ¹	9.D.Z		- Calib	<u>, , , </u> , e	wheat	100	0.09 straw	< 0.01	< 0.01	0.05 straw	0.04 grain
	~ DO	~~	- ~	C ^{IJ-} Q [©]	1	) L	turnip	301	0.01 leaf	< 0.01	< 0.01	< 0.01	< 0.01
	Congeotre	D ^t	RARA	Lettuce	800g		lettuce	301	0.01	< 0.01	< 0.01	< 0.01	< 0.01
~	NY AVE	Ĉ	)" *.	P.	*		wheat	363	0.01	< 0.01	< 0.01	< 0.01	< 0.01

Page 645 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram



									p ^Ĝ		- S		g ^{ilt} and
reference	author (report date)	formu- lation	Trial region plots	application on	dose ai.ha	rot. nb	crop	PBI .	FLU (mg/kg)	FLU-	چ⊾ FLU-PCA (mg/kg)		FLU- prethyl- sulfoxide (mg/kg)
				.1			carrot	30	0.05 Keot	50.01	\$0.01		<0.01
				soil (≤ 8cm)	500g	~C	OPettuce &	30	√ 9.03-0.09	<0.0L	50,09	\$ <0.01 \$ <0.01	\$ Q.01
				( <u> </u>		s 2,	ORettuce	.j.300 ^{t.(}	0.01 grain Q.15 straw	~ <0.01	0.01 ×	0.08 maw	0.03 grain
RA-2650/06		FLU	1 SEU	3	\$~~ }		wheat carror Vettuce	240	0.01 leas0.02	LC \$0.01	× <0.01 کر	<0.01	< 0.01
<u>M-296652-02-1</u>	(29/09/2008)	500SC	3 plots	Lettuce	500g	ġ	J. Tettucer	240	€ ⁹ 0.02	² 1009≳	\$0.01	wit × 0.01	< 0.01
			Å	Letture	Orp.	\$	wheat	_ 1 <b>20</b> +	<b>.</b>	0.01~V	0.04 <0.04	< 0.01	0.02 grain
		\$_ @	3 30 ⁶	al ⁰ "	C'I GILL	, De	carro	289	0.01 leaf 0.02 boot	< 0.01	\$0.01	< 0.01	< 0.01
		The star		Lettuco	500g	1	🖌 lettuce 🕥	×290	0 ¹ 9.01-0.03	<0. <b>6</b> 1	< 0.01	< 0.01	< 0.01
		V		ot s	\$	£ 0×.	wheat	36JC	0.08 straw	0.01	< 0.01	0.06 straw	< 0.01
			GULD)		TOON	ðj	\$ and	36	0.02 root	<0.01	< 0.01	< 0.01	< 0.01
		10 ^C	, Q	∫ SO11 (< & Barbar)		, I 	Dettuce	, 30°	<0.01	< 0.01	< 0.01	< 0.01	< 0.01
	TU	A ,	°°5 8	$\begin{array}{c} & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ &$	3 ^{t 1} . t	, at ¹	A heat	, 30 , 30	0.05 straw	0.14 straw	< 0.01	< 0.01	0.01 grain 0.06 straw
RA-2651/06 /-296671-02-1	(30/09/2008)	FLU	A SEU	Dull 1	2 ¹⁰ 2	19 ¹⁰	carrot	154	0.02 leaf 0.03 root	< 0.01	< 0.01	< 0.01	< 0.01
1-270071-02-1	(30/07/2008)		5 piots	Lettuce	500g 두	Ĉ	lettuce	155	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01
	~0 ⁴	çe ·	Ose	c ^{i de} c	CIPP.	15	wheat	154	0.19 straw	< 0.01	< 0.01	0.05 straw	0.04 grain
	a CITU	Ely "	ener'	<u> </u>	Dill	U	carrot	344	0.01 leaf/root	< 0.01	< 0.01	< 0.01	< 0.01
	COINS COINS	E C	MC Han	Wettuce ?	500g		lettuce	347	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01
F	Jer Colu	~1	JUE	10 ^e			wheat	357	< 0.01	0.05 straw	< 0.01	< 0.01	0.03 grain



Page 646 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

reference	author (report date)	formu- lation	Trial region plots	application	dose ai.ha	rot. nb	crop	PBI *	BC FLU (mg/kg)	FLL6 benzamide emg/kg)	(mg/kg)	FBU-7- OH (mg/kg)	a Mana/ka)
8-2160 -350816-01-	(03/07/2009)	FLU 500SC	2 NEU	soil (≤ 8cm)	500g	1	potato	28,30	0.00002		2 <0.01 2 	Cont Cont	50-0-01
3-2171 <u>I-350747-01-</u>	(03/07/2009)	FLU 500SC	2 SEU	soil (≤ 8cm)	500g		potato	3031	\$9.01		0.01 ³		<0.01
8-2161 <u>1-352225-01-</u>	(21/01/2009)	FLU 500SC	2 NEU	(< 8,610)	. 1 ⁰		al an	28-30	COV.01		0" <001 ⁰⁰ 00100	WILL	<0.01
8-2172 <u>1-355319-01-</u>	(07/09/2009)	FLU 500SC	2 SEL	U ^{LCU} soil ( (§ 8cm)	50000		Ovnion Ovnion UROCE	29-31		<80Cm	10091	<0.01	<0.01
8-2165 <u>1-352213-01-</u>	(23/07/2009)	FLO 500SC	2 NEU	o ^{ll b} soil O (≨ 8cm)	5005		> tomato	28-30	$0 \sim <0.01 \sim$	STEP O	<0.01	<0.01	<0.01
8-2176 <u>1-355320-02-</u>	(07/09/2009)		2300	sod (£8cm)	\$00g ¹			5 1100	ET <0.00 T	<0.01	<0.01	<0.01	<0.01
8-2167 <u>1-354235-01-</u>	(25/08/2009)	FLO 500SC	2 19 EU	C Scm)	500g		off peak De	28-30	<0.01	<0.01	0.02 dry	<0.01	<0.01
8-2178 <u>1-354237-01-</u>	(25/08/2009)	FLU 500S	28ÊU		~ O>		and a	28	<0.01	<0.01	0.02 green 0.03 dry	<0.01	<0.01
8-2168 <u>1-355324-01-</u>	(07/09/2000)	FLU 500SC	2 NEU	$ \begin{array}{c} & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & $	500g	j f ^e	corn	31-32	0.03 BBCH34	<0.01	<0.01	<0.01	<0.01
8-2179 <u>1-355327-01-</u>	2007/09/2009) CO ^{DE}	FLU 500SE	2 SEU	soil (≤ 8cm)	500g	1	corn	28-34	0.05-0.07 BBCH34	0.01 BBCH34	<0.01	0.03 BBCH34	<0.01



Page 647 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram

						•	-				a Dê		i the o
reference	author (report date)	formu- lation	Trial region plots	application	dose ai.ha	rot. nb	crop	PBI	FLU (mg/kg)	FLU- benzamide (mg/kg)	FEU-PCA (mg/kg)	FLU-7- C OH	methyl-
08-2164 <u>M-357777-01-</u> <u>1</u>	(22/10/2009)	FLU 500SC	2 NEU	soil (≤ 8cm)	500g	1	leek	30-31			2 6 81 C		(mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg) (mg/kg)
)8-2175 <u>M-357762-01-</u> L	(22/10/2009)	FLU 500SC	2 SEU	soil (≤ 8cm)	500g	~Q*	O ^P leek f	29 29		Sear C			<0.01
08-2166 <u>M-357953-01-</u>	(27/10/2009)	FLU 500SC	2 NEU	soil (≤ 8cm) ₅	500g		strawberts	31-32		\$9.01°	< 0.01	≤0.01	<0.01
)8-2177 <u>M-357930-01-</u> L	(27/10/2009)	FLU 500SC	2 SEU	500) 500) 8cm)	<b>500</b> g	³ ^{\$}	strawberry	28 ©	400) 100)	00001	0.01 (	<0.01 × <0.01	<0.01
08-2071 <u>M-357943-01-</u>	(27/10/2009)	FLU 500SC	2 NEU			t NC	spingen	28-29	Q.09	<b>@</b> .02-0.08	<0.01	0.05-0.26	<0.01
08-2170 <u>M-357959-01-</u>	(27/10/2009)	FLU 500SC	2 SEU	soil	\$500g	N ^{Oe}	spifach	-385I9		9.01-0.05	< 0.01	0.04-0.22	<0.01
8-2169 <u>4-350532-02-</u>	(10/09/2009)	FLU 5005C	Î NEU	Soil ≤ 8cm	500g		Summer	OT NI	¥01	<0.01	< 0.01	< 0.01	<0.01
8-2180 <u>4-359808-01-</u>	(02/12/2009)	FLU 500SC	2 SEUĈ	© soil, උ( (≤ 80m)	500g*		Vinter rape	29-30	0.01	<0.01	<0.01	< 0.01	<0.01
Ē	(27/10/2009) $(10/09/2009)$ $(02/12/2009)$ $(02/12/2009)$	ce ' At JY ' At JY ' At JY ' of	and any	$\frac{1}{2} \left( \leq 8 \operatorname{cm}^{3} \right)^{3}$ $\frac{1}{2} \left( = \frac{1}{2} \right)^{3}$	caise caise		J. O.C.						



Gap at 500 g ai/ha		FL	.U	FLU-ber	nzamide	FLU-	PCA	FLU-	7-OH	FLU-methy	-sulfoxide	Total r ca	
	Rotation	STMR	HR	STMR	HR	STMR	HR	STMR	HR	STMR	HR	STM	HR
Corn GM	R1	<0.01	<0.01	0.06	0.07	0.0.1	0.01	<0.01	<0.01	<0.00	<0.01	P.85	0.00
Corn kernel	R1	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01 🔊	<0.02	
Corn milky	R1	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	€ ₹0.01	<0.91	<0.00	<0.02
Tomato	R1	<0.01	<0.01	<0.01	<0.01	<0.01	\$9.91	<0.01	<0.00	<0.01	0,01	²⁰⁰ /02	<602
Spinach*	R1	0.01	0.07	0.02	0.08	<0.01	<0.01	0.07	<u>O</u> I0	<0.01 👷	<0.01	0.075	0.13
Potato*	R1	0.02	0.02	<0.01	<0.01	<0.01	<0.01	<0.01		。<0.01		0.05	0.03
Onion*	R1	0.01	0.02	<0.01	<0.01	0.01	<0.01	<0.01	<0.01	<0.62	001	8.02	603
Leek*	R1	0.025	0.04	<0.01	<0.01	0.01	0.02	<b>10</b> .01	\$0,01	<b>10</b> :01	0.01	¢ 0.03 م	0.05
Pea green seed	R1	<0.01	<0.01	<0.01	<001	0.00	0.02	<0.01	×0.01	°<0.01	<0.01	<0.02	<0.02
Pea dry seed	R1	<0.01	<0.01	<0.01	¥0.01	0025	0003	<0:0	<0.01	<0.01	<b>√</b> 001	40-02	<0.92
Strawberry	R1	<0.01	<0.01	<0.01	<0.01	<0.01	×0.01	@0.01	0.01	s. €0.01	Q<0.01	<0.02	€≪0.02
Rape pod	R1	0.02	0.06	\$001	\$2.01	<0:01	<0.01	<0.01	,<0.01	<0.01	<0.69	0.03	0.07
Rape seed	R1	0.01	0.01 /	<0.01	0.01	\$9.01	20.01	49.01	< ANY	<2.01	0.01	002	0.02
	R1	0.01	0.01	<0.00	<0.00	<0.01	€0.01	0.01	0.01	. 0.02	0.09 🔊	0.02	0.02
Wheat grain	R2	<0.01	9.01	¥0,01	<0.01	<0:01	<0,01	<0.01	Q<0.01	0.040	0.05	<0.02	<0.02
	R3	<0.01	<0.01%	5 · ·	Q.01	\$0.01	<i>6</i> 9.01	<0.01	<0.81	0.605	© ^{0.03}	<0.02	<0.02
	R1	219	0.12	0.00	0.00	<0.01		\$0.01	×\$0.01	0.035	0.05	0.12	0.13
Wheat GM	R2 🛠	.0.06	0.08	<i>©</i> 9.01	001	- Chi	<0.02	<0.61	<0.01	0.02	0.06	0.08	0.09
	R30	0.04	0.1~	L n	⊘<0.01		20.01	<0.01	<001	0.91	0.06	0.07	0.11
	S	674	028	0.85	1	<0.05	NP .	0.065	L0.11	@.055	0.07	0.20	0.33
Wheat straw	R2 C	1	0.19	\$0.05	60.05	50,05	₹0.05	0.05	0.1		<0.05	0.14	0.22
Ĉ	R30	0.055	0.08	0 [°] 0.05	V 0.05	ر) 2×0.05	0.05	005	066	<0.05	<0.05	0.11	0.13
Č.		2.915	ok04	<0.01	<0.0	<0.01	<0.01		Ø€0.01	<0.01	<0.01	0.025	0.05
Carrotterves	R1	0.01		\$0.01	<0.01	0.01	- CO1	<0.0	<0.01	<0.01	<0.01	0.02	0.03
carrowcaves	R2. 0	0.01	0.01	and the second sec		X0.01		20.01	<0.01	<0.01	<0.01	0.02	0.02
	No '	0.01 A.025	0.01	<0.01C	<0.03		<0.00					0.045	0.06
Connat	QR1	, <b>0</b> ,035	Call	Con I	<0.01 (0.01) (0.01)	5.01	<0.00	< 0.01	<0.01	<0.01	<0.01	0.025	0.04
Carrot root		0.02 č	0.03	0.01	(0.01) √ <0.01	×	4001		<0.01	<0.01	<0.01	0.02	0.03
×	R3	<b>~~</b>	0.01	<0.0	<0.00	<0.01	)×0.01	<0.01	<0.01	<0.01	<0.01	0.02	0.03
A A	R1	0.01	2002 Q	10,01	28,51	<0.01		<0.01	<0.01	<0.01	<0.01	10000000000	
Turnip body	R1 R2 R3	0.015	°0.02∧	<0.01	<0.90	<b>3</b> 0.01	<0.01	<0.01	<0.01	<0.01	<0.01	0.025	0.03
	R3	<001	<0.01	<0.00	<0.00	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.02	<0.02
	@ R1	<001 0.03 0.03 0.03	0.04	@.01	\$0,01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	0.04	0.11
Turnip leaves	B2	0.03	0.04	S<0.01	20 01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	0.045	0.05
<u> </u>		8ª	0,01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	0.02	0.02
Turnip leaves	Ø R1	0.025	0.11	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	0.035	0.10
Lettere	R2	0.02	0.02	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	0.02	0.03
	O'	\$01	0.03	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	0.02	0.04

Table 6.6.2- 3:	Result overview of all EU rotational trials conducted at 500 g ai/ha
-----------------	----------------------------------------------------------------------

* : at hap of GM : green material R1 : 1st rotation (Plant Back Interval ±30 days), R2 : 2nd rotation (PBI range 90-240d), R3 : 3rd rotation (PBI range 286-363d) Total residue calculated : Sum of Fluopyram + Fluopyram-benzamide



Data Point:	KCA 6.6.2/01
Report Author:	
Report Year:	2008
Report Title:	Determination of the residues of AE C656948 in/on the fight rotational cross
±	turnip, lettuce and winter wheat after spraying of AE C65948 (500 SC) in the C
	field in Northern France
Report No:	turnip, lettuce and winter wheat after spraying of AE C656948 (500 SC) in the field in Northern France RA-2649/06
Document No:	
Guideline(s) followed in	EU-Ref: Council Directive 91/41 EEC of July 5, 1991, Anne II, paga, section
study:	
	Residues in or on Treated Products, Food and Feed EC guidence working
	document 7524/VI/95 rev (1997-07-22)
	OECD Guideline for testing of Chemical, Residues in rotational crops filmited
	field studies), No. 504, g 3 V 2 V
	field studies), No. 504, 6 S S S S S S S S S S S S S S S S S S
Deviations from current	
test guideline:	
Previous evaluation:	yes, evaluated ind accepted @ rev. 1 to VoQ of DAR B7 sigust 2012 (revenence relied in) Yes, conducted under GIR Offickuly recognises sesting acilities
	rev. 1 to VoQ of DAR B7 agust 2912 (references relied on)
GLP/Officially recognised	Yes, conducted under GER/Offickally recognised Sesting Dicilities
testing facilities:	
Acceptability/Reliability:	$Y es q_1 \ll q_2 \qquad q_3 \qquad q_4 \qquad q_7 \qquad q_8 \qquad$
8/	
. <b>//</b>	

Methods

O

The purpose of the study was to determine the magnitude of the relevan residues of fluopyram (AE C656948) and its metabolites fluopyram-ben amide (AE F488) \$, fluopyram-pyridyl carboxylic acid (FLU-PCA, AF C657188), Oluopyram-7thydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122), in turnip, lettuce and wheat, grown as succeeding etops in northern Europe (Northern France) and following one sprist application of fluopyram SC500 on soil or on target crop lettuce. Residues of the active substance fluopyram and its metabolites were determined in the succeeding crops only. The target crop lettuce was not analysed.

The test item was applied to the reated plots if a different manner, but the application rate of 1.0 L of test item/ha (0.5 kg a.s. a) was the same.  $\sim$ 

For the plot A (trials R 2006 0864/9, R 2006 0865/9 and R 2006 0866/7) – the test item was applied to the bare soil followed by incorporation (maximum 8 cm depth) to avoid photodegradation. The investigated plant back interval was 30 days for all crops (turnip, lettuce and winter wheat) and corresponds to the standard plant back interval in case of crop failure.

For the plot B (trial  $\hat{R}$  2006 08675) – the test them was applied on lettuce as the target crop two weeks after planting. Plot B represents a plant back interval of 90-240 days.

For the plot C trial  $\mathbb{R}$  2006  $\mathbb{R}$  68/3) the test item was applied on lettuce as the target crop two weeks after planting. Plot C represents a plant back interval of 290-365 days.

Each Ploc was soldivided into 3 subplots for the 3 crops (turnip, lettuce, cereals) to be planted as rotational crops Explanation of the study plot designs is illustrated in the Table 6.6.2-4.



Table 6.6.2- 4:	Plot design and plant back intervals
-----------------	--------------------------------------

	Requested PBI	actual	Plant Back Interva	Remarks				
Trial No.	(days) / Application on	Root crop DAT (days)	Leafy crop DAT (days)	Cereals DAT (days)				
R 2006 0864/0 R 2006 0865/9 R 2006 0866/7	Plot A: 30 / soil	turnip 30 (R 2006 0864/0)	lettuce 30 (R 2006 0865/9)	winter wheat 30 ഛ (R 2006 0866/4)	Application on bace soil; planting/sowing of rotational crop after 30 days			
R 2006 0867/5	Plot B: 90-240 / lettuce	turnip 90*	lettuce	winter wheat	Application on lettuce two weeks atter planting; harvest proughing of lettuce; planting/sowing of rotational crops			
R 2006 0868/3	Plot C: 290- 365 / lettuce	turnip 320		Springwheat	Application on lettuce two weeks after planting; harvest bloughing of letting; cultivation break; planting/sowing of rotational grops			

#### DAT= days after treatment

In trials R 2006 0867/5 and R 2006 0868/3: of plot **B**, the carget crop lettice was harvested at normal harvest, 60 days after planting on plot C lettice was harvested after 43 days. No lettice samples were taken for analysis.

The harvest leftovers were destroyed by grinding and ploughed in (in order to capture all possible residues and not remove them from the plot prior to planting the rotational crops).

Untreated plots wergprepared before treated plots."

At the 30-day (Plot Å), 96240-day (Plot Å) and 290-365-day plant back intervals (Plot C) the plots were prepared for crop planning following normal agronomic practices for each crop type in the regions. For the longer-term Plot B (90-240 days) and Plot C4290-365 days a bare soil status had to be maintained after harvest of lettuce, i.e. no cover crop is sover.

Samples were taken, prepared on the field where necessary, gransported and stored.

The first sampling of rotational crops such as turnings and lettuce was taken at early harvest (14 days prior to normal harvest) followed by sampling at normal harvest maturity for each crop type. For wheat green material was sampled at growth stage BBCH 29-30 and at normal harvest maturity (BBCH 89) (grain and straw). All sampling equipment was cleaned poor to ontering any plot that was to be harvested.

The field samples from a trials were stored deep-frozen within 24 hours after sampling. All field samples were shipped by deep-freeze forry and arrived in good condition. The field sub samples were stored in a freezer at +18 °C or below until preparation of the examination samples. For the preparation of examination samples, the deep frozen field sub samples were shredded with dry ice in a cutter. Representative parts of the shredded samples were transferred into polystyrene boxes separately for analysis (UP samples) and archiving (UR samples) and stored at -18 °C or below until analysis.

Residues of Mopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (**1997**, 05/02/2007, <u>M-283301-00/1</u>, see MICA Section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SAN(0/3029/99 rev 4.

Residues of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitrile:water (80:20; v:v). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:



- One dilution was performed under acidic conditions: this extract allowed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed the determination of FLU, FLU-benzamide and FLU-7-OH.

An aliquot of the extracts was injected into LC-MS/MS operated in Electrospray Ionization mode:

- One injection in positive electrospray ionization for the determination of FLU, FLU-benzamide and FLU-7-OH.
- Another injection in negative electrospray ionization for the determination of FLU-PCA of FLU-methyl-sulfoxide under different conditions.

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established, with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standardization using isotopically stable labelled internal standards.

The Limit of Quantification (LOQ), expressed as the opyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat straw and 0.01 mg/kg for all other matrices

Full details and acceptable validation data to support this method are presented within accument M-CA 4, which comply with the EU regulatory requirements outlined within SANCO 3022999 rev 4.

# Findings

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and treated camples from the study in each set of analyses. The data demonstrate acceptable method performance during sample analysis. All the recovery results and details are given in the Table 6.6.2-5

natrices	Die 4			
mategal	<u>ک</u> FL (mg/kg) ??		OMean&value	RSD* (%)
Fluopyram (AE C65	69(48) 0.09 0.09 0.09	8 A S	N N	
RY 3	0.09	990 ***	∞ 99	
turnip leaf, normal		v v 0° 96≰)02 % v	A 99	
turnip leaf, normal	A Q"	Qyerall recovery (n=3)	99	3.0
-	$Q^{\prime} 0.01$	\$ \$\frac{1}{2}95; 81\$ \$\frac{1}{2}\$	88	
turnip body			100	
\		Overall recovery (4=4)	94	10.2
Å	0.01	<u>103</u> ≪	103	
lettore head	0.16	§96; 100	101	
	Y A a	Voverall receivery (n=3)	102	5.0
N N	<b>9</b> .01 ×	~Q~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	85	
wheat and	0.10	Q 4 97	97	
green material	4 V U S	S 100	100	
		Ov@all recovery (n=3)	94	8.4
		85	85	
	0.50	95	95	
vy meat strayv	1 2.S	95	95	
Wheat straw		Overall recovery (n=3)	92	6.3
	² 0.01	75; 96	86	
Waleat grain	0.10	103	103	
$\bigcirc$		Overall recovery (n=3)	91	16.0
Fluopyram-benzami	de (AEF14881	5)		
turnip leaf, normal	0.01	101	101	

# Table 6.6.2- 5: Recover data for fluopyram (AE 6656948) and its metabolites in rotational crop matrices



Coord Server le	FI		Maan malma	DCD*	
Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD* (%)	
material	0.10	93; 105	99	(70)	
	0.10	Overall recovery (n=3)	100	6.1	S S
	0.01	101; 89	95	0.1	, ¹⁰
turnip body	0.10	95; 99	97	S S	
turnip bouy	0.10	Overall recovery (n=4)	96	5.5 🔊	
	0.01	102	102	, 0	
lettuce head	0.10	91; 103	97 🗸	*	Y Q
		Overall recovery (n=3)	9 <b>9</b>	<b>6</b> .7 9	
	0.01	84 &	. ®4	× ~	
wheat	0.10	94 " [©]	^م 94 ه	<u> </u>	
green material	0.5	90 ° v	<u>90</u>		, S
		Overall recovery (n=3)	~ . <b>89</b>		~~
	0.05	\$89 Q	89 🔊	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	s,
Wheat straw	0.5	092 J 2	92 S	0 ^v - <del>,</del> ( , , , ,	
wheat straw	2.5		<u>~ 82</u>		Ű,
		Overall recovery (n=3)		∞_1.9	S.S.
	0.01	Ø 89×106	098 27	<u> </u>	
Wheat grain	0.10	<u> </u>	95 V V 95 V	S I a	
		Overall recovery (n=3)	2 90 č		
Fluopyram-methylsu	Ø	44122) Q O E			
	0.01	× 191** × V	×111	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
turnip leaf, normal	0.10	<u>\$104; 109</u>	1070		
		✓ Overall recovery (n≠3)	108	⁴ Ø <b>3.3</b>	
	ר.10		80		
turnip body	0.10	0 ⁷ 3; 82	× 78 0 <b>78</b>	<u>6</u> ³	
Ø		<u> VOverall recovery (n=3)</u>	<b>○`78</b>	[≫] 6.0	
lettuce head 5	0.01	× ~ 94 ~ ~			
lettuce nead ~	00.10		105 101 101	6.5	
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	\$ 0, <b>0</b>	Overall recovery (n=3)	101~ 123	0.5	
wheat	0.10		<u> </u>		
green material	0.10		101		
		Överall recovery (n=3)	<u> </u>	16.5	
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			109		
Ş	4 0.5 °		100		
Wheat straw	2.5	99 6	99		
a.		Overal recovery (n=3)	103	5.4	
~Ç~ (		98586	92		
Wheategrain	0.1 \$	\$\$\$97 J	97		
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Q Q	Overall recovery (n=3)	94	7.1	
Fluopyram-pyridy	arboxylic-aci	XAEC 57188			
		A. ~005	105		
"	Ø.01 📎				
turnip leaf, normal	0.10 C	Ø8; 103	101		
turnip leaf, normal	0.10		101 102	3.5	
	0.10 C	Overall recovery (n=3)	102 93		
	0.10	28; 103 OveraQ recovery (n=3)	102	3.5	
	0.10 0.10 0.10 0.10	Overall recovery (n=3) Overall recovery (n=3) 86 ; 99 92 ; 96 Overall recovery (n=4)	102 93 94 93	3.5 	
turnin body 2	0.10 C	Overall recovery (n=3) Overall recovery (n=3) Overall recovery (n=4) 78	102 93 94 93 78	3.5 	
turnin body 2	0.10 0 0.10 0	Ø8; 103 Overall recovery (n=3) 86; 99 92; 96 Overall recovery (n=4) 78 94; 99	102 93 94 93 94 93 93 94 93 93 94 93 93 94 93 93 94 93 93 94 93 93 93 94 93 97	3.5 6.0 	
	0.10 0 0.10 0 0 0.10 0 0 0.10 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Ø8; 103 Overall recovery (n=3) 86; 99 92; 96 Overall recovery (n=4) 78 94; 99 Overall recovery (n=3)	102 93 94 93 94 93 93 78 97 90	3.5 6.0 	
turnippody 2	0.10 C 0.10 C 0.10 C 0.10 C 0.00 0.01	Ø8; 103 Overall recovery (n=3) 86; 99 92; 96 Overall recovery (n=4) 78 94; 99 Overall recovery (n=3) 99	102 93 94 93 78 97 90 99	3.5 6.0 	
turnin body x	0.10 0.10 0.10 0.01 0.01 0.01 0.10	Ø8; 103 Overall recovery (n=3) Ø8; 99 Ø2; 96 Overall recovery (n=4) 78 94; 99 Overall recovery (n=3) 99 88	102 93 94 93 78 97 90 99 88	3.5 6.0 12.1	
turnippody	0.10 C 0.10 C 0.10 C 0.10 C 0.00 0.01	Ø8; 103 Overall recovery (n=3) 86; 99 92; 96 Overall recovery (n=4) 78 94; 99 Overall recovery (n=3) 99	102 93 94 93 78 97 90 99	3.5 6.0 12.1 	



Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD* (%)	
material	0.05	92	92		Q
	0.5	92	92		
Wheat straw	2.5	90	90	°> ⊘	
		Overall recovery (n=3)	91	S 1.3 🗸	
	0.01	100; 91	96	🔊	
Wheat grain	0.1	94	94	, 0, ,	Ø,
-		Overall recovery (n=🕉	95 న		Y Q
Fluopyram-7-hydrox	y (BCS-AA10	065)			L.
	0.01	90 K	<u>,</u> 90	× ~	Å,
Turnip leaf, normal	0.10	92; 101 °	Ø ⁹⁷ .		°, °
		Overall recovery (n=3)	94	Q 67 k	
	0.01	94; 90	@ ⁷ 92 @		
Turnip body	0.10	96;106	× 101 ×	A X	s, ser a ser
Ĩ		Overall recovery (n=4)	Ø 97 🔗	0° 7.1 🖉	
	0.01	A. 9.7 C	l		Children of the second s
Lettuce head	0.10	2 ⁹⁶ ,106		× ,	S
		Qerall recovery (n=3)	()Q100	§ 5.5	2 0
	0.01	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	79 Q 2 967 E		
winter wheat	0.10	§ Ø 969	X 96 6		
green material	0.5		93 0 ⁸⁹	<u> </u>	
-		•Overall recovery (n=3)	Q.89 O	☆ 10.2	
	0.05	\$\$ 83 _c	830	<u> </u>	
winter wheat	Q.5	S S St O	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Ø	
straw	∾. ¶ 5		\$\$1,59		
		Qveralbrecovery (n=30)	K, 90,	6.8	
• • • •	× 0.00	\$2; 9	0 87 × "	·	
winter wheat grain	Q.1 6	x ~ 100 2 0	100		
grain 🔊	<u>, 0' , y'</u>	Overall recovery (n=3)	91	9.9	

* some RSDs were not calculated as there were my two individual recoveries given ** Recovery corrected with the control interference (0.002) mg/kg/recovery not corrected

Final determination as: fluopyram Residues calculated as: fluopyram C

Final determination as: fluopyram residues calculated as: fluopyram Final determination as: FLU-benzamide Residues calculated as: fluopyram Final determination as: FLU-methylsulforde Residues calculated as: fluopyram Final determination as: FLU-Residues calculated as: fluopyram

Final determination as: FLO7OH Residues calculated a Thuopy an , st S

Ò

No residue of the opyram or related notabolities were found above the LOQs in any of the control samples of rotational Gop matrices analysed.

The residue levels of fluopyram and its relevant metabolites in the rotational crop matrices of turnip, lettuce and wheat are summarized in the tables befow.

The storage period of deep-frozen samples was up to 342 days for lettuce, 310 days for turnip leaves, 308 days for turnip body 169 days for wheat green material, 57 days for wheat grain and 66 days for wheat straw. Q

Residue measured in the relevant succeeding crop matrices are summarized below and overall trials and residue summaries are presented in the Dable 6.6.2-6.

Residues in Durnin

In grai R 2006 0864/0 (prot A, PBI 30 days), residues of fluopyram (AE C656948) were 0.10 and 0.04 mg/kg in jurnip leaf 91 and 105 days after treatment (DAT), respectively. In turnip body the residues of fluopyram were <0.01 mg/kg at DAT 91 and 105.

The residues of FLU-benzamide, FLU-methylsulfoxide, FLU-PCA, FLU-7OH in all turnip matrices were <0.01 mg/kg.



In trial R 2006 0867/5 (plot B, PBI 90 days) residues of fluopyram (AE C656948) were 0.03 mg/kg in turnip leaf, normal at DAT 91 and 105 and in turnip body residues of fluopyram were <0.01 mg/kg $^{\circ}$

The residues of FLU-benzamide, FLU-methylsulfoxide, FLU-PCA, FLU-7OH in all turnip matrices were <0.01 mg/kg.

In trial R 2006 0868/3 (plot C, PBI 320 days) residues of fluopyram (AE C656948) were 0.04 mg/kg in turnip leaf at DAT 381 and in turnip body residues of fluopyram were < 0.04 mg/kg. The residues of FLU-benzamide, FLU-methylsulfoxide, FLU-PCA, FLU-7OH in all turnip matrices were 0.06 mg/kg?

Residues in Lettuce

In trial R 2006 0865/9 (plot A, PBI 30 days), residues of fluopyram (AE C656948) were 0.11 mg/kg and 0.02 mg/kg in lettuce head 59 and 73 days after treatment (DAT), respectively of the second secon

The residues of FLU-benzamide, FLU-methylsuffoxide, FLU-PCA, FLU-70H in all lettuce matrices were <0.01 mg/kg.

In trial R 2006 0867/5 (plot B, PBI 90 days) residues of propyram (AE C656948) were 0.04 mg/kg in lettuce head samples at DAT 129 and 143 The residues of FLU benzanide, FEU-methylsulfoxide, ELU-PCA, FLU-7OH in all lettuce matrices were <0.01 mg/kg.

In trial R 2006 0868/5 (plot C, PBI 320 days) residues of Quopyram (ACC656948) were <0.01 mg/kg in lettuce head samples at DAT 354 and 368. The residues of FLU-benzamide, FLU-benzamide, FLU-benzamide, FLU-PCA, FLU-70H in all lettuce matrices were <0.00 mg/kg.

Residues in Wheat

In trial R 2006 0866/7 (plot A, PBI 30 days), residues of fluopyram (AE C656948) were 0.12 mg/kg (in green material), 0.28 mg/kg (in wheat straw), and 0.010 mg/kg in wheat gravit at DAT (days after treatment), 191, 308, and 308 respectively.

The residues of FLC-benzamide and FLO-PCA in all three wheat matrices were <LOQ.

The residues of CU-methylsuffoxide were at 0.05 mg/kg in greet material (DAT 191), 0.07 mg/kg in straw (DAT 308), 0.09 mg/kg in grain (DAF 308)

The residues of FLU-7OH were 40.01 mg/kg in wheat areen material and grain and 0.11 mg/kg in wheat straw.

In trial & 2006 0867/ (plot B, PBI 146 days), residues of fluopyram (AE C656948) were 0.05 mg/kg (in green material) 0.01 mg/kg in wheat grain), and 0.17 mg/kg in wheat straw at DAT (days after treatment), 307, 425, and 425, respectively.

The residues of FLU-benzamide and FLU-BCA in all three wheat matrices were <LOQ.

The residues of FLU-metholsulfoxide wore at 006 mg/kg in green material (DAT 307), 0.05 mg/kg in grain (DAT 425), <0.05 mg/kg in stray (DAT 425).

The residues of FLU-70H were <0.01 mg/kg in wheat green material and grain and 0.10 mg/kg in wheat straws

In trial R 2006 0868/5 (plot @ PBI 286 days)

residues of thoopyram (AEC656948) wele 0.10 mg/kg (in green material), <0.01 mg/kg (in wheat grain), and 0.06 mg/kg in wheat straw at DAT (days after treatment), 336, 425, and 425, respectively.

The restories of FLU-benzamide, FLU-PCA and FLU-70H in all three wheat matrices were <LOQ.

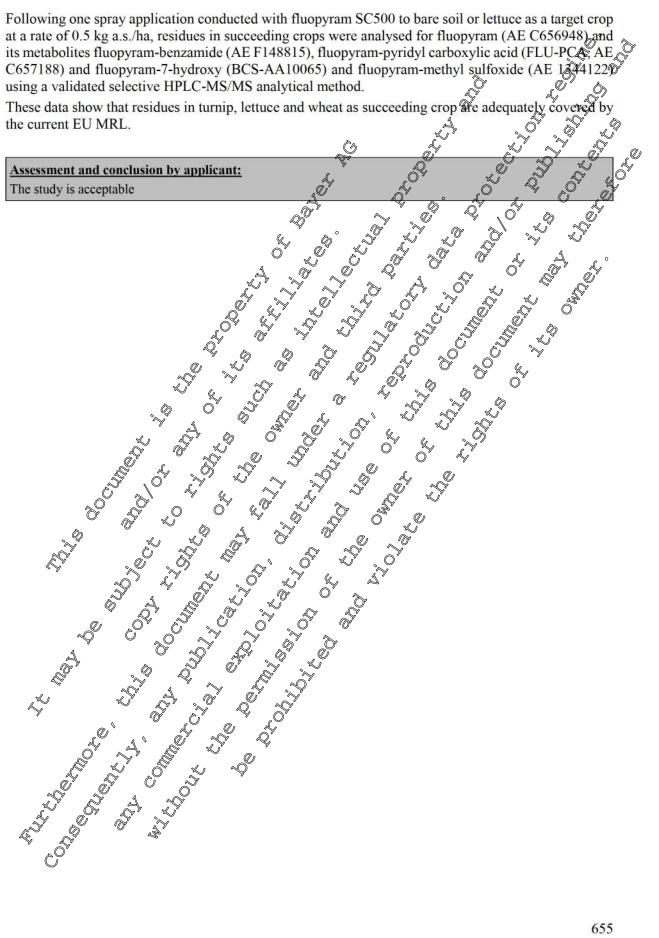
The residue of FL/2-methylsulfoxide were at 0.01 mg/kg in green material (DAT 336), 0.02 mg/kg in grain (DAT 425), <0.05 mg/kg in straw (DAT 425).

ĉ

Conclusion



Following one spray application conducted with fluopyram SC500 to bare soil or lettuce as a target crop at a rate of 0.5 kg a.s./ha, residues in succeeding crops were analysed for fluopyram (AE C656948) and its metabolites fluopyram-benzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE C657188) and fluopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122)



BAYER

Page 656 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

											2		°	
								10 ⁵ PC		ert 1	J. D. C. S.	A TES	O O D	ð
Table 6.6.2-	6: Results	s of rotational c	rop trials cond	lucted	with fluopy	ram	of Bô		1 ProP	° -*	ect ^{ijo}	l'ishi	t Ĝ	
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application ra treatmen <u>to bare soil or</u> <u>crop</u>	t <u>target</u>	Dates of treatment or no. a treatments and last date	Portion) apatysed	Growth stage at sam- pling	ectus ectus	1 ³ - 1	,» a	(mg/kg)	Jister 500t.er heref	,0 [°] L ^e	PHI (days)
	(a)	(b)	kg a.s./ha Water a.s./ha	°∑ ^g a.s.∕0∑Í	0 ¹ (c)G ^{UL}	A C		AE C656948 (656948) C656948	A FLU- benzamide S 636948	FLU- PCA as 0056948	FLU- 70H ac C656948	ELU- methyl- sulfoxide as AE C656948	Total residue calc.	(e)
R 2006 0864/0 0864-06 / 01 France, north	Plot A Application to bare soil PBI: 30 d	1) 05.07.2006 3) 15.09.2006 - 30.09.2008	2000 3300 320 3300 320 3300	0.16675	05.06.2006	leaver 1	47 1 1 0 1 1				<0.01 <0.01	<0.01 <0.01	0.11 0.05	91 105
F-95000 Cergy Europe, North F 2006	<u>Rotational</u> <u>crop:</u> Turnip, edible (Aramis)	, y,	ioject joji	LS DO	A Gje	and -	19 49 WILLET	~0.61 -901	<0.00 Å 5 C 20.00	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.02 <0.02	91 105
R 2006 0865/9 0865-06 / 01 France, north F-95000 Cergy Europe, North F	Plot A Application to bare soil PBI : 30 d Rotational crop: Lettuce (Estelle)	Thios is		20.1667 COL 20. 1667 S	25.06.2006 5.06.2006	head E	47 495 C	0.11 0.02	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0.12 0.03	59 73
2006 R 2006 0866/7	Plot A Application to	H36.10.2006	0.500 300	0.067	26.09.2006	green material	30	0.12	<0.01	<0.01	<0.01	0.05	0.13	191
0866-06 / 01 France, north	bare soil PBI: 30 C	NERTIZ COUR		eron.	» *	grain	89	<0.01	<0.01	<0.01	<0.01	0.09	<0.02	308
	Co _{llè} co	ant with	n, de	e						,		1		656

Page 657 of 801 2021-02-26



Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

											4		T Tuo	PJ
								A.	Ì	et I	1. D. O.	re ^g i	JIC JI	Ĵ.
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application r treatmen <u>to bare soil or</u> <u>crop</u>	nt	Dates of treatment or no. of treatments and last date	Portion analysed	Growth Stage at sam-C			°Residues P	mg/kg)	a ^{Obr} 6	o ^{fe}	PHI (days)
	(a)	(b)	kg Water a.s./ha (L/ha)	g a.s./hL		2 ⁵		C656948 as AE (C C656948	FLQ- benzamide as AE C656948	FO.U- PCA as AE C656948	×FLU- 70H as × AE C656948	FKO- wethyl- sulfoxide as AE	residue calc.	(e)
F-95000 Cergy Europe, North F 2006	Rotational crop: Wheat, winter		30 ^{CUMEDE}	ari Ori	D ^{t \$} g ^{y(}	WILL		5 4.28 5 C P T O 5 C P T O 5 C P T O	3000 3000 110		0.11 OWDS	₩0.07	0.33	308
R 2006 0867/5 0867-06 / 02 France, north F-95000 Cergy Europe, North F	Plot B: <u>Target crop</u> : lettuce, Admiration PB1: 90* days <u>Rotational</u> <u>crop</u> : Turnip edible	1) 19.05 2006 (lettuce) 1) 31.08.2006 (turnip)	Die tigi) 0.1667 (5 9 5 10 10	202.06.2006 E Dib N Dib Dib Dib	allo	47 49 49 47 47	0.03 0.03 0.01 0.01 0.01	<pre>0.01 <0.01 <0.01 <0.01 <0.01 <0.01</pre>	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	0.04 0.04 <0.02 <0.02	151 165 151 165
2006	Stanis Plot B : <u>Target crop</u> : lettuce, Admiration PBI: 90 d <u>Rotational</u> <u>crop</u> : Lettuce,	1) 31.08.2006 (lettuce)		C 8 667	02.402006 12.402006 10.200	Ehead Vi	0 48 9 49	0.01 0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.02 <0.02	129 143
	Estelle Plot B:		8300 300 F	0.1667	2.06.2006	green material	30	0.05	<0.01	<0.01	<0.01	0.06	0.06	307
	EULE COLLECT	ALLY COLU	N ^{TE DE}	₩ ₩										65'

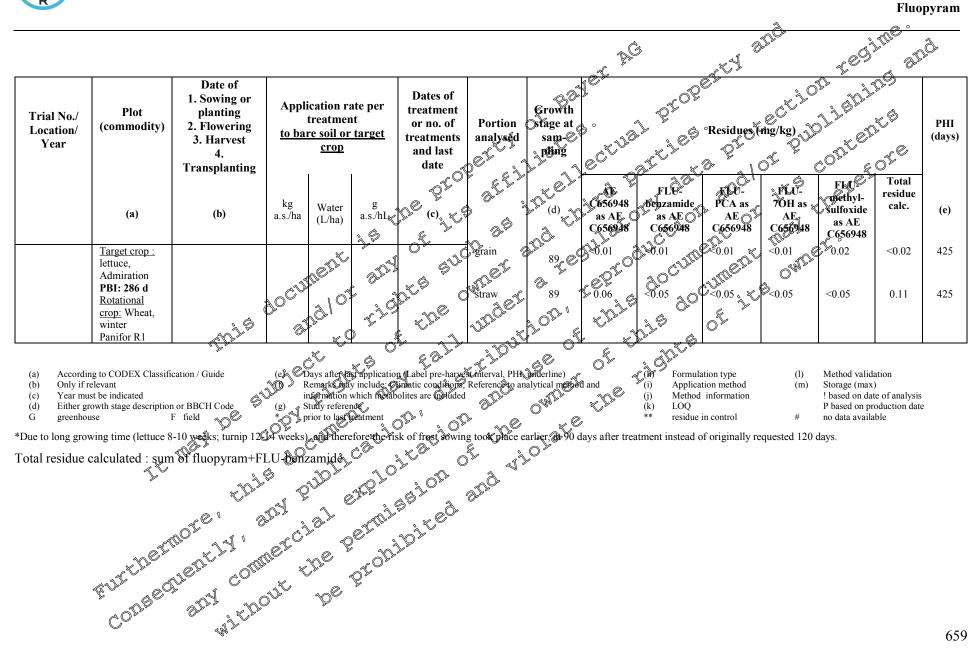
BAYER

Page 658 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

											A			ругаг
								Þ	Ď	et y	J.D.C.	re ^{gi}	J.C. O.L	1Ja
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application 1 treatme <u>to bare soil o</u> <u>crop</u>	ent <u>r target</u>	Dates of treatment or no. of treatments and last date	Portion analysed	Growth Ostage at sam-C pting	ec ^{tul}		°Residues	mg/kg)	¢°° ¢	07 ⁰	PH (day
	(a)	(b)	kg a.s./ha (L/ha)	g a.s./hL	. 1	0. ⁶	2 ¹⁰ (d) + 10 2 ¹⁰ (d) + 10	Ce56948 as AE (C656948	FL9- FL9- Senzamide as AE C656948	FLU- PCA as AE C6556948	×FLU- 7OH as AE C656948	FLU- unethyl- sulfoxide as AE C656948	Total residue calc.	(e)
	Target crop: lettuce, Admiration PBI: 146 days <u>Rotational</u> <u>crop:</u> Wheat, winter PR 22 R2	1) 26.10.2006 (wheat)	20 ^{CUMEDIC}		OT SUC		2 ^{12 89} 7 60 89 20 ^{20 1} 6	5 0.01 C 6.17 - D 2 6			<0.01	<0.05	<0.02 0.22	42.
R 2006 0868/3 0868-06 / 03 France, north F-95000 Cergy Europe, North F 2006	Plot C Target crop : lettuce, Admiration PB1: 320 d Rotational crop:	1)19.05.2006 (lettuce) 1)18.04.2007 (turnip) 3) 14.08.2006 – 25.08.2006 (lettuce)				leaver of the second	47 03 47 03 47 02 0 10 0 0 10 0 0 10 0	0.01 0 -0.01 -0.01 -0.01	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	<0.02 <0.02 <0.02	38 38 39
	Plot C Target crop : lettuce, Admiration PBI: 320 d Rotational crop: Lettuce Estelle	1) 18.04.2007			02.06.2006	head And green	41 49	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.02 <0.02	35 36
	Estelle Plot C	203.03.20070100 2011 2011 Witth	0.500 300 0.500 300	2004667	02.06.2006	green material	30	0.10	<0.01	<0.01	<0.01	0.01	0.11	

BAYER

Page 659 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram





Data Point:	KCA 6.6.2/02
Report Author:	
Report Year:	2008
Report Title:	Determination of the residues of AE C656948 in/on the ford rotational crops
	turnip, lettuce and winter wheat after spraying of AE C606948 (500 SC) in the field in Germany RA-2648/06
	field in Germany
Report No:	RA-2648/06
Document No:	M-296625-02-1 EU-Ref: Council Directive 91/414/EEC of July 5, 1991, Ann& II, p. A, so than 6 and Annex III, part A, section 8 Residues in or on Treated Deducts, Food and Feed EC guidance working document 7524/VI/95 reg 2 (1997-07-28)
Guideline(s) followed in	EU-Ref: Council Directive 91/414/EEC of July 25, 1991, Ann 27 II, p. A, section 6 and Annex III, part A, section 8 Residues in or on Treated Products, Food and Feed EC guidance corking 6 document 7524/VI/95 reg 2 (1997-07-28) OECD Guideline for testing of Chemic 95: Residues in protational cropy limits
study:	6 and Annex III, part A, section 8
	Residues in or on Treated Products, Food and Feed EC guillance working
	document 7524/VI/95 res 2 (1997-07-28) OECD Guideline for testing of Chemic 95; Residues in ordational cropt (limits) field studies). No. 504
	OECD Guideline for testing of Chemic Qs; Residues in Cotati all crops (limited
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated accepted y of y y y y
	yes, evaluated and accepted y rev. 1 to Vol of D&R B7 August 30 2 (references telied a)
GLP/Officially recognised	
testing facilities:	
Acceptability/Reliability:	Yes A A A A A A A A A A A A A A A A A A A
°/	

Materials and Methods

The purpose of the study was to determine the magnitude of the relevant residues of fluopyram (AE C656948) and its metabolites fluopyram-benzamide (AE FJ48815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AF C657458) and fluopyram. Thydrewy (BES-AA10065) and fluopyram-methyl sulfoxide (AE 1344122) in tunip, lettuce and wheat, grown as fotational crops in northern Europe (Germany) following one spray application of fluopyram SC500 on sold or on target crop lettuce. Residues of the active substance fluopyram and its metabolites were determined in the succeeding crops only. The target crop lettuce was not analysed.

The test item was applied to the reated plots for a different manner, but the application rate of 1.0 L of test item/ha (0.5 kg a.s. ha) was the same.

For the plot A trials R 2006 0858%, R 2006 0859/4 and R 2006 0860/8) – the test item was applied to the bare soil followed by incorporation (maximum 8 cm depth) to avoid photodegradation. The investigated plant back interval was 30 days for all crops (turnip, lettuce and wheat) and corresponds to the standard plant back interval in case of crop facture.

For the plot B (trial R 2006 0861 B) – the test item was applied on lettuce as the target crop two weeks after planting. Plot B represents a plant back interval of 100-240 days.

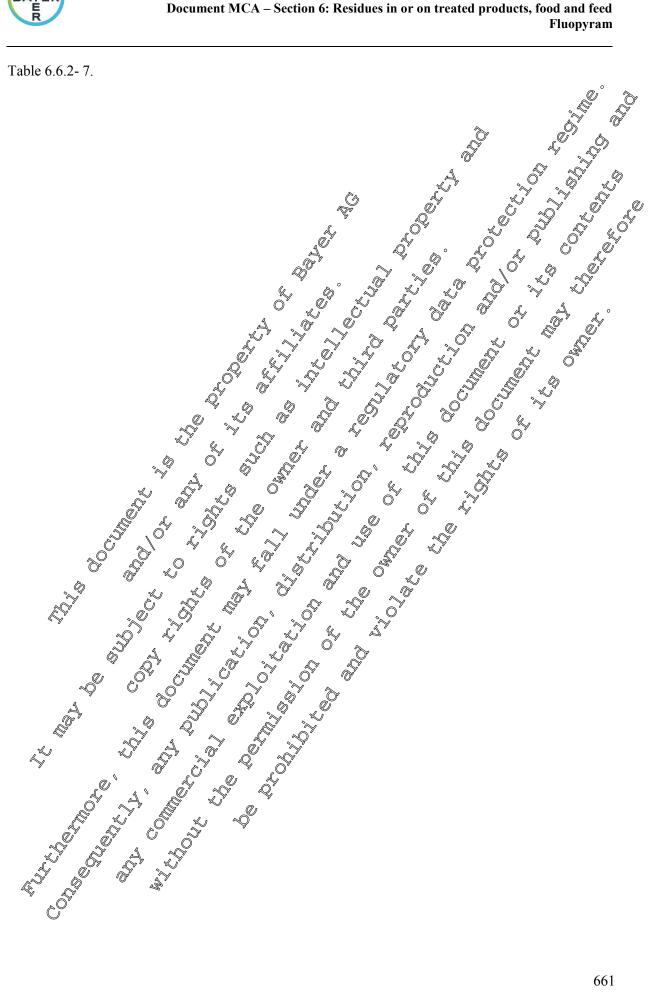
For the plot C trial R 2006 (862/4) the test item was applied on lettuce as the target crop two weeks after planting. Plot C represents a plant back interval of 290-365 days.

Plots B and C were subdivided into 3 subplots for the 3 crops (turnip, lettuce, cereals) to be planted as rotational crops. Explanation of the study plot designs is illustrated in the

E Star









R 2006 0859/4 Plot A. 507 30 30 28 planting/sowi R 2006 0860/8 soil (R 2006 0864/0) (R 2006 0865/9) (R 2006 0866/7) crop after 30	marks	Remarks	l (PBI)	Plant Back Interva	Requested PBI		
R 2006 0859/4 Plot A. 507 30 30 28 planting/sowi R 2006 0860/8 soil (R 2006 0864/0) (R 2006 0865/9) (R 2006 0866/7) crop after 30						· · /	Trial No.
- Application	© of rotational ↓ ↓ Yays ~	Application on bare s planting/sowin@of ro crop after 30 days	28	30	30		R 2006 0859/4
R 2006 0861/6 / lettuce 230 winter the lettuce winter the lettuce planting/sow	anting; ang of lettrice; (ng of rotational ()	Application on letter weeks after planting; harvest ploughing of planting/sowing of ro crops	190			/	R 2006 0861/6
R 2006 0862/4 Plot C: 290- 365 / 301 Several Action of the severa	anyting; ning of lettuce; eak;	Application on lettice weeks ofter planning; harvest/ploughing of cultivation break; planting/sowing apro crops	sprite wheat a			365 /	R 2006 0862/4

Harvest of target crop lettuce (Plor B, trial R 2006 0861/6 and Plot Cotrial R 2006 6862/4) On plots B and C the target crop lettrice was marvested at formal harves, 43 days after planting. No lettuce samples were taken for analysis.

The harvest leftovers were destroyed by grinding and ploughed in an order to capture all possible residues and not remove them from the plot prior to planting the rotational crops, Ô

Planting rotational crops:

Untreated plots were prepared before treated plots

At the 30-day (Plot A), the 100 - 240-day (Plot B) and the 290 - 365-day (Plot C) plant back intervals the plots were prepared for crop planting following normal agronomic practices for each crop type in the regions. For the longe cterm Plots B (100, -240 days) and C (290 - 365 days) a bare soil status had to be maintained after harvest of lettuce, i.e. no cover cropps sowo.

Samples wore taken, prepared in the field where necessary, gransported and stored.

Ŵ

The first sampling of turnips and lettuce was taken at early havest (14 days prior to normal harvest) followed by sampling at normal harves, maturity for each crop type. For wheat green material was sampled at growth stage BBCH 29-30 and at normal harves Omaturity (BBCH 89) (grain and straw). All sampling equipment was cleaned prior to entering my plot that was to be harvested.

The field samples from a trials were stored deep-forzen within 24 hours after sampling. All field samples were shipped by deep freeze forry and arrived in good condition. The field sub samples were stored in a freezer at 2-18 °C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field sub samples were shredded with dry ice in a cutter. Representative parts of the shredded samples were transferred into polystyrene boxes separately for analysis (UP samples) and archiving (UR samples) and stored at \leq -18 °C until analysis.

Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide were determined by LC-MS/MS according to method 00984 (method, 05/02/2007, M-28330 [283.4] and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 Dev 4.

Residue of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitrile:water (80:20; v:v). After



centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards: Q_n°

- One dilution was performed under acidic conditions: this extract allowed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions this extract allowed the determination of FLU, FLU-benzamide and FLU-7-OH.

An aliquot of the extracts was injected into LC-MS/MS operated in Electrospray Ionization mode

- One injection in positive electrospray ionization for the determination of FLIP, FLEDenzande and FLU-7-OH.
- Another injection in negative electrospray ichization for the determination of FLU-PCA are FLU-methyl-sulfoxide under different conditions.

The linearity was demonstrated in each analytical batch with a 0^{\times} weighted catibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standardization using isotopically stable labelled internal standards.

The Limit of Quantification (LOQ), opressed as floopyrand, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat straw and 0.01 mg/kg for all other matrices.

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within \$2000/3029/99 rev 4.

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and reated samples from the study in each set of analyses. The data demonstrate acceptable method performance during sample analyses. All the recovery results and details are given in the Table 0.6.2-8.

	·			
Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD* (%)
Fluopyram @E C65	$0^{(115)}$			(70)
Fluopyrain (St. Cos			02	2.6
4	Ø.01 %	90; 9 3, 92; 9 8	93	3.6
turnip leaf, normal	Ø 0.10	@103; 108; 102; 96; 85	99	8.9
40° -		Voverall recovery (n=9)	96	7.5
, KU KI	6,01 .	94; 100; 96; 97	97	2.6
turnip body	00.10 °	¥14; D5; 106; 99	106	5.8
Į (U)		Overative recovery (n=8)	101	6.5
	0.01 3	86; 97	92	
	9 .10	~ 105	105	
	C N	Overall recovery (n=3)	96	9.9
wheat green material		85; 85; 83; 80	83	2.8
wheat green material	× \$ \$	92; 88; 91; 90	90	1.9
		Overall recovery (n=8)	87	4.8
O'	0.05	86; 86	86	
wheatstraw	0.5	89	89	
		Overall recovery (n=3)	87	2.0
wheat grain	0.01	77; 78	78	



C	E.			DCD*
Crop/Sample material	FL (mg/lvg)	Single values (%)	Mean value (%)	RSD*
material	(mg/kg) 0.10	83	83	<u>(%)</u>
	0.10	Overall recovery (n=3)	79	4.1
Fluopyram-benzamic	le (AEF14881			
Thopyrum benzanik	0.01	98; 100; 107; 97	101	45
turnip leaf, normal	0.10	105; 97; 100; 98; 100	100 ,	3.1
1 /		Overall recovery (n=9)	100	· ○ 3.5 ◎ · · · ·
	0.01	101; 97; 89; 110 🖏	29	L 8.87 S
turnip body	0.10	98; 94; 100; 101	698	~ <u>\$</u> 2 ~ ~
		Overall recovery (µ=8)	¢0 [™] 99 ×	° 6.2 <i>€</i> 40°
	0.01	95; 101 ₃	6 ⁹ 98 0	<u> </u>
lettuce head	0.10	104	<u> </u>	
		Overall recovery (n=3)	° `>100 ~ `	X4 .6 ~ (7
	0.01	88; 84; 87; 760	84 %	₽ \$ 5.7 ₩
wheat green material	0.10	94; 86; 87, 92	<u> 7</u> %	4.3
	0.05	Overall recovery (n=8)	87	
1	0.05	89,107		
wheat straw	0.5			
	0.01	Överali řecov@v (n=S) Ø 91; 88		
wheat arain	0.01	N,	0124 0 124 0	
wheat grain	0.10	Ø Ø4 Øverall recover%(n=3)	Q, 101 8	× 19.8
Fluopyram-methylsu	Ifovido (A)E 13	A4122)		0 19.0
riuopyrani-metnyisu	Q.01	5; 83 3 ; 95 °	87 8	© 10.7
turnip leaf, normal	×0.10	164; 104, 900; 92; 107	101~~	5.7
turinp icar, normai	× \$9.10	Qveralbecovery (n=90	& <u>95</u>	11.1
	× 0.10	87; 84; 006 x	0 32 7	12.9
turnip body 🏾 🍣	0,10	404; 74; 89; 106, 24	87	17.7
ı		Overall recovery (n=8)	Å 89	15.2
0	» 0.01 ×	78; 99	K 84	
lettuce head	0,00		J07	
Ű'		Overall recovery (n=3)	92	15.9
	0.01	96; 106; 95 <u>; 1</u> 02	100 100	5.2
wheat green material	0,10	[™] 72;81;8©102 √ [∞]	<u>88</u>	11.9
		Overall recovery (n=8)	S 94	10.6
	0.05	<u>7 108; 112</u> O	110	
wheat straw	0.05	107 0	107	
	<u> </u>	Soversus recovery (n=3)	109	2.4
		796103 ° 202 v	91	
wheatgrain	0.1	Overall recovery (n=3)	102 95	
Fluopyram-pyridy			פע	14.3
		Q05; 85, 100; 101	98	7.9
turnip leaf, normal	0.10 V	91; 91; 89; 89; 97	98	3.6
	0.10	OveraQ , recovery (n=9)	91 94	6.8
		94; 80; 73; 106	88	16.7
turnip ody	0.10 🖉	[~] 988; 89; 93; 110	95	10.7
	0 2	Overall recovery (n=8)	92	13.4
	A 0,007	78; 96	87	
Aettuce bead	×0,10	92	92	
	4	Overall recovery (n=3)	89	10.7
<u> </u>	0.01	96; 101; 95; 90	96	4.7
wheat green material	0.10	79; 78; 78; 87	81	5.4
-		Overall recovery (n=8)	88	10.2
wheat straw	0.05	94; 103	99	



Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD* (%) © °
material	(mg/kg)	80	90	(70) °
-	0.5	80	80	
		Overall recovery (n=3)	92	12.6
	0.01	90; 81	86 📎	-0 6
wheat grain	0.1	95	95	<u> 4</u> . Ç [*]
		Overall recovery (n=1)	89	8.0
Fluopyram-7-hydroxy	y (BCS-AA10	065)	<hr/>	
	0.01	98; 93; 93; 96 💍	<u>95</u>	× 267 ×
Turnip leaf, normal	0.10	110; 103; 106; 95; 🕷	98	Q.9 K
		Overall recovery (n=9)	_ ©[™]97 _ ≴	∫ ~9.5 <i>~</i> ∉
	0.01	87; 86; 83; 46	N 88 0	6.4
Turnip body	0.10	106; 101; 98, 88	\$ 98 Q	7.7 24
		Overall recovery (n=8)	°~~93 ∞ /	\$.9
	0.01	90 97 Ø	94 🗸 🖉	P ~ ~ ~
Lettuce head	0.10	0 ₁₀₅	₩ 1 05° 0°	\$ \$ °
		Overall recovery (n=3)	<i>Q</i> <u>4</u> 97 ₄ ⊗	O LA AV
	0.01	82; 85; 82; 85	× 1.84 °	Q 2.1 Q
wheat green material	0.10	@ 97; 9¥; 94; 9¥	0 94	2.7
		Overall recovery (n=8)	89 8	0 6.8
	0.05	87; 88	N 888 A	<u> </u>
wheat straw	0.5	× & \$\$6 &	<u> </u>	Ŭ Ŷ
Willout Straw		•Øverall recovery (n=3)	<u>96</u> 0 96	% 5.5
	0.00	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		0
wheat grain		× × × × × ×	87 2	õ
wheat grain	<u>0.1</u>	Overall recovery (n=3)	87,9	5.7

FL: fortification level, RSD - Relative Statutard Deviation * some RSDs were not calculated as there were only two individual recoveries given ** Recovery corrected with the control interference (0.000) mg/kg/ recovery not corrected = Final determination as: fluopyram Residues calculated as fluopyram Final determination as: fDU-benzionide Residues calculated as fluopyram Final determination as: fDU-benzionide Residues calculated as fluopyram Final determination as fDU-benzionide Residues calculated as: fluopyram Final determination as fDU-benzionide Residues calculated as: fluopyram

n.

Final determination of FLU-PCA Residues calculated as floopyram Final determination as: FLU-TOH Residues calculated as: Pluopyram

Ô

Š No residue of fluopyram or related metabolites were found above the LOQs in any of the control samples of rotational crop matthes and used of rotational crop matrices analysed.

The residue levels of fluopyram and its relevant metabolites in the rotational crop matrices of turnip, lettuce and wheat are summarized in the Table 6.6.2-9.

The storage period of deep-frozen samples was up to 290 days for lettuce, 372 days for turnip leaves, 372 days for turnip body, 374 days for wheat given material, 71 days for wheat grain and 80 days for wheat straw.

Residues in Turnig

j S

In trial R 2006 0858/6 (ptot A, BI 30 days), Esidues of fluopyram (AE C656948) were 0.02 mg/kg in turnip leaf, normal at DAT (days after treatment), 86 and 100. In turnip body samples the residues of fluopyram were 0.02 and 0.01 mg/kg at DAT 86 and 100, respectively.

The residues of FUU-beoramide, FLO9methylsulfoxide, FLU-PCA, FLU-7OH in all turnip matrices were < 0.04 mg/kg.

In triat R 2006 0861 (plot B, PBI 216 days) residues of fluopyram (AE C656948) were 0.04 mg/kg in turnip leaf normal at DAT 323 and 337, and in turnip body residues of fluopyram were 0.02 mg/kg at DAT of 323 and 337. The residues of FLU-benzamide, FLU-methylsulfoxide, FLU-PCA, FLU-7OH in all turrup matrices were <0.01 mg/kg.

In trial R 2006 0862/4 (plot C, PBI 301 days) residues of fluopyram (AE C656948) were <0.01 mg/kg and 0.01 mg/kg in turnip leaf, normal at DAT of 372 and 386, respectively. In turnip body residues of



fluopyram were <0.01 mg/kg at DAT of 372 and 386. The residues of FLU-benzamide, FLU-methylsulfoxide, FLU-PCA, FLU-7OH in all turnip matrices were <0.01 mg/kg.

Residues in Lettuce

In trial R 2006 0859/4 (plot A, PBI 30 days), residues of fluopyram (AE C656948) were 0.03 mg/kg and 0.01 mg/kg in lettuce head at DAT (days after treatment), 66 and 80, respectively.

The residues of FLU-benzamide, FLU-methylsulfoxide, FLU-PCA, FLKFOH in all Aptruce matrices were <0.01 mg/kg.

In trial R 2006 0861/6 (plot B, PBI 216 days) residues of fluopyram (NE C656948) were (101 mg/kg in C lettuce head samples at DAT 261 and 275. The residues of FLU-benzamide, FLU-Dethylsuffoxide, FLU-PCA, FLU-7OH in all lettuce matrices were <0.01 mg/kg.

In trial R 2006 0862/4 (plot C, PBI 301 days) residues of fluororam (AE C656948) were & 1 mgRg in lettuce head samples at DAT 338 and <0.01 mg/kg at OAT 352. The residues of RCU-benZamide, FLU-methylsulfoxide, FLU-PCA, FLU-7OH in all lettuce matrices were <0.0 mg/kg.

Residues in Wheat

In trial R 2006 0860/8 (plot A, PBI 28 days), residers of thopyram (AE 656998) were 0.07 mg/kg (in green material), 0.07 mg/kg (in wheat straw), and <0.01 mg/kg in wheat grain at DAF (days after treatment), 190, 314, and 314, respectively.

The residues of FLU-benzamule, FLU-PCA and FLU-76H in on three wheat matrices were below relevant LOQ. The residues of FLU-meth uniformed were at <0.01 mg/kg in green material (DAT 190), <0.05 mg/kg in straw (DAP 314), 0.01 mg/kg in grain (DAT 314).

In trial R 2006 0861/6 (plot B PBI 100 days), residues of Nuoperam (AE C656948) were 0.08 mg/kg (in green material), 40.01 mg/kg (in wheat grain), and 0.09 mg/kg in wheat straw at DAT (days after treatment), 240, 328 and 328, respectively.

The residues of FLU-benzamide, FLU-PCA and FLU-70FI in all three wheat matrices were below relevant LOQ

The residues of FL@methylsulfaxide were at 0.02 mg/kg in green material (DAT 240), 0.04 mg/kg in grain (DAT 328), <0.05 mg/kg in straw straw (DAT 328), <0.05 mg/kg in straw straw straw straw

In trial (12, 2006, 0.0862) (plot (0, 200, 0.01) model grain), residues of fluor ram (AE C656948) were 0.02 mg/kg (in green material), (0.01, 0.01) (days after treatment), (14, 69), and (691, 120) (days after treatment), (14, 69), and (10, 120) (days after treatment), (14, 69), and (10, 120) (days after treatment), (14, 69), and (10, 120) (days after treatment), (14, 69) (days after treatm

The residues of FLU benzañide, ELU-methyls Fluide, FLU-PCA, FLU-70H in all three wheat matrices were below delevant LOQ?



Following one spray application conducted with fluopyram SC500 to bare soil or lettuce as a target crop at a rate of 0.5 kg a.s./ha, residues in succeeding crops were analysed for fluopyram (AE C656948) and its metabolites fluopyram-benzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE C657188) and fluopyram -hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122) using a variated selective HPEC-MS/MS analytical method.

These data show that residues in turnip, lettuce and wheat as succeeding crop are adequately covered by the correct MR_{0} .

Assessment and conclusion by applicant: The study is acceptable

Page 667 of 801 2021-02-26



Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

										4			ругаш
able 6.6.2-	9: Result		crop trials conducte	ed with fluop	yram	of Ba	j. Jer Je		orton a	ection ection	regi 1 129011 129011	19 19 19	ð,
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application rate per treatment to bare soil or target <u>crop</u>	Dates of treatment or no. of treatments and last date	Portion Ganalysed	Groven Stage at Sampling		DEC DEC DEC DEC DEC DEC DEC DEC DEC DEC	Residues (mg/kg)	peret()I)I	PHI (days
	(a)	(b)	kg a.s./bar (L/ha) 0	A SULA	WRET			•		FLASTON as AE C656948	FLU- methyl- sulfoxide as AE C656948	Total resude calc.	(e)
R 2006 0858/6 0858-06 / 01 Germany D-51399 Burscheid, Trial Station Höfchen Europe, North	Plot A Application to bare soil PBI: 30 d Rotational crop : Turnip, edible Rondo	1) 18.08.2006 G 3) 27.10 2006			to a file	2 2 49 2 49 3 49 49 47 49 6 10 10 10 10 10 10 10 10 10 10	802 0.02 0.02 0.01 0.01	0.01 0.01 0.01 0.01	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	0.03 0.03 0.03 0.02	86 100 86 100
F, 2006 R 2006 1859/4 1859-06 / 01 Germany D-51399 Burscheid Versuchsgut Höfchen) Europe, North F, 2006	Plot A <u>Application to</u> <u>bare soil</u> PBI: 30 d <u>Rotational</u> <u>crop</u> Lettuce Giselar Butterhead	ente i	0.500 300 M.1667		o ^E head at	42 49	0.03 0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0.04 <0.02	66 80
	CONGE	OLCY STELL	Op De										66

Page 668 of 801 2021-02-26



Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

					-			ler p	~0 [©]	JTEN 8	<u>, 0</u> 1	regij	1016 1016 1010	Ĵ.
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application treatme <u>to bare soil o</u> <u>crop</u>	ent er target	Dates of treatment or no. of treatments and last date	Portion] analysed	Growtle stage at sampling		arties	Resplues (onten onten	C ^{\$}	PHI (days)
	(a)	(b)	kg a.s./ha (L/ha)				J. D. C. C.	AE C656948 as AE O656948	FLU- benzamide AAE VE656948	FLU- PCA 98 AE C656948		Solution State	Total resude calc.	(e)
R 2006 0860/8 0860-06 / 01 Germany D-51399 Burscheid Europe, North F, 2006	Plot A Application to bare soil PBI: 28 d Rotational crop: Wheat, winter Thommy	1) 04.10.2006 2) 22.05.2007 - 29.05.2007 3) 17.07.2007			0 E E 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	green frail grain de straw	30 7 89 89 5 89 0 1 4 89 0 1 1 5 6 0 5	0.01 0.01 0.01 0.07 0.07 0 0 0 0 0 0 0 0 0 0 0 0 0	<0.01 <0.01 0.01 0.05	0.01°L C <0.01°L C <0.05	<0.01 <0.05	<0.01 0.01 <0.05	0.08 <0.02 0.12	190 314 314
R 2006 0861/6 0861-06 / 02 Germany D-51399 Burscheid (Versuchsgut Höfchen) Europe,	Plot B <u>Target crop:</u> Lettuce Gisela PBI:216 d <u>Rotational</u> <u>crop:</u> Turnip. edible Mairübe	1) 27.03.2007	20 ²¹ 20 ²¹			leaven Sbody E D E D E S D C E S S D C E S S S S S S S S S S S S S S S S S S			<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	0.05 0.05 0.03 0.03	323 337 323 337
North F 2006	Plot B <u>Target crop:</u> Lettuce Gisela PBI: 230 d Rotational crops: Lettuce Gisela	1) 10.04.2007 10 T C I I I I 10 C C I I I I I 10 C C I I I I I I 10 C C I I I I I I I I I I I I I I I I I	aner the	6.1667 P ^C 2 ^C P ^C		head	46 49	0.01 0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.02 <0.02	261 275

Page 669 of 801 2021-02-26

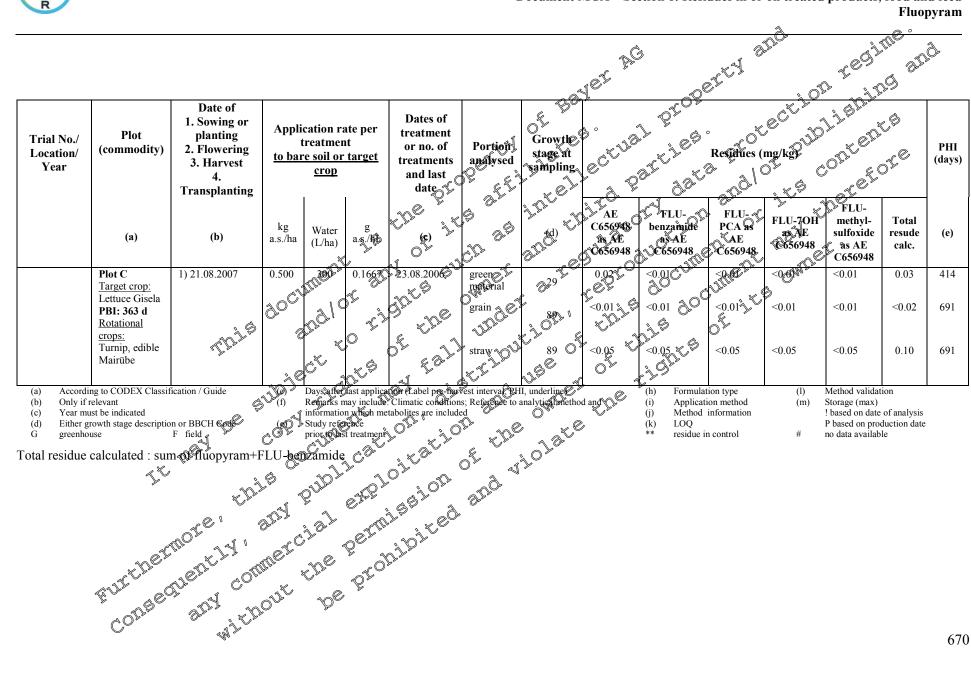


Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

									4			10
					Å	J ^{OL} P	3	ert d	TDO.	regi	J.G D.G	Ĵ.
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application rate per treatment <u>to bare soil or target</u> <u>crop</u>	Dates of treatment or no. of treatments and last date	Growthe stage at sampling		artiles dati	Respires (ECT IN CT IN mg/kgP D C FLU-70H	obten oref(.,\$) ^{r e}	PHI (days)
	(a)	(b)	kg a.s./ha Water g (L/ha) a.s./hb		O.L.	AE C656948 35 AE O656948	AS AE	AE 656948	**************************************	sulfoxide	Total resude calc.	(e)
	Plot B Target crop:	1) 01.12.2006	0.500	23.08.2006 green material Ograin	305	0.08	<0.010	~0.01, *C	<0.69N ^{N 21}	0.02	0.09	240
	Lettuce Gisela PBI: 100 d		2000 2102 rj	Ograin	89	×0.01		<0.01	<0.01 0.05	0.04 <0.05	<0.02 0.14	328 328
	<u>Rotational</u> <u>crop</u> : Wheat, winter	TULS	at to	of gall vite	L'IOBE		~0.01 ~0.05 ~0.05 ~0.05	S.0.3	0.03	<0.05	0.14	528
R 2006 0862/4	Plot C Target crop:	1) 20.06.2007	0.500 300 004667	23108.2006 Veaves	47 49 QI	<0.01 0.01	0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.02 0.02	372 386
0862-06 / 03 Germany D-51399 Burscheid (Versuchsgut Höfchen) Europe, North	Lettuce Gisela PBI: 301 d <u>Rotational</u> <u>crop:</u> Turnip, edible Mairübe Lettuce,Gisela	TRON De E	COPY CUMPLO	22708.2006 teaves	$\begin{array}{c} 1 & 47 \\ 49 & 67 \\ 0 & 47 \\ 2 & 49 \\ 1 & 2 \\ 1 $	0.01 39.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.02 <0.02	372 386
F 2006	Plot C <u>Target crop:</u> Lettuce Gisela PBI: 301 d		0.500 2300 04867 ART ART ART ART ART ART ART ART ART ART	010000 23982006 10101000 1001000	45 49	0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0.02 <0.02	338 352
	EV-CORSEC	Realt DY	Ont De F									669

BAYER

Page 670 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram





Data Point:	KCA 6.6.2/03
Report Author:	
Report Year:	2008
Report Title:	Determination of the residues of AE C656948 in/on the field rotational cops
	carrot, lettuce and winter wheat after spraying of AE C696948 (500 SC) in the field in Italy
	field in Italy
Report No:	RA-2650/06
Document No:	<u>M-296652-02-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/414/EEC of July 25, 1991, Ann & II, par A, section
study:	6 and Annex III, part A, section 8
	Residues in or on Treated Paducts, Food and Feed EC guidance working
	OECD Guideline for testing of Chemicus; Residues in otational crops (limited
Deviations from current	none
test guideline:	
Previous evaluation:	yes, evaluated and accepted revealed accepted by the second secon
	rev. 1 to Volo of Dal B7 august 20/2 (references welied 6)
GLP/Officially recognised	yes, evaluated and accepted rev. 1 to Vol. of Dal B7 august 20/2 (references velied 6) Yes, condiced under GLT Officially reconsised asting scilities
testing facilities:	
Acceptability/Reliability:	Yes a g g g g g g g g g g g g g g g g g g
2	

Materials and Methods

The purpose of the study was to determine the magnitude of residues of fluopyram (AE C656948) and its metabolite fluopyram-berzamide (AE 148845), fluopyram pyridyl carboxylic acid (FLU-PCA, AE C657188) and fluopyram-7-hydroxy (BCS-AA 10065) and fluopyram-methyl sulfoxide (AE 1344122) in carrot, lettuce, winter wheat grown as rotational crops in southern Europe (Italy) following one spray application of fluopyram SC 500. Residues of the active substance fluopyram and its metabolites were determined in the succeeding crops only. The target crop lettuce was not analysed.

The test item was applied to the treat d plots in a different manner, but the application rate of 1.0 L of test item/ha (0.5 kg a.s/ha) was the same.

For the plot A (trials R 2000 0869/I, R 2006 0870/5 and R 2006 0871/3) – the test item was applied to the bare soil followed by incorporation (maximum 8 cm depth) to avoid photodegradation. The investigated plant back interval was 30 days for all crops (carrot, lettuce and winter wheat) and corresponds to the standard plant back interval mease of crop failure.

For the plot B (trial R 2006 0872/1) – the test tem was applied on lettuce as the target crop two weeks after planting. Plot B represents a plant back interval of 100-240 days.

For the plot of trial R 2006 9874/8y – the test item was applied on lettuce as the target crop two weeks after planting. Plot represents a plant back interval of 290-365 days.

Plots B and C were subdivided into 3 subplots for the 3 crops (carrot, lettuce, cereals) to be planted as rotational crops, Explanation of the study plot designs is illustrated in the Table 6.6.2-10.



	Requested PBI	actual l	Plant Back Interva	ll (PBI)	Remarks
Trial No.	(days) / Application on	Root crop DAT (days)	Leafy crop DAT (days)	Cereals DAT (days)	
R 2006 0869/1 R 2006 0870/5 R 2006 0871/3	Plot A: 30 / soil	carrot 30 (R 2006 0869/1)	lettuce 30 (R 2006 0870/5)	winter wheat 30 (R 2006 65 1/3)	Application on bate soil; planting/Sowing Opotational crop after 30 days
R 2006 0872/1	Plot B: 90-240 / lettuce	carrot 240	lettice 240	winter where	Application on ettuce Ovo weeks after blanting; harvest/pl@ghing@f lettuce planting.sowing of rotational crops
R 2006 0874/8	Plot C: 290- 365 / lettuce	carrot 289	Kettuce 290 290 290 290 290 290 290 290	Spring wheat	Application on letture two weeks after planting barvest/ploughing of letture; cultivation break; planting/sowing of rotational crops

Harvest of target crop lettuce, Plot B, R 2006 0872/1 and Plot C, R 2006 0874/8

On plot B the target crop lettuce was harvested at normal harvest, 32 days after planting. On plot C the target crop lettuce was harvested at normal harvest, 56 days after planting, 9

No lettuce samples were taken for analysis. The harvest leftovers were destroyed by grinding and ploughed in (m order to capture all possible residues and not remove them from the plot prior to planting the rotational crops.)

Planting rotational crop

Untreated plots were prepared before treated plots.

At the 30° day (Plot A), the 100 240-day (Plot B) and the 290-365-day (Plot C) plant back intervals the plots were prepared for crop anting following normal agronomic practices for each crop type in the regions. 21 Å X

For the longer-term Plots $\vec{B}(100240 \text{ days})$ and $\vec{C}(290365 \text{ days})$ a bare soil status had to be maintained after harvest of lettuce Q.e. no Sover Gop is sown. S

Samples were taken, prepared in the field where necessary, transported and stored.

The first sampling of succeeding crops carrots and lettuce was taken at early harvest (14 days prior to normal harvest) followed by sampling at normal harvest maturity for each crop type.

For wheat, green material was sampled at growth stage 29-30 BBCH and at normal harvest maturity (grain and straw). All sampling equipment was deaned prior to entering any plot that was to be harvested. The field samples from all trials were stored deep-frozen within 24 hours after sampling. All field samples were shipped by deep-freeze lorry and arrived in good condition. The field sub samples were stored in a Greezer at \leq 30°C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field sub samples were shredded with dry ice in a cutter. Representative parts of the shredded samples were transferred into polystyrene boxes separately for analysis (UP) samples) and archiving (UR samples) and stored at \leq -18°C until analysis.

Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxid, were determined by LC-MS/MS according to method 00984 (283301-01-1, see MCA section 4.1.2). Full details and acceptable validation data to support this method



are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4. Q_n°

Residues of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitrile:water (80:20; v:3). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

- One dilution was performed under acidic conditions: this extractationed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed determination of FLU, FLU-benzamide and FLU-7-OH.

An aliquot of the extracts was injected into LC-MSTMS operated in Electrospray Ionization mode:

- One injection in positive electrospray ionization for the determination of FDU, FLU-benzamide and FLU-7-OH.
- Another injection in negative electrosprationization for the determination of FLUPCA and FLU-methyl-sulfoxide under different conditions.

The linearity was demonstrated in each analytical batch with a /x weighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standardization using isotopically stable labelled internal standards.

The Limit of Quantification (LOQ) expressed as fluopyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat straw and 0.01 mg/kg for all other matrices

Full details and acceptable validation data to Support this nothod are presented within document M-CA 4, which comply with the EU/regulatory requirements outlined within SANCO/3029/99 rev 4.

Findings

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and treated samples from the study in each set of analyses. The data demonstrate acceptable method performance during sample analysis. All the recovery results and details are given by the Table 66.2-11

Table 6.6.2- 11:	Recovery data for fluopy am (AE C636948) and its metabolites in rotational crop matrices (carrot leaf and root, lettuce head, winter wheat green material, winter wheat straw, and winter wheat grain)	
~	crop matrices (carrot leaf and root. Lettuce head, winter wheat green material.	
	winter wheat straw and winter wheat grain)	
	Gite Oneu Straw, and where shear grain)	

Crop Sample	FL (mg/kg)	Single values (%)	Mean value (%)	RSD* (%)
Fluopyram (AE C65	<u>6948) (*) (*)</u>	<u> </u>		
	0.01 U	98; 194; 96; 100	100	3.4
carrot leaf, normal	s 0.1⊘ ^y	🔊 10 \$ 2,108; 101; 97	102	4.5
.0. ~.		[♥] Ov <i>g</i> rall recovery (n=8)	101	4.0
caret root	0.01 💉	* 903; 93; 105; 106	102	5.9
carget root	0.10	94; 101; 104; 99	100	4.2
J Q +		Overall recovery (n=8)	101	4.9
	2,01	104; 105	105	
Ettuce head	۵.10 هگ	105; 99	102	
Í "Ô ^y		Overall recovery (n=4)	103	2.8
	0.01	100	100	
winter wheat green material	0.10	91	91	
material	0.5	86	86	



	1		Γ	
Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD* (%)
		Overall recovery (n=3)	92	7.7 2
	0.05	87; 83	85	
winter wheat straw	5.0	108	108	
Whiter Whiter Straw	0.0	Overall recovery (n=3)	93	. 44.5
	0.01	85; 92; 84	87,	<u></u> , 0 [°] 5.0 6 [°] , 2 [°]
winter wheat grain	0.10	96 (**	26	
		Overall recovery (n¥)	89	
Fluopyram-benzami	de (AEF14881		,0× *	
• •	0.01	98; 85; 100; 405	97° 0	8.8
carrot leaf, normal	0.10	102; 99; 102; 100		
		Overall recovery (n=8)	<u>~</u> 99	6.1
	0.01	99; 80; 93; 100	93 KU K	y *≫10.1 [®]
carrot root	0.10	95; 99; 100, 107	<u>~</u> 980° ~	£ 5.7 °
		Overall recovery (n=8)	<u>~ 96 ~ </u>	<u> </u>
	0.01	105,90	Ø <u>(</u> 98 . 0`	<u> </u>
lettuce head	0.10	U 100; 109 ~		
		Overall recovery (n=0)	<u>6</u> 107 S	<u> </u>
	0.01	<u>96</u> 9	N 396 N	<u>S</u>
winter wheat green	0.10		0 87,0 0 107 0 6	J '¥
material	0.5	<u>407</u>		<u> </u>
	₩ ^v	Överall recovery (n=3)	\$7 \$7	0 10.4
• • • • •	0,05	10/0/01		<u> </u>
winter wheat straw	<u>~</u> 3.0		× √ 96 √ ×	
	0.00	Overal recovery (n=30	$\begin{array}{c c} & 101 & 57 \\ \hline 0 & 91 & 77 \\ \end{array}$	5.4
winter wheat are in		2, <u>89; 9</u> 7 , 7 7 , 9 7 , 7	97	
winter wheat grain		Overall recovery (n=3)	97 27 9 3	4.4
Fluopyram-methylsu		4\$(122)		7.7
		94; 92; &1; 92	\$ @90	6.6
carrot leaf normal	0.10 Ø	<u>91; 88, 93; 88</u>	× 90	2.7
		Overall recovery (n=8)	~ 90	4.7
	0,10	83; 978; 8©100 V	s. 0 ³ 87	10.9
carrot root	Q.10	\$5; 91; 9 6; 93,	§ 91	5.1
Jan Standard Standa		Qverall recovery (n=8)	89	8.2
Q.	0.01	× \$2; 88 ×	85	
lettuce head	0.00	0 109; 95 0	102	
~Q (Overall recovery @=4)	94	12.4
A	0.01	80	80	
winter wheat green	9 0.1Q	\$ 100°	100	
material	0.50		100	
¥¥	S N	Oxorall recovery (n=3)	93	12.4
- 	0.05 C	25; 108	117	
winter wheat straw	\$ 5.00	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	92	
<u>Q`</u> >		Overall recovery (n=3)	108	15.2
A A	00.01	<i>∞</i> 110; 96	103	
winter wheat gram	0.1	91	91	
		Overall recovery (n=3)	99	9.9
Flugpyram pyridy			70	24.6
carrot Caf, normal	<u>لافًان 0.01</u>	61; 60; 64; 96	70	24.6
carrot (eat, normal	0.10	66; 68; 69; 90	73	15.3
~	0.01	Overall recovery (n=8)	72 98	18.9 7.3
carrot root	0.01 0.10	101; 94; 91; 107 86; 85; 95; 88	98 89	5.1
	0.10	00, 03, 73, 88	07	J.1



	1			
Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD* (%)
		Overall recovery (n=8)	93	8.2
	0.01	102; 98	100 🔗	07 &
lettuce head	0.10	101; 96	99	4
		Overall recovery (n=4)	99	2.8
	0.01	109	109	<u> </u>
winter wheat green	0.10	93 🖏	<u>9</u> \$	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
material	0.5	80 🔗	080	
		Overall recovery (n=3)	^{0%} 94 ×	J A15.5 A 4
	0.05	95; 101 ₄ ©	0 ⁵ 98 0	
winter wheat straw	5.0	93 6	\$ \$\$	
		Overall recovery (n=3)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	×4.3 ~~
	0.01	19; 76 Q	× 78 × 2	
winter wheat grain	0.1		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	L L . 0
0		Overall recovery (n=3)	^Q ₄ 78 ₄ ⊗	
Fluopyram-7-hydrox	y (BCS-AA10	065)		
	0.01	Ø 93; 89; 94; 94	0 93	3.5
carrot leaf, normal	0.10	[∞] 102 102; 100; 96 [∞]	~ 1.00 .S	2,8
,		Overall recovery (n=8)	N 897 A	A 4.8
	0.01	©99; 91@86; 100 6	94,0	Ŷ [™] 7.4
carrot root	0.10	96; 89 ; 92; 89	Q 92 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	\$ 3.6
	×,	Overal recovery (n=8)	1. \$ 93	©‴ 5.7
	0.01	97 695 0	×~96 ~	ò
lettuce head	° 0.10	\$ 1497; 90 L	97, 97	۲ <u></u>
		Qveral recovery (n=40)	<u> </u>	6.0
4	0.00	× 970 × 1	0° 397 1.7	
winter wheat green			91	
material S	\00.5 Å	× ~96 × v	<i>6</i> , 96, 96, 96, 96, 96, 96, 96, 96, 96, 96	
C C		Overall recovery (n=3)	£. 95	4.0
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u> </u>	0 × 90;29 0	a 85	
winter wheat straw	5.0 Ø	1 299 8	× 99	
<u>`</u>		Ørerall recovery (n=3)	~ 89	11.2
<u> <u></u></u>	0.005	87; 80° V	<u></u> 0 ³ 87	
winter wheat grain		87% 4.	<u>م</u> لا 100 87	
A A A A A A A A A A A A A A A A A A A		Qverall recovery n=3)	<u>87</u>	0.7
L fortification lavel	Ratalina Standard			

FL: fortification level, KD - Refairve Standard Desiation * some RSDs were not calculated as there were only two individual proveries given ** Recovery corrected with the control interference (0.002) mg/kg/ recovery not corrected = 132% Final determination as: fluopyram residues calculated as fluopyram Final determination as: FLU-benzamide Residues calculated as fluopyram Final determination as: FLU-methylsulforde Residues calculated as fluopyram

Final determination as: FLU-PCA Residues calculated as: flipopyrano Final determination as: FLQ-PCH Residues calculated as fluopyrano

°~ S , O K, Ą, Ô

No residue of floopyram or related merabolites were found above the relevant LOQs in any of the control samples of rotational drop watrices analysed.

The residue levels of fluopyrant and its relevant metabolites in the rotational crop matrices of carrot, lettuce and when are summarized in the tables below.

The storage period of deeperfozen samples was up to 363 days for lettuce, 315 days for carrot leaves, 315 days for carrolroot, 221 days for wheat green material, 109 days for wheat grain and 107 days for wheat straw.

Residue measured in the relevant succeeding crop matrices are summarized below and overall trials and residue summaries are presented in Table 6.6.2-12.



#### **Residues in Carrot**

In <u>trial R 2006 0869/1</u> (plot A, PBI 30 days), residues of fluopyram (AE C656948) were 0.02 mg/kg and 0.04 mg/kg in carrot leaf 108 and 122 days after treatment (DAT), respectively. In carrot root samples, the residues of fluopyram were 0.05 mg/kg at DAT 108 and 122.

The residues of FLU-benzamide, FLU-methylsulfoxide, FLU-PCA and FLU-70H in all carrot matrices were <0.01 mg/kg.

In <u>trial R 2006 0872/1</u> (plot B, PBI 100-240 days) residues of fluopyram (AF C656948) were 0.00 mg/kg² in carrot leaf, normal at DAT 338 and 352, and in carrot residues of fluopyram were 0.02 mg/kg² at DAT of 338 and 352. The residues of FLU-benzamide, FLU-methylsuboxide, FLU-PCA and FLU-TOH in all carrot matrices were <0.01 mg/kg.

In <u>trial R 2006 0874/8</u> (plot C, PBI 290-365 days) residues of fluopyram (AE C656948) were 0.01 mg/kg in carrot at DAT of 363 and 377, respectively. In carrot root residues of fluopyram were 0.02 mg/kg and 0.01 mg/kg at DAT of 363 and 377, respectively. The residues of FLU4benzamide, FOU-methylsulfoxide, FLU-PCA and FLU-7OH in all carrot root matrices. Were <0.01 mg/kg.

#### **Residues in Lettuce**

In trial <u>R 2006 0870/5 (plot A, PBI 30 days</u>), residues of fluopyram (AE C656948) were 0.09 mg/kg and 0.03 mg/kg in lettuce head 58 and 72 days after treatment (DAT), respectively. The residues of FLU-benzamide, FLO-methylsulforide, FDU-PCA and DLU-70H in all lettuce matrices were <0.01 mg/kg.

In trial <u>R 2006 0872/1</u> (plot **B**, PBI 100 – 240 days) residues of fluopyram (AE C656948) were 0.02 mg/kg and <0.01 mg/kg in lettuce head samples at DAT 296 and 340, respectively. The residues of FLU-benzamide, FLU-methylsulfoxide, FLU-PCA and FLU-7OH in all lettuce matrices were <0.01 mg/kg.

In trial <u>R 2006 0874/8</u> (plot C, PBI 290 – 365 days) residues of Rhopyram (AE C656948) were 0.03 mg/kg and 0.0 mg/kg in lettice head samples at DAT 318 and 332, respectively. The residues of FLU-benzamide, FLU-methylsinfoxide, FLU-PCA and FLC-70H in all fettuce matrices were <0.01 mg/kg.

#### Residues in Wheat

In trial <u>RC2006 0871/3</u> (plot A PBI 36 days), residues of thopyrand (AE C656948) were 0.11 mg/kg (in green material), 0.15 mg/kg (in wheat strow), and 0.01 mg/kg in wheat grain 139, 265, and 265 days after treatment (DAP), respectively.

The residues of PLU-methyls floxide in wheat green material were 0.02 mg/kg (DAT 139), in straw <0.05 mg/kg (DAT 265), and 0.03 mg/kg m wheat green material DALT 265).

The residues of FLU-7OH in wheat green material and grain were <0.01 mg/kg (DAT 139 and 265) and at 0.08 mg/kg in wheat straw.

The residues of FLU-benzamide and FLU-PCA in all wheat matrices were below their respective LOQs.

In trial <u>R 2006 0872/1</u> (plot **B** PBIQ00-24) days), residues of fluopyram (AE C656948) were 0.07 mg/kg (in green material) 0.01 mg/kg (in wheat grain), and <0.05 mg/kg in wheat straw 242, 352, and 352 days after treatment (DAT), respectively.

The residues of FL/5-methodsulfoxide were at 0.01 mg/kg in green material (DAT 242), 0.02 mg/kg in grain (DA1, 352), 0.05 mg/kg in straw (DAT 352).

The residues of FLU-benzaroide, FLU-PCA and FLU-7OH in all three wheat matrices were below relevant LOQS

In trial <u>K 2006 0874/8</u> (plot C, PBI 290-365 days), residues of fluopyram (AE C656948) were 0.06 mg/kg (in green material), <0.01 mg/kg (in wheat grain), and 0.08 mg/kg in wheat straw 478, 611, and 611 days after treatment (DAT), respectively.



The residues of FLU-methylsulfoxide in wheat green material were at the level of 0.01 mg/kg at DAT 478, <0.01 mg/kg in wheat grain, and <0.05 mg/kg in wheat straw at DAT 611. The residues of FLU-7OH in wheat green material and grain were <0.01 mg/kg at DAT 478 and 611 and at the level of 0.06 mg/kg in wheat straw (DAT 611). The residues of FLU-benzamide and FLU-PCA in all wheat matrices were below their respective I A or letting incurs allowing of incurs and the original of t Ő Conclusions Following one spray application conducted with fluopyram SC500 to bare soil or lettuce as a target cop at a rate of 0.5 kg a.s./ha, residues in succeeding crops were analysed for fluopyram AE CO6948 and its metabolites fluopyram-benzamide (AE F148815), fluopyram-pyri@ carboxylicacid (FU-PCA, AE C657188) and fluopyram-7-hydroxy (BCS-AA1006) and fluopyram-methyl sphoxide (AE 644120) These data show that residues in carrot, lettuce and wheat as speceeding croppare adequately covered by the current EU MRL.



Page 678 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Гаble 6.6.2	- 12: Results	s of rotational	crop trials conducte	ed with fluo	oyram	B	ter p	ç	perty at	til Of	regi i zegi	ng gig	Ĵ.
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application rate per treatment <u>to bare soil or target</u> <u>crop</u>	Dates of treatment or no. of treatments and last	3 9 E V	Growth Stage at sampling	ectul Lectul	and .	A A	PUD g/kg) (	herer	, ^y ^g	PHI (days)
	(a)	(b)	kg a.s./ha Water (L/ha) a.s./hL			J.S.(d)	AE C656948 O as AE C656948	FLX- benzamide as AE C656948	FICU-PCA as AE C656948	<b>EÚ</b> - SOH as AE C655948	FLU- methyl- Ssulfoxide as AE C656948	Total residue calc.	(e)
R 2006 0869/1 0869-06 / 01 Italy	Plot A Application to bare soil PBI:30 d	1) 10.08.2006 3) 05.11.2006 - 15.11.2006	0.50 0 1 300 0 1667	11.00.2006	JII DE		20.02 0.04	<0.01 ><0.01 3.0	OF		<0.01 <0.01	0.03 0.05	108 122
I-37050 Albaro Europe, South F 2006	<u>Rotational crop :</u> Carrot, Nantese di Chioggia	T l de	ND TROPIES	or fai		39 49 10 10 10 10 10 10 10 10 10 10 10 10 10		~0.01 <0.01 ~	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0.06 0.06	108 122
R 2006 0870/5 0870-06 / 01 Italy I-37050	Plot A <u>Application to</u> <u>bare soil</u> PBI: 30 d Rotational cfop	1) 10.08,2006 3) 17.09,2006 - 24.09.2006	0.50 300 00667 COP CUTUR 20667		De head		0.09 0.03	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0.10 0.04	58 72
Albaro Europe, South F 2006	Rotational crop Lettuce,Potomac (Numens); Butterhead variety	re '	any al exp	Lesion Lesion	and								
R 2006 0871/3 0871-06 / 01 Italy	Plot A <u>Application to</u> <u>bare soil</u> PBI: 30 PBI: 30	©26.10.2006 2) 25.05 2007 - 1506.2007 3©5.06.2007 05.07.2009		26.09 [°] 2006	green material grain	30 89	0.11	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0.02	0.12	139 265
	Colle	all th			1	1	1	1	1	1	I	I	673



Page 679 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

												4			PJ
										Ġ	, O	^p lO ^p	d'	100-70	ð
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	t	cation rat treatment <u>ce soil or t</u> <u>crop</u>	-	Dates of treatment or no. of treatments and last date	Portion analysed	Growth stage at sampling	Ner P.	al prof	Residues (n	rent for the second sec	Lighir Lighir	50 50 50 50 50 50 50	PHI (days)
	(a)	(b)	kg a.s./ha	Water (L/ha)	g a.s./hL	the Pr	P B B	j. Moel	AE C656948 ASAE C656948	benzanute sal AE	FLU IÔA BÂAE C656948	FLA- 570H as AE C656049	FLU- methyl- soffoxide as AE C656948	) Total residue calc.	(e)
I-37050 Albaro Europe, South F 2006	Rotational crop: Wheat, winter Guadalupe			ARCA	19 19 1	N ST	Straw O.B C.D. OWD.E.T	89 d 70	Tebto Dr. Para	3000111	CULTRE DIV	CU30748	<0.05	0.20	265
R 2006 0872/1 0872-06 / 02 Italy I-37050 Albaro Europe,	Plot B <u>Target crop:</u> lettuce (target crop) PBI: 240 d <u>Rotational crop:</u>	1) 28.02.2007	05° (		0.1000	93.07.200 5 0 5 6 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	leaves de		0 [°]		<0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.02 <0.02 <0.02 <0.02	338 352 338 352
South F 2006	Carrot N/A Plot B		0.5 0.5		0 1805		· (1)	NOW DE	0.02	<0.01	<0.01	<0.01	<0.01	0.03	296
	Target crop: lettuce (target & crop) PBI: 240 d <u>Rotational</u> crops:	The Los	STUT .	5 9.7 6 7 9.7 6 9.90 7 9.90 7 9.90 7 9.90 7 9.90 7 9.90 7 9.90 7 9.7 7 9	0.1000		head to her	2049	<0.02	<0.01	<0.01	<0.01	<0.01	<0.02	310
	Lettuce Funly Plot BC Rayed crop:	551.10.2006O	0.5	500		03.07.2006	green material	30	0.07	<0.01	<0.01	<0.01	0.01	0.08	242
	Co _{lf} e	ALL ALL		OE		1		1		'	1				67

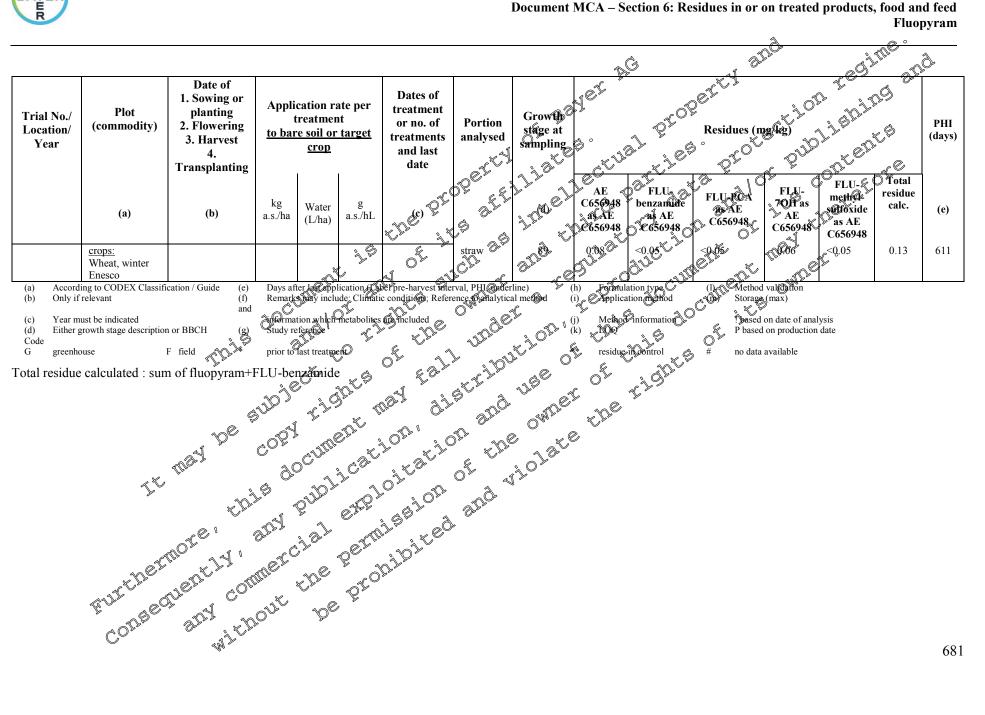


Page 680 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

									Ģ	- I	⁷ O ^s	J.	TUC .	ð
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application r treatme <u>to bare soil or</u> <u>crop</u>	nt	Dates of treatment or no. of treatments and last date	Portion analysed	Growth stage at sampling	N ^{CT}	al prof	Residues (n		Lishir Lishir		PHI (days)
	(a)	(b)	kg Water a.s./ha (L/ha)	g a.s./hL	the Pr	DP OFF	i 1000	AE C656948 ASAE C656948	FLU benzantute at AE 656948	FLU-ROA 8 AE C656948	FLU- 70H as AE C656948	methyl- softoxide	) Total residue calc.	(e)
	lettuce (target crop) <b>PBI: 120 d</b> Wheat, winter Serio		d.oc. anen		N OF GI	grain d. ^g Graw	8- C.	L ^{CE}	~0.64.5 m 30.05 30.05		<0.05 0 0 0 0 0 0 0 0 0 0	0,02 <0.05	<0.02 0.10	352 352
R 2006 0874/8 0874-06 / 03 Italy I-37050 Albaro Europe, South	Plot C Target crop: lettuce PBI: 289 d Rotational crop: Carrot N/A	1) 09.08 200 1			24.10.2006 Ear	leaves	2 47 2 49 1 647 49 0 1 647 49 0 1 647 49 0 1 647 49	0.01 0.01 0.02 0.01 0.01		<pre></pre>	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	0.02 0.02 0.03 0.02	363 377 363 377
F 2006	PBI: 290 d	Mee 1	0.50 0.500	0.1000 C		head to like	4502	0.03 0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0.04 0.02	318 332
	Plot C Target crop: lettuce PBI: 368 of Retational	1022.10.2007 1121 1121 1121 1121 1121 1121 1121	0.50 CJ500	-2100 2000	24.182006	green material grain	29 89	0.06 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0.01 <0.01	0.07 <0.02	478 611
	COIDE	Oiles the												68



Page 681 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram





Data Point:	KCA 6.6.2/04
Report Author:	
Report Year:	2008
Report Title:	Determination of the residues of AE C656948 in/on the feed rotational gops
_	carrot, lettuce and winter wheat after spraying of AE C606948 (500 SC) in the
	carrot, lettuce and winter wheat after spraying of AE C696948 (500 SC) in the field in Spain
Report No:	RA-2651/06
Document No:	<u>M-296671-02-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/414/EEC of July 25, 1991, Ann & II, pro A, section
study:	6 and Annex III, part A, section 8
	EU-Ref: Council Directive 91/414/EEC of July 5, 1991, Ann 4 II, p. A, section 6 and Annex III, part A, section 8 Residues in or on Treated Products, Food and Feed EC guidance working 6 document 7524/VI/95 reg 2 (1997-07-28) OECD Guideline for testing of Ghemic 45; Residues in grotational crops (limited)
	document 7524/VI/95 res 2 (1997-07-22) OECD Guideline for testing of Ghemis US; Residues in potational crops (limited field studies), No. 50
	OECD Guideline for testing of Ghemic Is; Residues in potational crops (limited
	field studies), No. 50
Deviations from current	
test guideline:	
Previous evaluation:	yes, evaluated and accepted rev. 1 to Vol of D&R B7 August 20/2 (reference velied a)
	rev. 1 to Vol of D&R B7 August 29/2 (references velied @) C O
GLP/Officially recognised	yes, evaluated and accepted rev. 1 to Vol of Dor B7 August 20/2 (ret Gences telied of) Yes, condiced under GLP officially reconsed osting scilities
testing facilities:	
Acceptability/Reliability:	Yes y a a a a a a a a a a a a a a a a a a
\$	
Ĩ.	Y S Y S' Y S' V S

V Naterials and Methods

The purpose of the study was to determine the magnitude of the relevant residues of fluopyram (AE C656948) and its metabolites fluopyram-benzanide (AF F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA AE C657188) and fluopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344022) in carrot, letture and winter wheat as rotational crops in southern Europe (Spain) following one spray application of fluopyram SC 00 on soil or on target crop lettuce. Residues of the active substance fluopyram and its metabolites were determined in the succeeding crops only. The target crop lettuce was not analysed.

crop lettuce was pot analysed. The test item was applied to the treated plots in a different manner, but the application rate of 1.0 L of test item/ha (0.5 kg a.s./ha) was the same of 2.0 L of

For the plot A (trials R 2006 0855/6, R 2006 6876/4 and R 2006 0877/2) – the test item was applied to the bare soil followed by incorporation (maximum 8 cm depth) to avoid photodegradation. The investigated plant back interval was 30 days for all crops (carrot, lettuce and winter wheat) and corresponds to the standard plant back interval in case of crop failure.

For the plot B (trial R 2006 0878/0) The test item was applied on lettuce as the target crop two weeks after planting Plot B tepresents a plant back interval of 120-240 days.

For the plot C (triat R 2006 0879/9): - the test item was applied on lettuce as the target crop two weeks after planting. Plot C represents a plant back interval of 290-365 days.

Plots Brand Covere subdivided into 3 subplots for the 3 crops (carrot, lettuce, cereals) to be planted as rotational crops. Explanation of the study plot designs is illustrated in the



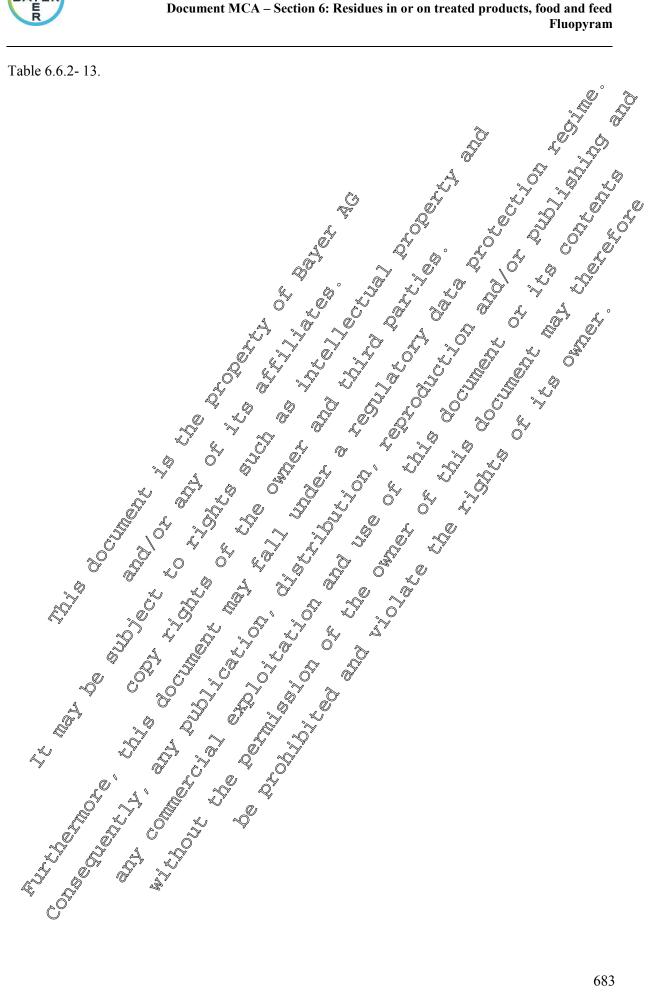




Table 6.6.2-13:	Plot design and plant back intervals
-----------------	--------------------------------------

	Requested PBI	actual	Plant Back Interva	Remarks	
Trial No.	(days) / Application on	Root crop DAT (days)	Leafy crop DAT (days)	Cereals DAT (days)	
R 2006 0875/6 R 2006 0876/4 R 2006 0877/2	Plot A: 30 / soil	carrot 36 (R 2006 0864/0)	lettuce 30 (R 2006 0865/9)	winter wheat 49 (R 2006 0866/A)	Application on bare soil; planting/sowing of rotational crop after 30% ays
R 2006 0878/0	Plot B: 90-240 / lettuce	carrot 154	lettuce	winter wheat	Application on lettuce two weeks after planting; harvest broughing of lettuce; planting sowing of rotational cross
R 2006 0879/9	Plot C: 290- 365 / lettuce	carrot 344		Springwheat	Application on lettuce two weeks after planting; harvestoloughing of lettuce; cultivation break; planting/sowing of rotational crops

#### DAT= days after treatment

Harvest of target crop lettuce (Plot B, R

On plots B, the target crop lettuce was harvested at normal harvest, \$6 days after planting. On Plot C the target crop lettuce was harvested at normal harvest, of days after planting

No lettuce samples were taken for analysis

The harvest leftovers were destroyed by grinding and ploughed in (in order to capture all possible residues and not remove them from the plot prior to planting the cotational crops

m

## Planting rotational crops

Untreated plots were prepared before treated plots.

At the 30-day Plot A, the 90-240-day (Not B) and the 290-365-dag (Plot C) plant back intervals the plots were prepared for crop planting following normal agronomic practices for each crop type in the regions.

For the longer-term Plots B, 100-240 days and C, 290-365 days a bare soil status had to be maintained after harvest of lettiee, i.e. no cover crop is sover.

Samples were taken, prepared in the field where necessary transported and stored.

The first sampling of carrots and setuce was taken at early harvest (14 days prior to normal harvest) followed by sampling at normal harvest maturity for each crop type.

For wheather material was sample that growth stage 30 BBCH and at normal harvest maturity (BBCH 89) (grain and straw) All sampling equipment was cleaned prior to entering any plot that was to be harvested.

The field samples from all trials were store deep-frozen within 24 hours after sampling. All field samples were shipped by dego-free lorry and arrived in good condition. The field sub samples were stored in a freezer  $t \leq -1$  C until preparation of the examination samples. For the preparation of examination samples, the deep frozen field sub samples were shredded with dry ice in a cutter. Representative parts of the shredded samples were transferred into polystyrene boxes separately for analysis/(UP samples) and atchiving (UR samples) and stored at  $\leq$ -18 °C until analysis.

Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 ( 283301-01-1, see MCA section 4.1.2). Full details and acceptable validation data to support this method



are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.  $Q_{p}^{\circ}$ 

Residues of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitrile:water (80:20; v.o). After centrifugation the extract volume was adjusted. Then, the extracts were diluted for times by adding the internal standards:

- One dilution was performed under acidic conditions: this extractationed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed determination of FLU, FLU-benzamide and FLU-7-OH.

An aliquot of the extracts was injected into LC-MSTMS operated in Electrospray Ionization mode:

- One injection in positive electrospray ionization for the determination of FDU, FLU-benzamide and FLU-7-OH.
- Another injection in negative electrosprationization for the determination of FLUPCA and FLU-methyl-sulfoxide under different conditions.

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standardization using isotopically stable labelled internal standards.

The Limit of Quantification (LOQ) expressed as fluopyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat straw and 0.01 mg/kg for all other matrices

Full details and acceptable valuation data to Support this method are presented within document M-CA 4, which comply with the EU regulatory requirements of lined within SANCO/3029/99 rev 4.

indinăs

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and treated samples from the study in each set of analyses. The data demonstrate acceptable method performance during sample analysis. All the recovery results and details are given in the Table 6.6.2–14.

 Table 6.6.2-14:
 Recovery data for fluopyram (AF C656948) and its metabolites in rotational crop matrices (carrot leaf normal, carrot root, lettuce head, winter wheat green material, whiter wheat straw, winter wheat grain)

Crop/Sample	FL (h0g/kg)~	Single values (%)	Mean value (%)	RSD*(%)
Fluopyram (AE G65	694 <b>8)</b> کُ			
	\ 0.0 <b>€</b> [×]	Q Q 109	109	
Lang Que t	> <u>0</u>	100; 91 🖉	96	
carrot leaf pormal	<u>∂</u> 9.15 ≪	~Q 100	100	
	0 à	Overall recovery (n=4)	100	7.3
	0:00	83	83	
Carrot pot	<u>∘0</u> 10	96; 97	97	
Searrot poot	Å	Overall recovery (n=3)	92	8.5
()	0.01	86; 98	92	
lettuce head	0.10	102; 98	100	
		Overall recovery (n=4)	96	7.2
winter wheat green	0.01	92	92	



<b>C</b>	TJT			]
Crop/Sample	FL	Single values (%)	Mean value (%)	RSD*(%)
material material	(mg/kg) 0.15	95	95	
material	0.13	85	85	&
	0.5	Overall recovery (n=3)	<u>91</u>	5.7
	0.05	91; 81	86	3.0
winter wheat straw	0.5	108	108	
whiter wheat straw	0.5	Overall recovery (n=3)	93	. 0 14 6
	0.01	93; 78 (%	86	
winter wheat grain	0.10	84	84	
Willeer Wileat Bruill	0.10	Overall recovery (n=3)	"O [°] 85 ×	
Fluopyram-benzami	de (AEF14881			
	0.01	109	169 Q.	
carrot leaf, normal	0.10	95; 104		
,	0.15	×98 Ø	98 %	P ~ ~ ~
		Overall recovery (n=4)	N 102 N	£ 6.2 °
	0.01	A 890 0	Q 489 40	
carrot root	0.10	86;91	× × × × × × × × ×	() . <del></del> . ()
		Qeerall recovery (n=3)	89	2.8
	0.01	6 <b>(</b> 92; 98 , 5	~ 26 Q	<u> </u>
lettuce head	0.10	§ 0°99; 109	2 304 8	5° 4-
		Værall recovery () ()		⊘ ≫7.1
winter wheat green	0.01	108;90	Q 99 3	×
winter wheat green material	0.10	2 93 93 V		O
material		✓ Overall recovery (n [@] 3)	97 ×	Ôg 9.9
	°~0.05	§ 967103 K		y
winter wheat straw	0.5	6 6 87 ° 0	<u>k</u> 87 . 6	
	Ç Ø	<ul> <li>✓Overall recovery (n=3)</li> </ul>	0° 395 2	8.4
	0,01	<u>× ~~ 85; 403 ~ (</u>	94	
winter wheat grain	O.10 ~~~~		ý 100-	
<u> </u>	°, , , , , , , , , , , , , , , , , , ,	Øverall recovery (n=3)	<u> </u>	10.0
Fluopyram-methyls		44122)	<u>o</u> , Q	
, Ô	0.01	A 2004 0	[™] 104	
carrot leaf, normal	<u>0.10</u>	86; 89	~~ 88	
,	0,10	1040 [°] ⁽¹ )	<u> </u>	
		Overall recovery (n=4)	<b>96</b>	10.0
carrot root		× 096 0 ~	96	
carrot root 🤏	0.10	87; 82	85	
~~~~		Overal recovery (n=3)	88	8.0
1 (1 . 1			78	
lettucehead	0.10	1 f0; 102	106	
		Overaltrecovery (n=4)	92	18.7
	0.01		109	
winter wheat green			107	
material	0.5 0		99	
		Overal recovery (n=3)	105	5.0
winter 1	00.5 ×	113; 119 101	116	
winter wheat straw		V	101	
		Overall recovery (n=3)	111	8.3
witter wheat grain	0,07 \$0,1	99; 106	103	
winner wheat grain	2 ° 0.1	97	97	
	-	Overall recovery (n=3)	101	4.7
Fluopx@m-pyridyl-			00	
	0.01	89	89	
carrot leaf, normal	0.10 0.15	<u> </u>	83 98	



Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD*(%)
		Overall recovery (n=4)	88	9.8
	0.01	89	89	🏹 🗸
carrot root	0.10	96; 83	90 🔗	07 &
		Overall recovery (n=3)	89	7.3
	0.01	99; 93	96	Q X
lettuce head	0.10	96; 91	94	, 0 [°] 0 [°] x
		Overall recovery (n=0)	25	J 3.7% S
	0.01	74	4	
winter wheat green	0.15	92 &	_0 [×] 92 ×	1 2 5 U
material	0.5	84 4U [*]	× 84 °	
		Overall recovery (n=3)		10.8
	0.05	101,97	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
winter wheat straw	0.5	×90 0	× 90 ×	P - V
		Overall recovery (n=3)	0 890 O	L 13 A
	0.01	A.96; 1 @ ~	Q 104 ~	O Q A
winter wheat grain	0.1	84	84.0 3	() <u></u> (Q
		Querall recovery (n=3)	.0 97.	13.9
Fluopyram-7-hydrox	v (BCS-AA10			
<u></u>	0.01	937	N N3 N	
	0.10	6 10 2 91 Or 6	096.0	Ŭ
carrot leaf, normal	0.15		0 ⁵ 100 ⁵ %	<u> </u>
		Overal recovery (n=4)	<u> </u>	[♥] 5.2
	0.01		× ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u>م</u>
carrot root	×0.10	\$ 9 \$, 83 4	89.9	Р
currot root		Qveralbrecovery (n=30	<u> </u>	8.8
	× 0.00	78: 95 x x	0 87 x 7	
lettuce head		× ~~ 103,91 ~~ (97	
lettuce head		Overall recovery (n=4)	<u> </u>	11.4
Ö	0.01			11.7
winter wheat green		0 K 96 0	2 0,96	
material	0.50 Ø	- · · · · · · · · · · · · · · · · · · ·	[∞] 93	
matchai	0.30 Q	Øverall recovery (n=3)	<u>94</u>	1.8
	0,00		<u> </u>	
winter wheat street		<u>~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~</u>	× 80 × 83	
winter wheat straw			<u>83</u> 85	
		Overall recovery (n=3)		2.4
	0.01	89;83	86	
winter wheat grain			81	
I : fortification loval PSD	1 🖉 🗳	Overall recovery ()=3)	84	4.9

FL: fortification level, RSD - Relative Standard Deviation * some RSD over and calculate as there were only two individual recoveries given ** Recovery corrected with the control interference (0.002/ mg/kg) recovery not corrected = 132% Final determination as: fluopy an Residues calculated as fluopy ram Final determination as: FLU-benzariote Residues calculated as fluopy ram Final determination as: FLU-benzariote Residues calculated as: fluopy ram Final determination as: FLU-PCA Residues calculated as: fluopy ram Final determination for FLU-PCA Residues calculated as: fluopy ram Final determination for FLU-PCA Residues calculated as: fluopy ram Final determination for FLU-PCA Residues calculated as: fluopy ram Final determination for FLU-PCA Residues calculated as: fluopy ram Final determination for FLU-PCA Residues calculated as: fluopy ram Final determination for FLU-PCA Residues calculated as: fluopy ram

No residue of flugpyrant or related metabolites were found above the LOQs in any of the control samples of rotational coop matrices analysed, except for the trial R 2006 0879/9 in which the residue of AEC657188 in carrot root was at 0.02 mg/kg.

The residue levels of Fluopyram and its relevant metabolites in the rotational crop matrices of carrot, lettuce and wheat are summarized in the Table 6.6.2-15.



The storage period of deep-frozen samples was up to 290 days for lettuce, 139 days for carrot leaves, 145 days for carrot root, 334 days for wheat green material, 71 days for wheat grain and 80 days for wheat straw.

Residues in Carrot

In trial R 2006 0875/6 (plot A, PBI 30 days), residues of fluopyram (AE C656948) were 0.01 mg/kg and 0.01 mg/kg in carrot leaf 206 and 220 days after treatment (DAT), respectively. In carrot root samples the residues of fluopyram were 0.02 mg/kg at DAO 206 and 220

The residues of FLU-benzamide, FLU-methylsulfoxide, FLU-PCA FLU-7OH in Call carbot matrices were <0.01 mg/kg.

In trial R 2006 0878/4 (plot B, PBI 120-240 days) residues of fluopyram (AE C656948) were 0.01 mg/kg and 0.02 mg/kg in carrot leaf (DAT 271 and 285), and in carrot root residues of fluopyram were 0.02 mg/kg and 0.03 mg/kg (DAT of 271 and 285), respectively. The residues of FLU-benzamide, FLUmethylsulfoxide, FLU-PCA, FLU-70H in all carrot matrices were 0.01 mg/kg.

In <u>trial R 2006 0879/9</u> (plot C, PBI 290, 565 days) residues of fluopyram (AE C656948) were 01 mg/kg in all carrot matrices DAT of 532 and 56. The residues of FLU-benzamide, FLU-methybulfoxide, FLU-PCA, FLU-7OH in all carrot matrices were 0.01 mg/kg

Residues in Lettuce

In trial <u>R 2006 0876/4</u> (plot Å, PBF30 days), residues of Duopyram (ÅE C656948) were <0.01 mg/kg in lettuce head 136 and 150 days after treatment (DAT). The residues of FLU-benzamide, FLU-methylsulforide, FDU-PCA, FLU-70Hb in all lettuce matrices were <0.01 mg/kg.

In trial <u>R 2006 0878/0</u> (plot B PBI 20 – 240 days) residues of fluopyram (AE C656948) were <0.01 mg/kg in retuce head samples at DAT 225 and 239. The residues of FLU-benzamide, FLU-methylsulfoxide, FLU-PCA FLU-70H in all lettree matrices were <0.01 mg/kg.

In trial <u>R 2006 0879/9</u> (plot CAPBI 290 – 365 days) residues of fluopyram (AE C656948) were <0.01 mg/kg in lettuce head complex at DAT 449 and 463. The residues of FLU-benzamide, FLU-methylsuffoxide, FLU-PCA, PLU-7OH in all letture matrices were <0.01 mg/kg.

Residues in Wheat

In trial <u>R 2006/0877/2</u> (plot A, PBP30 days), residues of fluopyram (AE C656948) were 0.11 mg/kg (in green material), 0.05 mg/kg (in wheat spaw), and <0.11 mg/kg in wheat grain 126, 219, and 219 days after treament (DAT), aspectively.

The restrives of FLU benzamide were 0.01 mg/kg (in green material), 0.14 mg/kg (in wheat straw), and <0.01 mg/kg in wheat grain at DAT 126 219, and 219, respectively.

The residues of FLU-methylsul (0xide were 0 02 mg/kg (in green material), 0.06 mg/kg (in wheat straw), and 0.01 mg/kg (in wheat grain at DAY 126 219, and 219, respectively

The residues of FLU-DCA and FLU-70H in all three wheat matrices were below relevant LOQ.

In trial <u>R 2006, 0878/0</u> (plot B, PBI 120-240 days), residues of fluopyram (AE C656948) were 0.05 mg/kg (in green material), 0.19 mg/kg (in wheat straw), and <0.01 mg/kg in wheat grain at DAT (days after treatment), 211, 266, and 266, respectively.

The residues of FLU-benzamide and FLU-PCA were below relevant LOQ in all wheat matrices.

The residues of FLU-methylsulfoxide were 0.02 mg/kg in green material at DAT 211, <0.05 mg/kg in wheat straw at DAT 266, and 0.04 mg/kg wheat grain at DAT 266.

The residues of FLU-7OH in wheat green material (at DAT 211) and wheat grain (at DAT 266) were <0.01 mg/kg and 0.05 mg/kg in wheat straw (at DAT 266).



In trial R 2006 0879/9 (plot C, PBI 290-365 days), residues of fluopyram (AE C656948) were 0.02 mg/kg (in green material), <0.05 mg/kg in wheat straw and <0.01 mg/kg (in wheat grain) at DAT The residues of FLU-methylsulfoxide were 0.06 mg/kg (in green material), <0.05 mg/kg in wheat straw and 0.03 mg/kg (in wheat grain) at DAT (days after treatment). 427, 592 - 1568 The residues of FLU-benzamide were <0.01 mg/kg (in green material and grain) and 0.05 mg/kg in wheat straw.

The residues of FLU-PCA and FLU-7OH in all three wheat matrices were below relevant

Conclusion

Following one spray application conducted with fluopyram SC500 to bars soil of Actuade as a target crop at a rate of 0.5 kg a.s./ha, residues in succeeding goops were analysed for fluopyram AE C696948 and its metabolites fluopyram-benzamide (AE F148815), fbuopyram-pyridyl carbbxylicacid (FLU-PCA, AE C657188) and fluopyram-7-hydroxy (BCS-AA10069) and fluopyram-relative side (AE 1344122) using a validated selective HPLC-MS/MS analytical method. These data show that residues in carrot, leftuce and when as succeeding cropare adequately covered by the current EU MRL. C657188) and fluopyram-7-hydroxy (BCS-AQ 10069) and fluopyram-methyl softoxide (AE 1344122) n and a second Ş using a validated selective HPLC-MS/MS analytical method.



Page 690 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Гаble 6.6.2-	15: Result	s of rotational	crop trials conduct	ed with fluo	pyram	B	at ^{er p}	Č "C ^O	pertil		regi	ING OID	ð,
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application rate per treatment <u>to bare soil or target</u> <u>crop</u>	Dates of treatment or no. of treatments and last date	Portion Apalysed	Growth stage at sampling		201 21 000 201 7 1000	Besidues (R	ec pjykg) it ^c	perer	ý ⁹	PHI (days)
	(a)	(b)	kg a.s./ha Water g (L/ha) a.s./hL	Che j		O.L.	AE C656948 AF C656948 C656948	benzamide	FLQ-PCA (as AE C656948	FLU- TOH as AE C656908	methyl-	Total residue calc.	(e)
R 2006 0875/6 0875-06 / 01 Spain E-41310	Plot A Application to bare soil PBI: 36* d	1) 14.11.206 3) 15.04.2007 – 15.06.2007	0.50 JIDO 0.1669	09.10.2006	UILOLE	49 5 49	\$0.01 \$0.01 \$0.02	<000 \$<0.01 0.25	€0.01 5 5 5 5 5 5 5 5 5 5 5 5 5	<0.01 <0.01	<0.01 <0.01	<0.02 <0.02	206 220
Brenes Sevilla Europe, South F 2006	<u>Rotational</u> <u>crop :</u> carrot, Navarino F1	L'II.	upi crishts	aay di		10 45 49 C	0.02	~0.01 ~1901 ~2 ¹ 901	<0.01	<0.01 <0.01	<0.01 <0.01	0.03 0.03	206 220
R 2006 0876/4 0876-06 / 01 Spain E-41310 Brenes,	Plot A <u>Application to</u> <u>bare soil</u> PBI: 30 d <u>Rotational</u>	1) 15.11.2006 3) 30, µ1.2006 – 15, 93, 2007	0.500 300 2147667		Shead Thead	e 45 49 0 t 1 0 0 t	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.02 <0.02	136 150
Sevilla Europe, South F, 2006	<u>crop</u> lettuce, Carolus	ere '	ant pur exp		9.DO								
R 2006 0877/2 0877-06 / 01 Spain	Plot A <u>Application</u> <u>bare soit</u> PBL 49* d	(V) 18.12.2006 2) 12.04.2007 – 20.04.2007 (V) 15.06.2007 15.07.2007	0.46C 276 @1667	30,50.2006	green material grain	30 89	0.11 <0.01	0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0.02 0.01	0.12 <0.02	126 220
	Corre	O.G.J. J. J.		1	J	I	I	I	I	I	I	I I	69

690

BAYER

Page 691 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

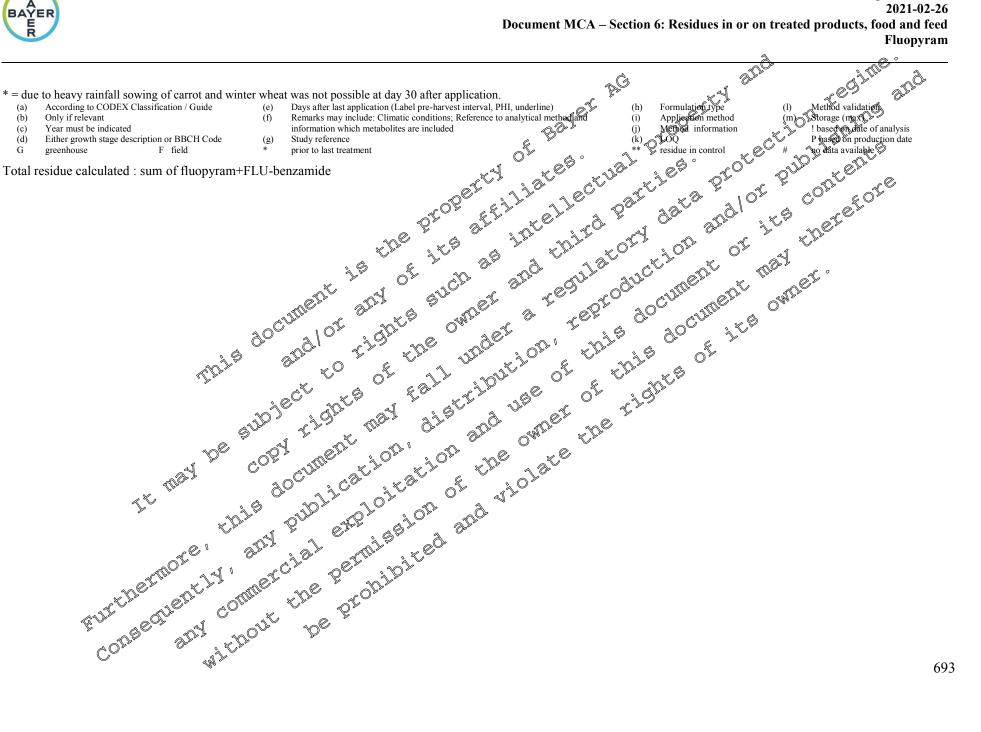
											<u>ð</u> .			
					1	1		-	Ĝ	Ő			The C	ð
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application treatm <u>to bare soil o</u> <u>crop</u>	ent or target	Dates of treatment or no. of treatments and last date	Portion analysed	Growth stage at sompling		et et	$\frac{e^{t}}{e^{t}}$ Residues (n	,	Lishir	L L D D D D D D D D D D D	PHI (days)
	(a)	(b)	kg Water a.s./ha (L/ha)		(c) 2 ^T			AE C656948 as AD C656948	benzamide as AE C636948	FLU-PGA 33 39 C656948 0.05	FLU- 7016as XE C656948	FLU- methyl- sulfoxide as AE C656948	O [≫] Total residue calc.	(e)
E-41310 Brenes Sevilla Europe, South F 2006	<u>Rotational</u> <u>crop:</u> Winter wheat, Don Pedro		2.0CJURE	07 3. N 3.		straw 2,9 2,010 0,100 0,100 0,100 2,00 2,00	89 3.D.D. T.C.	Tebt	8 90 900,112		TI	0.06	0.19	220
R 2006 0878/0 0878-06 / 02 Spain E-41310 Brenes, Sevilla Europe, South F	Plot B <u>Target crop:</u> <u>lettuce, Stilo</u> PBI: 154 d <u>Rotational</u> <u>crop:carrot,</u> <u>Navarino F1</u>	1) 07.03.2007	0.47 Digo		04.10,2000	leaven voot	J.G. M.D.C.	0.01 5 0.02 0.03 0.03 5 5 5 5 5 5 5 5 5 5 5 5 5	~0.0 0.01 ~0.01 7 2 9 7	<0.61 <001 >001 >0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	0.02 0.03 0.03 0.04	271 285 271 285
г 2006	Plot B <u>Target crop:</u> lettuce, Silo PBI: 155 d <u>Rotational</u> <u>crops</u> : lettuce, Carolus	COT LI	0.972 3.074 2.074	ere	≥04 10 2006 »	head the	1.7044	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.02 <0.02	225 239
	Plot B Target-brop: letting, Silo	1) 07 05 2007	NOFT EFFE	0.125 ©	04.10.2006	green material grain	30 89	0.05 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0.02 0.04	0.06 <0.02	211 266
	Corre	an itr	j0 ž	I										69

BAYER

Page 692 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

									4	Ő	<u>n</u> ð.	\$	The °	
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application treatm <u>to bare soil</u> <u>cro</u>	ent or target	Dates of treatment or no. of treatments and last date	Portion analysed	Growth stage at sompling	SI ^{CT}	G P ^{I PIO}	Residues (n	1g/kg)	OFLU- methal suttoxide	PP -	PHI (days)
	(a)	(b)	kg Wate a.s./ha (L/ha	r g a.s./hL	(c) D ^T			AE C656948 as AE C656948	offLU- benzamide as AE C656948	* FLU-PGA * FLU-PGA * G656948 * 0.05 * 0.05	FLU- 7016as XĚ C656948	FLU- methad- sulfaxide as AE C656948	Total residue calc.	(e)
	PBI: 154 d <u>Rotational</u> <u>crop</u> : winter wheat, Cajeme		CULLE		NT 5	straw D.C. D.C.D. O.W.D.C.C.	10.0 0.0	0.19 2 9 V	dire di	all'and all all all all all all all all all al	OWLE	<0.05	0.24	266
R 2006 0879/9 0879-06 / 03 Spain E_41310 Brenes (Sevilla) Europe,	Plot C <u>Target crop:</u> <u>lettuce, Filipo</u> PBI: 344 d <u>Rotational</u> <u>crop:</u> carrot, Navarino F1	1) 09.10.2007		NO CONTROL	9.10.2006 50 6 5 6 5 5 6 5 5 6 5 6 5 6 5 6 5 6	root				<0.01 <0.01 <0.01/0.02**	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	0.02 0.02 0.02 0.02	532 546 532 546
South F 2006	Plot C <u>Target crop:</u> <u>lettuce, Filipo</u> PBI:337 d <u>Rotational</u> <u>crop:</u> lettuce, Filipus	Those and	0.50 400 COP COP COP CO CO CO CO CO CO CO CO CO CO CO CO CO			a O>		~0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.02 <0.02	449 463
	Plot C <u>Target crop:</u> <u>lettuce, Flipo</u> PBI: 357 d <u>Rotational</u>	n ⁰ .11	3.0.7			groun material grain	30 89	0.02 <0.01	<0.01	<0.01 <0.01	<0.01 <0.01	0.06	0.03	437 582
	Rotational crops: wintee wheat took Pedrol	plent con	ULLET EDE			straw	89	<0.05	0.05	<0.05	<0.05	<0.05	0.10	582
	College	Orgen A. T. T.	J											69

Page 693 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed



BAYER



LIARA POINT.	KCA 6.6.2/05
Data Point: Report Author:	
Report Year:	2008
Report Title:	
Report Thie.	AE C656948 500 SC - Magnitude of the residue in alfalfa (rotational crop tolerance)
Report No:	RAGMP105
Document No:	M-306501-01-1
Guideline(s) followed in	FPA Ref : OPPTS 860 1500 Crop Field Trials
study:	EPA Ref.: OPPTS 860.1500, Crop Field Trial S PMRA Ref.: DACO 7.4.4, Field Crop Rotational Trial Study
Deviations from current	
test guideline:	
Previous evaluation:	
GLP/Officially recognised	Yes, conducted under GLEOfficially recognised tosting facilities
testing facilities:	
Acceptability/Reliability:	
This US study was part of	f the baseline dossier but is not summarized here as EU data are required for
his renewal dossier	
٥,	
4	
Data Point:	KGX 6.6.2016 X X X X
Report Author:	
Report Year:	
	AE C656948 500 SY - Maduitude of the residue in Cotton (rotational crop to@ranceO
Report Title:	
Report No:	RAGM& 004
Report No:	RAGN& 004 A A A A A A A A A A A A A A A A A A
Report No: "O" Document Vo: X	RAGN& 004 A A A A A A A A A A A A A A A A A A
Report No:	RAGNO 004 M-307306-047 ORO S 8669 500, Grop Ford Tried O LOCO 3/4 4. Field Crop Rotational Tried Study
Report No: Document No: Guidelia (s) followed in	RAGNO 004 M-307306-047 ORO S 8669 500, Grop Ford Tried O LOCO 3/4 4. Field Crop Rotational Tried Study
Report No: Document No: Guidelings) followed in study: Deviations from current test guideline:	RAGNO 004 M-307306-04 ORO S 8669 500, Grop Ford Trieds DRO S 4 4 Field Crop Rotational Tried Study
Report No: Document No: Guidelings) followed in study: Deviations from current test guideline:	RAGN& 004 A A A A A A A A A A A A A A A A A A
Report No: Document So: Guidelice (s) followed in study: Deviations from current test guideline: Previous evaluation:	RAGNO 004 M-307806-0451 OPE S 86651500, Grop Ford Trials DXCO 724.4, Field Crop Kotational Trial Study
Report No: Document No: Guideling S) followed in study: Deviations from current test guideline: Previous evaluation:	MAGMØ 004 M-30(*306-04) OPOTS 86651500 Grop Förd Trial DXCO 74.4, Fight Crop Rotational Trial
Report No: Document No: Guideling S) followed in study: Deviations from current test guideline: Previous evaluation:	MAGMØ 004 M-30(*306-04) OPOTS 86651500 Grop Förd Trial DXCO 74.4, Fight Crop Rotational Trial
Report No: Document No: Guideling S) followed in study: Deviations from current test guideline: Previous evaluation:	MAGMØ 004 M-30(*306-04) OPOTS 86651500 Grop Förd Trial DXCO 74.4, Fight Crop Rotational Trial
Report No: Document No: Guideling S) followed in study: Deviations from current test guideline: Previous evaluation:	MAGMØ 004 M-30(*306-04) OPOTS 86651500 Grop Förd Trial DXCO 74.4, Fight Crop Rotational Trial
Report No: Document No: Guideling S) followed in study: Deviations from current test guideline: Previous evaluation:	MAGMØ 004 M-30(*306-04) OPOTS 86651500 Grop Förd Trial DXCO 74.4, Fight Crop Rotational Trial
Report No: Document No: Guideling S) followed in study: Deviations from current test guideline: Previous evaluation:	MAGMØ 004 M-30(*306-04) OPOTS 86651500 Grop Förd Trial DXCO 74.4, Fight Crop Rotational Trial
Report No: Document No: Guideling S) followed in study: Deviations from current test guideline: Previous evaluation:	MAGMØ 004 M-30(*306-04) OPOTS 86651500 Grop Förd Trial DXCO 74.4, Fight Crop Rotational Trial
Report No: Document No: Guideling S) followed in study: Deviations from current test guideline: Previous evaluation:	MAGMØ 004 M-30(*306-04) OPOTS 86651500 Grop Förd Trial DXCO 74.4, Fight Crop Rotational Trial
Report No: Document No: Guideling S) followed in study: Deviations from current test guideline: Previous evaluation:	MAGMØ 004 M-30/206-0451 OPSTS 86651500 Grop Förd Trial DXCO 74.4, Fight Crop Rotational Trial Study
Report No: Document No: Guideling S) followed in study: Deviations from current test guideline: Previous evaluation:	MAGMØ 004 M-30/206-0451 OPSTS 86651500 Grop Förd Trial DXCO 74.4, Fight Crop Rotational Trial Study
Report No: Document No: Guideling S) followed in study: Deviations from current test guideline: Previous evaluation:	MAGMØ 004 M-30/206-0451 OPSTS 86651500 Grop Förd Trial DXCO 74.4, Fight Crop Rotational Trial Study
Report No: Document No: Guideling S) followed in study: Deviations from current test guideline: Previous evaluation:	MAGMØ 004 M-30/206-0451 OPSTS 86651500 Grop Förd Trial DXCO 74.4, Fight Crop Rotational Trial Study
Report No: Document No: Guideling S) followed in study: Deviations from current test guideline: Previous evaluation:	RAGNO 004 M-307806-0451 OPE S 86651500, Grop Ford Trials DXCO 724.4, Field Crop Kotational Trial Study



Data Point:	KCA 6.6.2/07
Report Author:	
Report Year:	2008
Report Title:	AE C656948 500 SC - Magnitude of the residue in field rotational crops (240 day
*	plant back interval)
Report No:	RAGMP061
Document No:	<u>M-306586-01-1</u>
Guideline(s) followed in	EPA Ref.: OPPTS 860.1900, Field Accumulation or Protational Crops
study:	PMRA Ref.: DACO 7.4.4, Field Cop Rotational Trial Study
Deviations from current	
test guideline:	
Previous evaluation:	
GLP/Officially recognised	Yes, conducted under GP/Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	
This US study was part of	in the based me dossiler but is not summarized note as to data are required for
this reliewal dossiel	
. 1	
Į,	
S, o	
The second se	
<i>6</i> ¹	
ky	
\sim	
¥	
A Co	
	KCA 6.6.2/07 2008 AE CoS6948 500 SC - Magnitude of the residue in field rotational crops (2004a) plant back interval) RAGMP061 M-306586-01-1 EPA Ref.: DPTS 860.1900, Field Accumulation of Potational Costs PMRA Ref.: DACO 7.4.4, Field (Cop Rotational Heal Study Yes, conducted under OP/Officially recents desting fieldiths Yes, conducted under of the residue desting field field field field field fieldiths Yes, conducted under of the residue desting field field field field field field fieldiths Yes, conducted under of the residue desting field



Data Point:	KCA 6.6.2/08
Report Author:	
Report Year:	2009
Report Title:	Determination of the residues of AE C656948 in/on potato after spraying
	fluopyram SC 500 in the field in France (North) and Germany
Report No:	08-2160
Document No:	<u>M-350816-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/4140 EC of July 15/1991,
study:	Annex II, part A, section 6 and Ashex III, part A section 8
	Annex II, part A, section 6 and Ashex III, part A section 8 Residues in or on Treated Products, Food and Deed EC guidance working
	document 7029/VI/95 rev. 5(9997-07-22)
Deviations from current	none
test guideline:	
Previous evaluation:	No, not previously submitted a star with a
	Study was not found DAR RAR and the Addened of a second se
GLP/Officially recognised	Yes, conducted under GLDO Officially recognised testing facilitie
testing facilities:	
Acceptability/Reliability:	Yes Of Y O Y Y Y Y

Materials and Methods

The purpose of the study was to determine the magnitude of residues of fluopyram (AE C656948) and its metabolites fluopyram-benzamide (AE #148805), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE C657188),fluopyram-7-hodroxy (BCS-AA10065) and fluopyram-methyl suffoxide (AE 1344122), in/on potato (tuber) harvested after one spraying application with Fluopyram SC 500 on bare soil 30 days before planting of potatoes in northern Europe (Northern France and Germany). The investigated plant back interval was 30 days.

For application the formulation Fluopyram SC 500 was used, a suspension concentrate formulation containing 500 g/L of Fluopyram. The application was done on bare soil followed by incorporation into the soil (< 8 cm) trial 08-2160-01) and 28 days (trial 08-2160-02) before the planting of potatoes.

In both trials the appreciation was done with $1 \oplus L$ of rest item/ha and a water rate of 300 L/ha, corresponding to a spray concentration of the test item of 0.33% (0.17% of active substance in the spray liquid). The application rate was 9.50 kg fluops am /ka.

For residue analysis samples of potato (tuber) were taken from the treated and the control plots. In order to obtain representative samples of the raw commodity, samples were taken at random along the treated and the control plot.

Samples of potato (tuber) were taken from the treated and untreated plot in both trials 14 days before harvest and at harvest

The field samples were stored deep-frozen within 24 hours after sampling and until dispatch. The field samples of trial 08-2160-01 were shipped by deep-freeze lorry, the field samples of trial 08-2160-02 were shipped by car with dry dee and arrived in good condition. The field samples were stored in a freezer at ≤ -48 °C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field samples were shredded with dry ice in a cutter. Representative parts of the shredded field samples were transferred into polystyrene boxes separately for analysis or archiving and stored at ≤ -18 °C.



Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (**1999**, 05/02/2007, <u>M-283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitiele:water (8030; v: 3) After centrifugation the extract volume was adjusted. Then, the extracts were diffuted ten times by adding the internal standards:

- One dilution was performed under acidic conditions: this extract allowed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed the determination of FLU, FLU-benzamide and FLU-7-QP.

An aliquot of the extracts was injected into LO-MS/MS operated in Electrospray Jonization mode:

- One injection in positive electrospray ionization for the determination of FLU, FLUebenzauide and FLU-7-OH.
- Another injection in negative electrospray conization for the determination of FLU-PCA and FLU-methyl-sulfoxide under different conditions

The linearity was demonstrated in each analytical batch with a fix weighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by nternal standardization using isotopically stable labelled internal standards.

The Limit of Quantification (100), expressed as fluopyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat straw and 0.01 mg/kg for all other matrices.

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

	<u>ن</u>	1 Con	×	Å	Ť
<u>Findings</u>	Q 1	Č			
		<i>a</i> .	~~~~	· · · ·	~

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the malyses of control and treated samples from the study in each set of analyses. The means of the concurrent fectoreries were for all fortification levels within the acceptable range of 70 - 110 % except for FLO-methyl-sulfoxide at 114% and 115 % respectively at 0.1 mg/kg and 1 mg/kg. All overall mean recoveries are in the acceptable range of 70 - 110 %; therefore, the results are considered valid. Recovery results are presented in Table 6.6.2-16.

No residue of fluopyram or related metabolites were found above the LOQ in any of the control samples of rotational crop matrices analysed.

The residue levels of fluopyrand and its relevant metabolites in the rotational crop matrices of potato tubers are summarized in the able 6.6.2-19.

The storage period of deep frozen samples ranged between 271 and 316 days.

Residuces in porato tubers

In trial 08-2 60-01 PBI 30 days), residues of fluopyram (AE C656948) were 0.02 mg/kg in potato tuber 14 days before harvest and at harvest.

The residues of the metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methyl-sulfoxide) were < 0.01 mg/kg 14 days before harvest and at harvest.

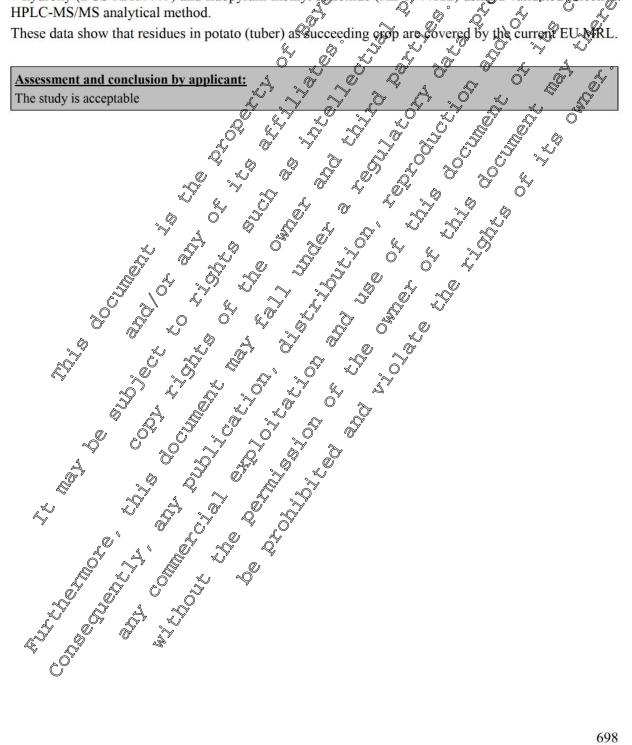


In trial 08-2160-02 (PBI 28 days) residues of fluopyram (AE C656948) were 0.02 mg/kg and 0.01 mg/kg in potato tubers 14 days before harvest and at harvest, respectively.

The residues of the metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methyl-sulfoxide) we < 0.01 mg/kg 14 days before harvest and at harvest.

Conclusions

Following one spray application conducted with fluopyram SC500 to bare soil at a rate of 0.5 kg a.s./ba residues in succeeding crops were analysed for fluopyram AE C656948 and its metabolites Thiopyrambenzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE C657 1288) and fluopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl solfoxide (AE 1044122) using a validated elective





	•	for fluopyram (AE C6569	948) and its metabol	lites in potato,
Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD(%)
Fluopyram (AE C65	6948)		4	ST ST
	0.01	82; 95; 84	87	× 8.0
Potato, tuber	0.10		<u></u>	C AN C'
i otato, tubei	1.0	* *	<u></u>	
		Overall recovery (n=7)		
Fluopyram-benzami	de (AEF14881	5)		
	0.01	89; 78; 84	@ ⁷ _`^%84 @	√ √6 .6 √
Potato, tuber	0.10	90 91; 90 2		<i>™</i> 0.6 <i>™</i>
i otato, tabei	1.0			
		Overall recovery (n=7)	87	<u>\$4</u>
Fluopyram-pyridyl-c	carboxilic-acid	(AE C657188)		
	0.01	Q 72,70; Q ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	× 76 ×	2.2 ⁰
Potato, tuber	0.10	87;97 <u>,</u> 97 4		\$ 6 2
i otato, tabei	1.0			\$ <u>}</u>
		Overall recovery (n= 7)		15.1
Fluopyram-7-hydrox	y (BCS AA10	965) <u>S</u>		0
	. 4	× 5, 89; 92 , 87 ⁰	~~ ⁹⁰ ~~	l 3.4
Potato, tuber	×90.10		<u>97</u>	
Potato, tuber				
tuber FL (mg/kg) Single values (%) Mean value (%) RSD (%) Fluopyram (AE C656948) 0.01 82; 95; 84 87 8.9 Potato, tuber 0.01 97; 96; 96 96 96 96 Potato, tuber 0.01 82; 95; 84 87 8.9 96 Potato, tuber 0.01 97; 96; 96 96 96 96 96 Potato, tuber 0.01 97; 96; 96 96				
riuopyram-metnysa			8787	9.0
Č,			AC 194	
Potato, tuber	\$ <u>1.9</u>	\cap $(0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0$	A LAS	
0' Ø	9	Overall recovery (n= 7)	103	15.2
L: fortification level, RSD -	Relative Standard	Douteman	\sim	
mai determination as. nuop	main residence call	ulated as sudopyram	×	
inal determination as: FLO	benzannide Resident	s calculated as: ftuppyram		
inal determination as: $\mathbb{A}_{\mathbb{P}}$ -	PCA Residue Calc	ulated as: fluored am		
inal determination as: FLU-	7615 Residues calc	utated as: fuopyram		
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~				
4	° ,\$'			
	Q			
	Y A.	, , , , , , , , , , , , , , , , , , ,		
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		Q A		
an [®]	·• ~	O A		
Å.	1`&`	Ş Q		
	' L' .			
	8 N	¥		
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u> </u>			
Let 2 10	N. N.			
× Å				
Ű				

BAYER

Page 700 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No./	17: Results Plot (commodity)	s of rotational of Date of 1. Sowing or planting 2. Flowering	crop trials conducted Application rate per treatment	d with fluopyram Dates of treatment or no. of	Greavith	yer A	2 Prof	ertry	rect ^{il}	DIA TEGA DIA TEGA COINTER COINTER HEIL- methyl- sylfoxide	20 20 20	PHI
Location/ Year	(commonly)	3. Harvest 4. Transplanting	<u>to bare soil or target</u> <u>crop</u>	treatments analyser and last date			101 Jai	Residue	( <b>m)2</b> /kg)	co. eref	0*	(days)
	(a)	(b)	kg a.s./ha (L/ha) a.s/hL			AF C656948 AS AE C656948	C656948	C656948	C656948		Total residue calc.	(e)
08-2160-01 France, north 37230 Fondettes Centre Europe, North F 2008	Application to bare soil PBI: 30 d Rotational crop: Potato Juliette	1) 16.05.2008 2) 07.07.2008 - 23.07.2008 3) 10.09.2008 - 25.09.2008		16.042008 Where Falle Fall Fall Fall Fall Fall	JK 10m 1		2001 2001 201 201 2001 2001 2001 2001 2		0.01 0.01	<0.01 <0.01	0.03 0.03	141 155
08-2160-02 Germany 51399 Burscheid Nordrhein- Westfalen Europe, North F 2008	Application to bare soil PBI: 28 d Rotational crop: Potato Cilena	1) 02.05.2008 2) 15.06.2008 - 30.06.2008 3) 20.08.2008	0001 3000 0.17 COPY COPY CUIREDIT COPY CUIREDIT COPY CUIREDIT COPY		47 er or dr er or dr er or dr er or dr er	0.02 0.04 C	≪0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0.03 0.02	124 138
<ul> <li>(a) Accordin</li> <li>(b) Only if ro</li> <li>(c) Year musical</li> <li>(d) Either group</li> </ul>	st be indicated owth stage description	BBCH Code	Daysafter last applica (i) Daysafter last applica Reparts may include information which me Study reference prior to last freatment LU-benzamide		PHI, underline) to analytical metho	od and	(i) Applic (j) Method (k) LOQ	lation type ation method d information e in control	(l) (m) #	Method valida Storage (max) ! based on dat P based on pro no data availal	e of analysis oduction date	
	C	L'IN .										7



Data Point:	KCA 6.6.2/09
Report Author:	
Report Year:	2009
Report Title:	Determination of the residues of AE C656948 in/on potato after spraying of
	fluopyram SC 500 in the field in Italy and Spain
Report No:	08-2171
Document No:	<u>M-350747-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/41 EEC of July 16, 1991, Annex II, part X, section 6 and Annex III, part A, section 8; Residues in C on Treated Products Food and
study:	6 and Annex III, part A, section 8; Residues in 2 on Treated Products Food and
	Feed; Equivalent to US EPA PTS 860.1500 (Supplementa)
Deviations from current	none A Q o A A
test guideline:	
Previous evaluation:	No, not previously submitted or a gradient of the second sec
	Study was not found in DAR AR and the Addenda
GLP/Officially recognised	Yes, conducted under GLP Officially recognised testing facilities
testing facilities:	Yes, conducted under GLP Officially recognised testing facilities
Acceptability/Reliability:	Yes A A A A

# Materials and Methods

The purpose of the study was to determine the magnitude of residues of fluopytam (AE C656948) and its metabolites fluopytam-ben amide (AE F148815), fluopytam pyridy carbox vic acid (FLU-PCA, AE C657188), fluopytam 7-hydroxy (BCS-AC10065) and fluopytam-methyl sulfoxide (AE 1344122), in/on potato (tuber) has ested after one spraying application with Fluopytam SC 500 on bare soil 30 days before planting of potatoes in southern Europe (Sprain and Italy). The investigated plant back interval was 30 days.

For application the formulation Fluopytam  $30^{\circ}$  500 was used, a suspension concentrate formulation containing 500 g/L of fluopytam. The application was done on bare soil 31 days (trial 08-2171-01) and 30 days (trial 08-2171-02), before planting of potatoes. After the application the test item was incorporated into the soil (08-217)-01: 8, 10 cm depth and 08-2171-02: < 8 cm depth).

In both trials the application was done with 1.0 L of test item/ha and a water rate of 300 L/ha, corresponding to a spray concentration of the test them of 0.33% (0.17% of active substance in the spray liquid). The application rate was 0.50 kg fluopy am /ha

For residue analysis samples of potato tuber, were taken from the treated and the control plots. In order to obtain representative samples of the raw commodity, samples were taken at random along the treated and the control plot.

Samples of potato (tubef) were taken from the treated and untreated plot in both trials 14 days before harvest and at harvest

The field samples were stored deep-frozen within 24 hours after sampling and until dispatch. The field samples were shipped by deep-freeze lorry and arrived in good condition. The field samples were stored in a freezer at  $\leq 0.8^{\circ}$ C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field samples were shredded with dry ice in a cutter. Representative parts of the shredded field samples were transferred into polystyrene boxes separately for analysis or archiving and store at  $\leq -18^{\circ}$ C

Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (**1997**, 05/02/2007, <u>M-283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method



are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.  $Q_{\mu}^{\circ}$ 

Residues of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitrile:water (80:20; v:6). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

- One dilution was performed under acidic conditions: this extract allowed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed determination of FLU, FLU-benzamide and FLU-7-OH.

An aliquot of the extracts was injected into LC-MSMS operated in Electrospray Ionization mode:

- One injection in positive electrospray ionization for the determination of FDU, FLU-benzamide and FLU-7-OH.
- Another injection in negative electrospray ionization for the determination of FLUPCA and FLU-methyl-sulfoxide under different conditions.

The linearity was demonstrated in each analytical batch with a 1/x veighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standard ation using sotopically stable abelled internal standards.

The Limit of Quantification (LOO), expressed as fluopyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat straw and 0.01 mg/kg for all other matrices.

Full details and acceptable variation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements patilined within SANCO/3029/99 rev 4.

#### **Findings**

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and treated samples from the study in each set of analyses. The means of the concurrent recoveries were for all fourification levels within the acceptable range of 70 - 110 % except for FDU-methyl-sulfoxide at 111 % and 120 % respectively at 0.1 mg/kg and 1 mg/kg. All overall average recoveries are in the acceptable range of 70 - 110 %; therefore, the results are considered valid. Recovery results are presented in Pable 6.6.2-18.

No residue of luopy cam or clated metabolites were found above the LOQ in any of the control samples of rotational crop matrices analysed.

The residue levels of flaopyron and its relevant metabolites in the rotational crop matrices of potato tubers are summarized in the Table 6.6.2 9.

The storage period of deep frozen samples ranged between 316 and 345 days.

## Residues in potato tubers

In trial 08-2771-01 (PBLO) days), residues of fluopyram (AE C656948) were 0.02 mg/kg in potato tuber 14 days before for vest and at parvest.

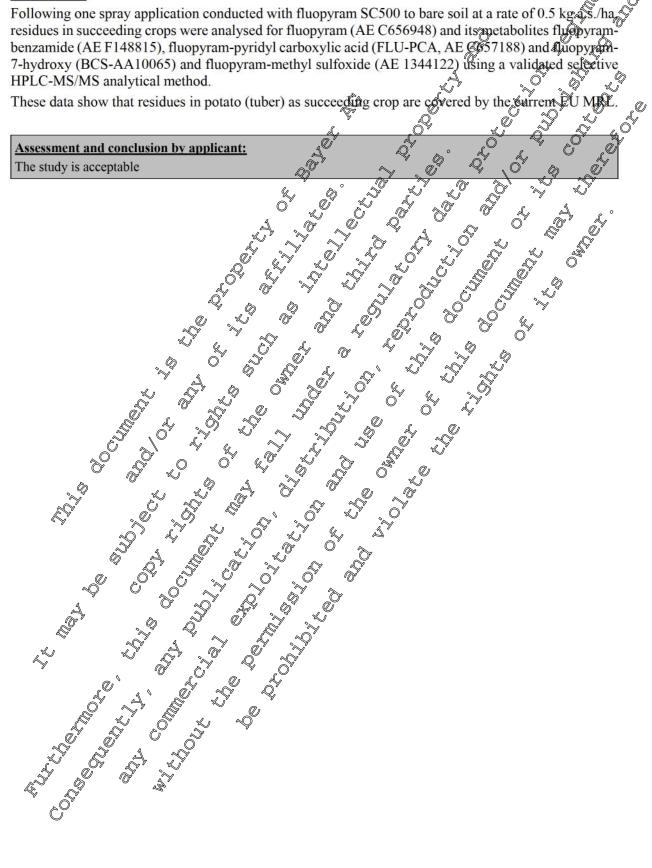
The residues of the metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methyl-sulfoxide) were < 0.01 mg/kg 14 days before harvest and at harvest.

In trial 08/2171-02 (PBI 30 days) residues of fluopyram (AE C656948) were 0.02 mg/kg in potato tubers 14 days before harvest and at harvest.

The residues of the metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methyl-sulfoxide) were < 0.01 mg/kg 14 days before harvest and at harvest.



<u>Conclusions</u> Following one spray application conducted with fluopyram SC500 to bare soil at a rate of 0.5 kg as./ha residues in succeeding crops were analysed for fluopyram (AE C656948) and its metabolites fluopyrambenzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE (\$57188) and Quopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122) using a validated selective HPLC-MS/MS analytical method.





	ecovery data Iber	for fluopyram (AE C656)	948) and its metabol	lites in potato,
Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD(%)
Fluopyram (AE C65	6948)		,	
•• •	0.01	88; 93	91	<u></u>
Datata tuban	0.10	98 🖉	28	
Potato, tuber	1.0	106	0.06	6 2 V X
		Overall recovery (n=4)	<u>0[™]96</u> ×	
Fluopyram-benzami	de (AEF14881	5)		
	0.01	80; 70 *	<u>~ ' 78 Q'</u>	<u>, ov a av</u>
Potato, tuber	0.10	<u></u>	<u>~ ~94 ~ (</u>	$\sqrt{\sqrt{-\sqrt{2}}}$
i otato, tubei	1.0	×98	98 4 6	ý ý <u></u> ~
		Overall recovery (n=40		
Fluopyram-pyridyl-		(AE C657188)		
	0.01	74,85		
Potato, tuber	0.10	<u> </u>		<u> </u>
1 000000, 00000	1.0		<u> X S</u>	- Ø
		Overall recovery (n= 7)	<u> 86 87 </u>	<u>N 10.6</u>
Fluopyram-7-hydrox	<i>[7]</i> .			
	0.01	<u>\$0;93</u>		
Potato, tuber	0.10			
, ,	j. d. C			Q
Fluopyram-methylsu	lforido (ATA 2	$\frac{\text{Overall recovery (n=7)}}{44222}$		6.8
r luopyram-metnyist		<b>440022)</b> 0 3; <b>A</b>		
	<b>0.00</b>			
Potato, tuber 🔊				
Ò		Øveralk recovery (n= 7)		20.7
L: fortification level, RSD 4	Relative Standard	Peviation		20.7
Final determination as: FLU- Final determination as: FLU- Final determination as: FLU-	benzimide Revidue næhylsulförde Re PCA Revidues cale	Deviation only two individual recoveries given ulated as: fluor@ram es calculated as: fluopycam esidues calculated as Duopyram ulated as fluopyram ulated as fluopyram		
inal determination as: F	70H Residues only	ulatedas fluopularin ov		
	E C C			



Page 705 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application rate per treatment <u>to bare soil or target</u> <u>crop</u>	Dates of treatment or no. of treatments and last date	Portion analysed	Growth stage of sampling		arties	Residues		CONTER CONTER CONTER CONTER CONTER	0 ⁷⁶	PHI (days)
	(a)	(b)	kg Water kg a.s./ha (L/ha) a.s./hL	€ ¹²⁰ (c) 3,5	310- J.Ş		as Ac C656948	C656048	000000	CORIN	as AE	Total residue calc.	(e)
08-2171-01 Spain 46230 Alginet Comunidad Valenciana Europe, South F 2008	Application to bare soil <b>PBI: 31 d</b> <u>Rotational</u> <u>crop:</u> Potato, Nicola	1) 14.04.2008 2) 01.06.2008 - 20.06.2008 3) 01.07.2008 - 30.07.2008	3000 r r	914.03.2008 911+5 911+5 5100 51 5100	UIDEL UIDEL UIDEL					<0.01 N S	<0.01 <0.01	0.03 0.03	116 130
08-2171-02 Italy 00055 Ladispoli (RM) Lazio Europe, South F 2008	· eronie	1) 01.05.2008 2) 13.06.2008 - 07.07.2008 3) 15.07.2008 - 15.08.2008	copy rangent			UP95 99 0WDE1 012te	0.02 0.02	0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0.03 0.03	113 127
(b) Only if r	g to CODEX Classif elevant st be indicated owth stage descriptio ise calculated : Sim B ULL C	1 Br	(e) Bays after last apprice (f) Remarks may hiclude information which may (g) Study reference (h) Bays after last apprice (h) Remarks may hiclude (h) Remarks may hic	: Clineatic conditions:	Weterence to	I, underline) analytical method	d and	(i) Applic (j) Method (k) LOQ	lation type ation method d information e in control	(l) (m) #	Method valida Storage (max) ! based on dat P based on pro no data availa	e of analysis oduction date	
	Co».	WI Tr.											70



Data Point:	KCA 6.6.2/10
Report Author:	
Report Year:	2009
Report Title:	Determination of the residues of AE C656948 in/on onion after spraying of
	fluopyram SC 500 in the field in France (North) and Germany
Report No:	08-2161
Document No:	<u>M-352225-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/41 EEC of July 16 1991
study:	
Deviations from current	
test guideline:	
Previous evaluation:	No, not previously submitted
	Study was not found in DAR/RAR and the Addenda T
GLP/Officially recognised	Yes, conducted under GLP/Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes A A A

#### **Materials and Methods**

The purpose of the study was to determine the magnitude of residues of fluopyram (AE C656948) and its metabolites fluopyram-benzamule (AE F148875), fluopyram-pyrich carboxylic acid (FLU-PCA, AE C657188), fluopyram-7-hydroxx (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122), in/on onion (bulb) harvested after one spray application with Fluopyram SC, 500 on bare soil followed by incorporation, 30 days before sowing of pairons in northern Europe (northern France and Germany).

For application the formulation Fluopyram SC 500 was used, a suspension concentrate formulation containing 500 g/L of Fluopyram. The application was done with 7.0 L test item per ha and 300 L water per ha on bare coil followed by incorporation into the soft (< 8 cm) 30 days before the sowing of onions (28 days in trial 08-2161-02). The investigated plant back interval was 30 days.

In both trials the application was done with 1.0 L test item per ha and 300 L water per ha, corresponding to a spray concentration of the test item of 0.33 % (0.17%) of active substance in the spray liquid). The application rate was 0.50 kg fluoryram da.

For residue analysis samples of onion (bulb) were taken 14 days before harvest and at harvest in both trials corresponding to 160 and 174 days (08-2161-01) and 124 and 138 days (08-2161-02) after last treatment. Samples of onion (bulb) were taken from the treated and the control plots at both sampling events. In order to obtain representative samples of the raw commodity, samples were taken according to different sampling procedures from various parts of each treated and control plot.

The field samples were stored deep-frozen within 24 hours after sampling and until dispatch. The field samples of trial 08-2161 01 were shipped by deep-freeze lorry, the field samples of trial 08-2161-02 were shipped by car with dry ice and arrived in good condition. The field samples were stored in a freezer at  $\leq$ -18°C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field samples were stredded with dry ice in a cutter. Representative parts of the shredded field samples were transferred into polystyrene boxes separately for analysis or archiving and stored at  $\leq$ -18°C

Residues of Tuopytam and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (**1999**, 05/02/2007, <u>M-283301-07-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.



Residues of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitrile:water (80:20; v:v). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

- One dilution was performed under acidic conditions: this extract allowed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed the determination of FLU, FLU-benzamide and FLU&OH.

An aliquot of the extracts was injected into LC-MS/MS operated in Electrospray Ioferation mode

- One injection in positive electrospray ionization for the determination of PLU, FLU-berzamide and FLU-7-OH.
- Another injection in negative electrospray ionization for the determination of FKU-PCA and FLU-methyl-sulfoxide under different conditions.

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standardization using isotopically stable tabelled internal standards.

The Limit of Quantification (LOQ), expressed as fluopyram, defined as the lowest alidated fortification level, was 0.05 mg/kg for wheat straw and 0.01 mg/kg for all other matrices.

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the BU regulatory requirements outlined within SANCO/3029/99 rev 4.

#### **Findings**

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and treated samples from the study in each set of analyses. The overall means of the concurrent recoveries were for all fortification levels within the acceptable range of 70 - 110 %, except for FLU-methyl-sulfoxide at 114 % at 0.1 mg/kg All overall mean recoveries are in the acceptable range of 70 - 140 %; therefore the results are considered valid. Recovery results are presented in Table 6.62-20.

No residue of fluopyram orcelated metabolites were found above the LOQ in any of the control samples of rotational crop matrices analysed.

The residue levels of Puopyram and its relevant metabolites in the rotational crop matrices of onion bulbs are summarized in the Table 8.6.2-21.

The storage period of deep-frozen samples ranged between 262 and 301 days.

#### Residues in onion balls

In trial 08-2161-01 (PBI 30 days), residues of Puopyram (AE C656948) were at the level of 0.01 mg/kg in onion tuber 14 days before harvest and acharvest.

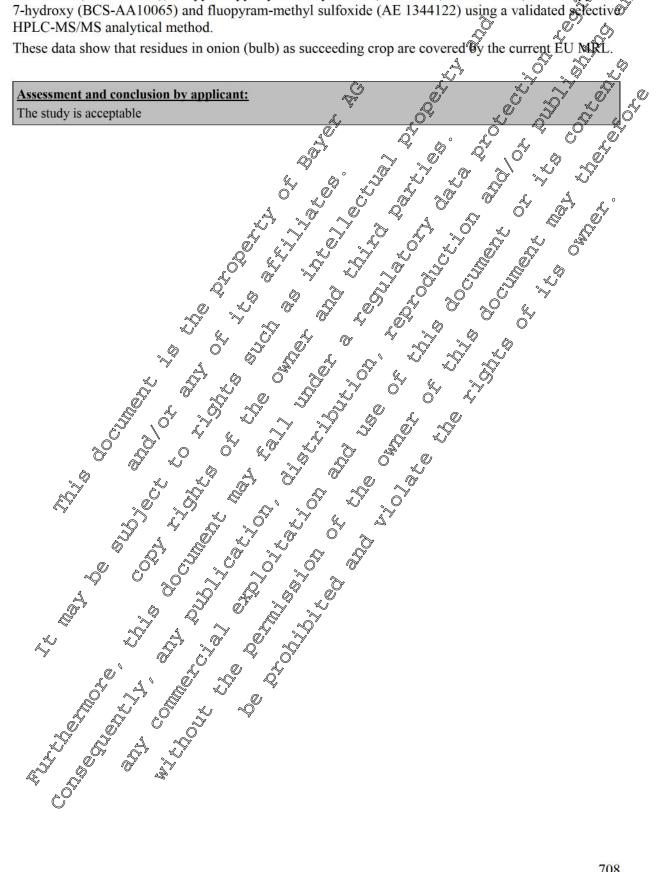
The residues of metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methyl-sulfoxide) were < 0.01 mg/kg, 14 days before harvest and at harvest.

In trial 08-216 02 (PBI 28 days) residues of fluopyram (AE C656948) and its metabolites (FLUbenzamide, FDU-PCA, FLU-7-OH, FLU-methyl-sulfoxide) were < 0.01 mg/kg, 14 days before harvest and at harvest.





Following one spray application conducted with fluopyram SC500 to bare soil at a rate of 0.5 kg a.s./ha, residues in succeeding crops were analysed for fluopyram (AE C656948) and its metabolites fluopyrambenzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE C657188) and fluopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122) using a validated selective HPLC-MS/MS analytical method.





Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD*((25))
Fluopyram (AE C65	56948)		"S	
<b>**</b> \	0.01	81; 74; 83; 79	79 🔬	_Q4.9
Onion, bulb	0.10	97; 97; 98; 91	96	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
Onion, buib	0.10	(4)	 	
		Overall recovery (n 8)		
Fluopyram-benzami		- 7		
	0.01	83; 73; 73;		
Onion, bulb	0.10	92; 96; 92, 95		
		Overall recovery (n=8)	<u> 786</u>	<u> </u>
Fluopyram-pyridyl-	carboxilic-acid	(AE C657188)		
	0.01	65; 66; 77; 70	Q 19 ~	0 7 <b>8</b> 4
Onion, bulb	0.10	89; 89; 94; 94	€ £92 °	S.2 (C
,		Overalkrecovery (n=8)		j 15.40
Fluopyram-7-hydro				
- aopyram-/-nyul0	0.01 a	82; 77; 83; 103	N Q6 A	\$\$ \$\$ \$\$ \$\$ \$\$.3
		<pre></pre>	91° ~ C	$\nu \rightarrow$
Onion, bulb	0.10			<u> </u>
	L V,	Overall recovery (n=8)		O` 9.0
Fluopyram-methyls				<u>Ô</u>
	°~Ø.01	@90; 1 <b>6</b> 4; 96; <b>8</b> 4	y 94 y Q	9.1
Onion, bulb	<i>≪</i> 0.10¢	2 114; <b>Q</b> 19; 1 <b>0</b> ; 114	\$14 ×	4.0
G		Overall recovery (n=8)	Q104 ~	12.1
inal determination as fluo inal determination as: FLU inal determination as: FLU inal determination as: FLU inal determination as: FLU	Senzamid Residu methylstifoxide B -PCA Residue calc -70 Residue	eScalculated as: fluoryram esidues calculated as: fluoryram culated as: fluoryram culated as: fluoryram		



Page 710 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

able 6.6.2-	21: Result	s of rotational o	crop tri	ials conducted	l with fluop	oyram		1° ^L	3	erti	O'TO'S	TR TRONT	100 Sil	jð.
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	t	cation rate per reatment <u>e soil or target</u> <u>crop</u>	Dates of treatment or no. of treatments and last date	Portion analysed	Growth stage af sampting	<b>\$</b> ~ _	arties	Residues		plienter conten conten	jî Cî ^e	PHI (days)
	(a)	(b)	kg a.s./ha	Water (L/ha) kg a.s./hL	CALC (c) j.t	S.D. O.S.		as AE C656948	benzamides as AB Co56948	PLU- PCA as AE	FLU- 7OH as AF C636948	methyl- sulfoxide as AE C656948	Total residue calc.	(e)
08-2161-01 France, north 8410 Bouafle Ile-de-France Europe, North F 2008	Application to bare soil <b>PBI: 30 d</b> Rotational <u>crop:</u> Onion Paille des vertus	MOL S	0.5 20000		19.03.2008 30 ^E 50 ^E	J.D.J.C.					<0.01 <0.00 ;5	<0.01 <0.01	0.02 0.02	160 174
08-2161-02 Germany 51399 Burscheid Nordrhein- Westfalen Europe, North F 2008	Application to bare soil PBI: 28 d Rotational crop: Onion Sherpa	Went De S	0.5 30 ³ 0 c ⁰²¹ c ⁰²¹	A DIRE RAT			US 99		22 500 3001	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0.03 0.03	124 138
(a) Accordin (b) Only if r (c) Year mu (d) Either gr G greenhoo Total residue	ng to CODEX Classifi elevant st be indicated owth stage descriptio ise calculate C sun B UC	ication / Guide		Pays after Graphical Remarks may include information which the addy reference prior to las Greatment 2000 C	tion (abel pre-har Chinatic condition abolites are field	vestinterval, PH is; Reference to ed	II, underline) analytical metho	d and	<ul> <li>(i) Applica</li> <li>(j) Method</li> <li>(k) LOQ</li> </ul>	ation type ation method l information in control	(l) (m) #	Method valida Storage (max) ! based on dat P based on prr no data availa	) e of analysis oduction date	
	Ċ ^Q [*]	W. L.V.												71



Data Point:	KCA 6.6.2/11
Report Author:	
Report Year:	2009
Report Title:	Determination of the residues of AE C656948 in/on onion after spraying of
	Determination of the residues of AE C656948 in/on onion after spraying of fluopyram SC 500 in the field in Italy and Spain
Report No:	08-2172
Document No:	<u>M-355319-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/41 EEC of July 10, 1991, Annex II, part A, section
study:	6 and Annex III, part A, section 8 Residues in Fron Treated Products, Food and
	EC guidance working document 7029/VI/9 Prev. 5 (1997-07-22) 2
Deviations from current	none of the second seco
test guideline:	
Previous evaluation:	No, not previously submitted
	Study was not found in DAN RAR and the Addenda
GLP/Officially recognised	Yes, conducted under GLP/Offreially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes a ky ky ky ky ky ky ky
	$\frac{Yes}{Q} \xrightarrow{Q} \xrightarrow{Q} \xrightarrow{Q} \xrightarrow{Q} \xrightarrow{Q} \xrightarrow{Q} \xrightarrow{Q} $

### Materials and Methods

The purpose of the study was to determine the magnitude of residues of the pyram (AE C656948) and its metabolites fluopyram beneamide (AE F 148815) fluopyram pyridyl carboxylic acid (FLU-PCA, AE C657188), fluopyram f-hydroxy (BCS-A/20065) and fluopyram-methyl sulfoxide (AE 1344122), in/on onion (bulb) harvested after one praying application with Fluopyram SC 500 on bare soil followed by incorporation 30 days before stwing/planting of onion in souther Europe (Spain and Italy).

For application the formulation Fluopyram SC 500 was used a suspension concentrate formulation containing 500 g/L of Fluopyram. The application was some with 1.0L test item per ha and 300 L water per ha on bare soil followed by picorporation into the soil (58 cm) 50 days before the sowing of onions (31-29 days in trials 06 2161 of 1 & 02 respectivelo). The investigated plant back interval was 30 days.

In both trials the application was none will 1.0 K test item per ha and 300 L water per ha, corresponding to a spray concentration of the test item of 0.33% (0.17% of active substance in the spray liquid). The application rate was 0.30 kg thropyram /ha

For residue analysis samples of onion (bub) were taken 14 days before harvest and at harvest in both trials corresponding to 139 and 53 days (082172-02) and 133 and 146 days (08-2172-02) after last treatment Samples of onion (bub) were taken from the treated and the control plots at both sampling events. In order to obtain representative samples of the raw commodity, samples were taken according to different sampling procedures from various parts of each treated and control plot.

The field samples were stored deep-frozen within 24 hours after sampling and until dispatch. The field samples were shipped by deep-freeze lorry and arrived in good condition. The field samples were stored in a freezer of  $\leq -18$  °C until preparation of the examination samples. For the preparation of examination samples, the deep frozen field samples were shredded with dry ice in a cutter. Representative parts of the shredded field samples were transferred into polystyrene boxes separately for analysis or archiving and stored at  $\leq 18^{\circ}$  °C

Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (**1999**, 05/02/2007, <u>M-28330 01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.



Residues of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitrile:water (80:20; *v:v*). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

- One dilution was performed under acidic conditions: this extract allowed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extra@ allowed the determination of FLU, FLU-benzamide and FLU(7)OH.

An aliquot of the extracts was injected into LC-MS/MS operated in Electrospray Ioferation mode

- One injection in positive electrospray ionization for the determination of PLU, FLU-benzamide and FLU-7-OH.
- Another injection in negative electrospray ionization for the determination of FKU-PCA and FLU-methyl-sulfoxide under different conditions.

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve stablished with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standardization using sotopically stable tabelled internal standards.

The Limit of Quantification (LOQ), expressed as fluopyram, defined as the lowest falidated fortification level, was 0.05 mg/kg for wheat straw and 0.01 mg/kg for all other matrices.

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

#### **Findings**

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and treated samples from the study in each set of analyses. The means of the concurrent recoveries were for all fortification levels within the acceptable range of 70 - 110 % except for FUU-methyl-sulfoxide at 116 % for the fortification 0.1 mg/kg. All overall mean recoveries are in the acceptable range of 70 - 110 %; therefore, the results are considered valid. Recovery results are presented in Table 6.2-22.

No residue of fluonyram or celated metabolites were found above the LOQ in any of the control samples of rotational crop matrices analysed.

The residue levels of Phopyram and its relevant metabolites in the rotational crop matrices of onion bulbs are summarized in the Table 8.6.2-23.

The storage period of deep-frozen samples ranged from 272 to 326 days.

#### Residues in onion ballbs

In trial 08-2172-01 (PBI 1 days), residues of Gesidues of fluopyram (AE C656948) and its metabolites (FLU-benzamide, FLU-PCA, FLU-GOH, EU-methyl-sulfoxide) were < 0.01 mg/kg, 14 days before harvest and a marvest  $\sim$ 

In trial 08-2172-02 (PBL 99 days) residues of residues of fluopyram (AE C656948) and its metabolites (FLU-benzamide, FLU-PCA 0 LU-7-OH, FLU-methyl-sulfoxide) were < 0.01 mg/kg, 14 days before harvest and at harvest at harves

## <u>Conclusions</u>

Following one spray application conducted with fluopyram SC500 to bare soil at a rate of 0.5 kg a.s./ha, residues in succeeding crops were analysed for fluopyram (AE C656948) and its metabolites fluopyrambenzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE C657188) and fluopyram-



ed sets rei 7-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122) using a validated selective HPLC-MS/MS analytical method. 

These data show that residues in onion (bulb) as succeeding crop are covered by the current EU MRL And and and the second to be and and the second and

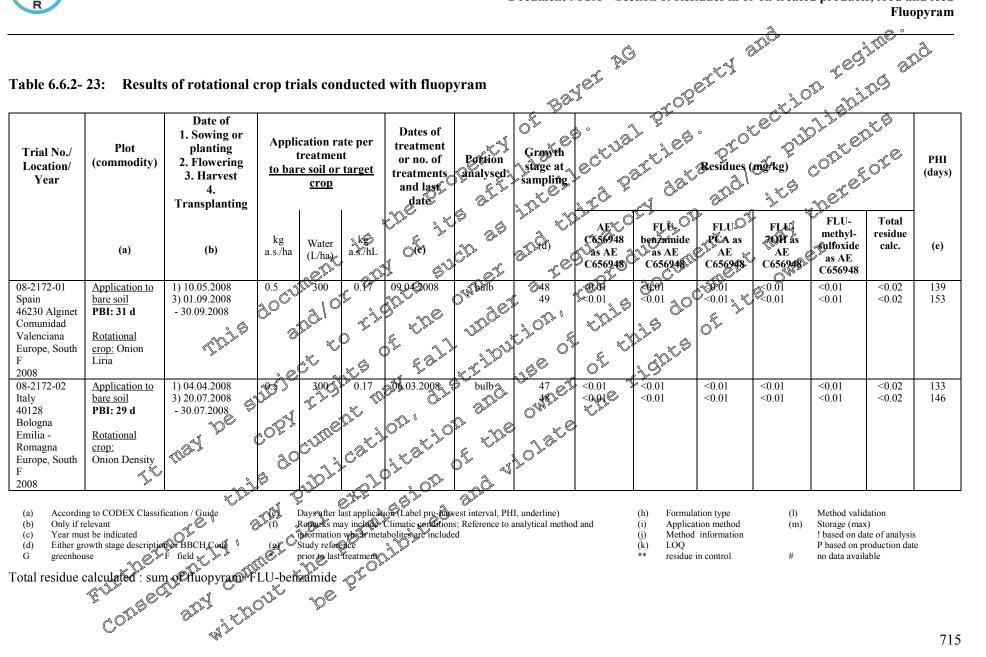
without the second and the second an



Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD*
Fluopyram (AE C65	6948)	•		
	0.01	87	87 🔬	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
Onion, bulb	0.10	83; 85	84	, O' 1.7 Q v
		Overall recovery (n=3)	85	× 24 ×
Fluopyram-benzami	1			
	0.01	91	<u>0*91</u>	
Onion, bulb	0.10	88; 89	<u> </u>	× 0.80 @
		Overall recovery (n=3)	<u> </u>	0 [×] 1,7 0 [×]
Fluopyram-pyridyl-				
	0.01	\$77 0		
Onion, bulb	0.10	100; 96		
		Overall recovery (n=3)	1 1 1	<u> </u>
Fluopyram-7-hydro:	<b>*</b> `			
<b>0</b> · · · ·	0.01			
Onion, bulb	0.10	<u>\$ \$ \$ 95; 925</u> ~ *		
		Overall recovery (n=3)	<u>5</u> 889 5	<u>\$</u> 40.5
Fluopyram-methylsi	ulfoxide (AEI:			
	0.01		$\sqrt{\frac{9}{10}}$	
Onion, buib	0. KU			0.0 <b>0 10.0</b>
some RSDs were not calcu nal determination as: fluop nal determination as: FLU nal determination as: FLU nal determination as: FSU nal determination as: FSU	lated as there were over Resides cal or Reside Reside of Reside Reside rectangle and reside PCA Reside Scal -70 Reside Scal	only two individual recoveries give culated as: fluopyram scalculated as: fluopyram sidues calculated as: fluopyram culates s: fluopyram		<i>°</i>
some RSDs were not calcunal determination as: fluop nal determination as: FLU nal determination as: FLU nal determination as: FLU nal determination as: FLU	lated as there were write Residnes cal prizamide Residnes methy pulfoxide B -PCA Residues cal -70 Residues cal	only two individual recoveries give culated as: fluopyram scalculated as: fluopyram culated as: fluopyram culated as: fluopyram culated as: fluopyram		°
some RSDs were not calcunal determination as: fluop nal determination as: FLU nal determination	lated as there were syntax Residence and prizamide Residence and the syntax and the syntax and the syntax and the syntax and the syntax and the syntax and the syntax and the syntax and the syntax and the syntax and the syntax and the syntax and the syntax and the syntax and the syntax and the syntax and the syntax and the syntax and the syntax and the syntax and the syntax and t	only two indicated are coveries give culated as: fluopyram sidues calculated as: fluopyram culated as: fluopyram culated as: fluopyram culated as: fluopyram culated as: fluopyram		2
some RSDs were not calcunal determination as: fluop nal determination as: fluop nal determination as: FLU nal determinatio	lated as there were syntax Residnes cal penzamide Residnes rethylgulfoxide R -PCA Residues rate of Residues rate of A residues rate rate of A residues rate of A resi	Verail recovery (n=3) 44122 44122 97 116; 116 Overail recovery (n=3) Deviation only two individual recoveries give calculated as: fluopyram culated as: fluopyram culated as: fluopyram culated as: fluopyram culated as: fluopyram culated as: fluopyram		2

BAYE

Page 715 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram





Data Point:	KCA 6.6.2/12
Report Author:	
Report Year:	2009
Report Title:	Determination of the residues of AE C656948 in/on tomate after spraying of fluopyram SC 500 in the field in France (North) and Germany
	fluopyram SC 500 in the field in France (North) and Germany
Report No:	08-2165
Document No:	<u>M-352213-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/41 EEC of July 16 1991
study:	
Deviations from current	none of A of A
test guideline:	
Previous evaluation:	No, not previously submitted
	Study was not found in DAR/RAR and the Addenda or Study was not found in DAR/RAR and the Addenda
GLP/Officially recognised	Yes, conducted under GLP/Officially recognized testing facilities
testing facilities:	
Acceptability/Reliability:	Yes A A A A
	$\frac{\operatorname{Yes}}{\operatorname{Q}^{4}} \xrightarrow{\operatorname{Q}^{4}} \xrightarrow{\operatorname{Q}^{$

#### **Materials and Methods**

The purpose of the study was to determine the magnitude of the relevant residues of fluopyram (AE C656948) and its metabolites theopyram-benzamide (AE F148815), fluopyram byridyl carboxylic acid (FLU-PCA, AE C657188), fluopyram 7-hydroxy (BCS-A710065) and tuopyram-methyl sulfoxide (AE 1344122), in/on tomato (fruits) has rested after one spraying application with Fluopyram SC 500 on bare soil 30 days before sowing/planting of tomato in northern Europe (northern France and Germany). The investigated plant back interval was 30 days

For application the formulation Fluopyram SC 500 was used a suspension concentrate formulation containing 500 g/L of Fluopyram. The application was done on bare soil followed by incorporation into the soil (58 cm) 30 days before the sowing of tomate.

In both trials the application was done with 1.9 L of test item per ha and 300 L of water per ha, corresponding to a spray concentration of 0.33% (0.7% of active substance in the spray liquid). The application rate was 0.59 kg fluopyram ha.

In both trials the appreciation was done or bare soil 30 days (08-2165-01) and 28 days (08-2165-02) before the planting of tornato. The test item was incorporated into the soil (08-2165-01: 5-6 cm depth) and 08-2165-02: < 8 cm depth).

For residue analysis samples of tomato (fruit) were taken from the treated and the control plots. In order to obtain representative samples of the raw commodity, samples were taken at random along the treated and the control plot. Samples of tomato (fruit) were taken from the treated and untreated plot in both trials at harvest

The field samples were stored deep-frozen within 24 hours after sampling and until dispatch. All field samples were shipped bo deep freeze forry (08-2165-01) and by car with dry ice (08-2165-02) and arrived in good condition. The field samples were stored in a freezer at  $\leq$  -18°C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field samples were shredded with dry ice in a cutter. Representative parts of the shredded field samples were transferred interpolystyrene boxes separately for analysis or archiving and stored at  $\leq$  -18°C.

Residuce of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (**1997**, 05/02/2007, <u>M-283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method



are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.  $Q_n^{\circ}$ 

Residues of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitrile:water (80:20; v:6). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

- One dilution was performed under acidic conditions: this extractation of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed the determination of FLU, FLU-benzamide and FLU-7-OH.

An aliquot of the extracts was injected into LC-MSINS operated in Elegrospray Ionization mode:

- One injection in positive electrospray ionization for the determination of PDU, FLU-benzamide and FLU-7-OH.
- Another injection in negative electrosprationization for the determination of FLUPCA and FLU-methyl-sulfoxide under different conditions.

The linearity was demonstrated in each analytical batch with a /x weighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standardization using isotopically stable labelled internal standards.

The Limit of Quantification (LOQ) expressed as fluopyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat straw and 0.01 mg/kg for all other matrices

Full details and acceptable validation data to support this nothod are presented within document M-CA 4, which comply with the EU/regulatory requirements outfined within SANCO/3029/99 rev 4.

#### **Findings**

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and treatest samples from the study in each set of analyses. The overall means of the concurrent recoveries were within the acceptable range of 70 - 110 % and all the results are considered calid. Recovery results are presented in Table 6.6.2- 24.

No residue of fluoporam or related metabolites were found above the LOQ in any of the control samples of rotational croponatrices analysed.

The residue levels of thopy and its reprvant octabolities in the rotational crop matrices of tomato fruits are summarized in the Table  $\beta.6.2-25$ .

The storage period of deep-frozen samples ranged from 290 to 321 days.

#### Residues in tomato Truits

In trial 08-2172-01 (PBF 30 days), residues of fluopyram (AE C656948) and its metabolites (FLUbenzamide, FLU-PCA, FLU-OH, FLU-methyl-sulfoxide) were all < 0.01 mg/kg in tomato fruit at harvest.

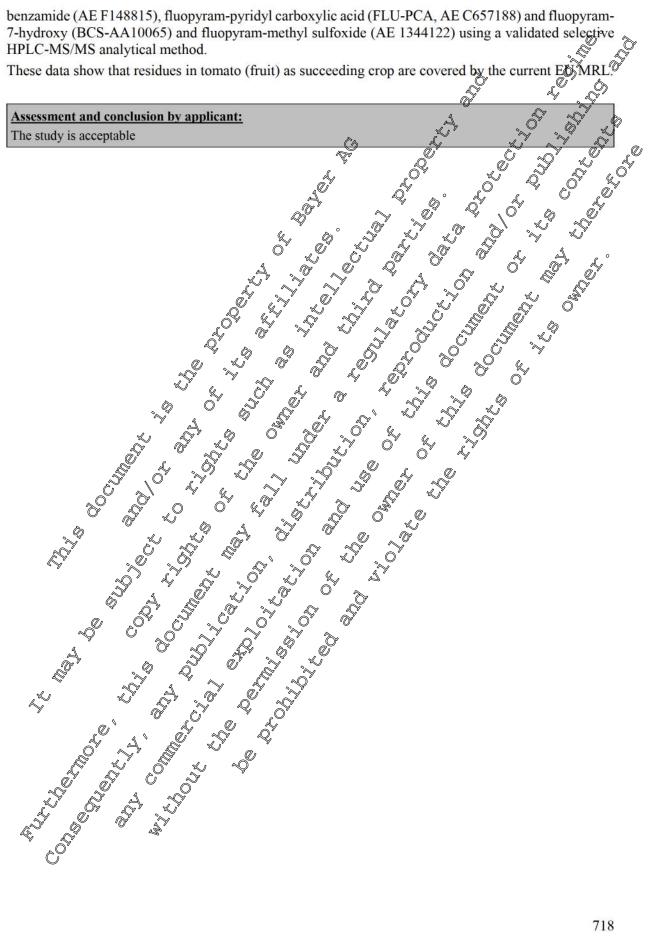
In trial 082172-02 (PBP 28 days) residues of fluopyram (AE C656948) and its metabolites (FLUbenzamice, FLU-PCA, FLU-OH, FLU-methyl-sulfoxide) were all < 0.01 mg/kg in tomato fruit at harvest.

#### **Conclusions**

Following one spray application conducted with fluopyram SC500 to bare soil at a rate of 0.5 kg a.s./ha, residues in succeeding crops were analysed for fluopyram (AE C656948) and its metabolites fluopyram-



benzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE C657188) and fluopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122) using a validated selective





	ecovery data uit	for fluopyram (AE C6569	948) and its metabol	lites in tomato,
Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD(%)
Fluopyram (AE C65	6948)		<u>س</u> ريد ۵	
	0.01	83	83	<u>, 0 -, 0 x x</u>
Tana (a. Cart	0.10	91 🖏	24	N AN AS A
Tomato, fruit	1.0	97 🚿	.097	
		Overall recovery (n=3)	× 0°90 ×	√ [∞] 7.8 [∞] [∞]
Fluopyram-benzami	de (AEF14881:	5)		
	0.01	81.07 *	s st Q	, OY 75 OY
Tomato, fruit	0.10		@ <u>`</u> `~~90 @``	$\sim$ $\sim$ $\sim$
Tomato, mun	1.0	×93 Q	<u> </u>	× ·· ·
		Overall recovery (n=3)	<u></u>	<b>7.4</b> °
Fluopyram-pyridyl-c		(AE C657188) 0 ~	× 1 ×	
	0.01		p 275 2	
Tomato, fruit	0.10	<u> </u>		<u> </u>
Tomato, mun	1.0	$0^{\circ}$ $y^{\circ}$ $92$ $y^{\circ}$ $y^{\circ}$	<u> </u>	5
		V Overall recovery (n=3)	S 085 S	<u>N</u> 40.6
Fluopyram-7-hydrox		<u>165) &amp; /u>		
	0.01	× 1086 ~ v	Q' 86 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u> </u>
Tomato, fruit	0.10		× × ×	<u> </u>
				Q
		Overall recovery (n=3)	83	3.5
Fluopyram-methylsu	0.00			
_Ű				
Tomato, fruit 🔊				
Ď		Overall recovery (n=3)		10.7
L: fortification le@, RSD	Relative Gandard	eviation	29. 0 <b>A</b>	10.7
some RSDs were not calculation inal determination as: fluopy inal determination as: FLU- inal determination as: FLU- inal determination as: FLU-	ated as there were yram Residues calc bergamide Residue nothylsulfoode Re PCA Residues calc	only two individual recoveries given ulated as: fluoro am s calculated as: fluoro am sidues calculated as Duopyram ulated as fluopyram ulated as fluopyram		
inal determination as: Fige		ulateday: fluopyfam		
	-			



Page 720 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram 4

$\left( a \right) \left( b \right) \left( b \right) \left( b \right) \left( c	Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application 1 treatme <u>to bare soil o</u> <u>crop</u>	nt r target	Dates of treatment or no. of treatments and last date	Portion analysed	Growth stage of sampling		arties	Residues		on reg		PHI (days)
0.6-2-105-01       Application to bare soil       1) 02.04-2008       0.3       3.0       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1       0.1 <td< th=""><th></th><th>(a)</th><th></th><th>" "utor</th><th>kg a.s./hL</th><th>CC) JUC OF</th><th>ju de</th><th></th><th>AE C656948 as AE C656948</th><th>FLU- benzamide as AB (7658948</th><th>PLU- PCA as AE</th><th>FEU- 7OH as AF</th><th>FCU- methyl- sulfoxide as AE CG56948</th><th>Total residue</th><th></th></td<>		(a)		" "utor	kg a.s./hL	CC) JUC OF	ju de		AE C656948 as AE C656948	FLU- benzamide as AB (7658948	PLU- PCA as AE	FEU- 7OH as AF	FCU- methyl- sulfoxide as AE CG56948	Total residue	
S1399     F bit. 20 d     - 01.09.2008       Burscheid     3) 08.09.2008     10 a       Nordrhein-     Rotational crop:       Tomato     De       Europe, North     Hoffmanns       F     Rentita       2008     10 a	France, north 37230 Fondettes Centre Europe, North	bare soil PBI: 30 d Rotational crop: Tomato Super	1) 16.05.2008 2) 09.06.2008 - 04.07.2008 3) 04.08.2008 - 15.08.2008	20 ^{CURE}			WILCH UIDOCT					<0.01 J	<0.01	<0.02	114
	Germany 51399 Burscheid Nordrhein- Westfalen Europe, North 7 2008	bare soil <b>PBI: 28 d</b> <u>Rotational crop:</u> Tomato Hoffmanns Rentita	2) 15.06.2008 - 01.09.2008 3) 08.09.2008				and	V ⁶ ®9	a.		<0.01	<0.01	<0.01	<0.02	136
		to CODEX Classifica levant be indicated wth stage description of e F alculated :	tion / Guide	~ \\	last application of the lude: ( a which mean ence the bent of the bent	on (Labe Pre-harve Linge conditions bolites are incitited	est enerval, PHI Weference to a	I, underline) Inalytical method	l and	<ul> <li>(i) Applica</li> <li>(j) Method</li> <li>(k) LOQ</li> </ul>	tion method information	(m)	Storage (max ! based on da P based on p	<ul> <li>x)</li> <li>ate of analysi</li> <li>roduction data</li> </ul>	



Data Point:	KCA 6.6.2/13
Report Author:	
Report Year:	
Report Title:	Determination of the residues of AE C656948 in/on tomato after spraying of
	fluopyram SC 500 in the field in Italy and Spain
Report No:	08-2176
Document No:	<u>M-355320-02-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/41 EEC of July 16, 1991, Annex II, par A, section 6 and Annex III, part A, section 8 Residues in Son Treated Products, Food and
study:	6 and Annex III, part A, section 8 Residues in from Treated Products Food and
	Feed
	EC guidance working document 7029/VI/9Qrev. 5 (1997-67-22)
Deviations from current	none Que a construction of the construction of
test guideline:	
Previous evaluation:	No, not previously submitted & & &
	rev. 1 to Vol.3 of DAR B7 August 2012 (references relied on)
GLP/Officially recognised	Yes, conducted under GLP/Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes a way to be a construction of the construc

# Materials and Methods

The purpose of the study was to determine the magnitude of residues of fluopyram (AE C656948) and its metabolites fluopyram-benzantide (AF F148815), fluopyram-pyradyl carboxylic acid (FLU-PCA, AE C657188), fluopyram-7 bydroxy (BCS AA10065) and fluopyram-prethyl sulfoxide (AE 1344122), in/on tomato (fruits) harvested after one spray application with Fluopyram SC 500 on bare soil 30 days before sowing/planting of tomato in southern Europe (in Italy and Spain). The investigated plant back interval was 30 days.

Samples were taken a growth stage BBCH 87 (corresponding to DALT 125, trial 08-2176-01) and BBCH 89 (corresponding to DALT 114 real 08 2176 02).

For application the formulation Fluoryram SC 500 was used, a suspension concentrate formulation containing 500 g/L of Fluoryram. The application was done on bare soil followed by incorporation into the soil (< 8 cm) 30 days before the sowing of tomato.

In both trials the application was done with 01.0 L of test item per ha and 300 L of water per ha, corresponding to a spray concentration of 633% (0.17% of active substance in the spray liquid). The application rate was 650 kg luopyram /ha.

In both trials the application was done on bare soil 30 days (08-2165-01) and 28 days (08-2165-02) before the planting of tomato The test item was incorporated into the soil (08-2176-01: 8-10 cm depth; 08-2176-02: 2, cm depth)

For residue malysic samples of tomatoes were taken from the treated and the control plots. In order to obtain representative samples of the raw commodity, samples were taken at random all along the treated and the control plot. Samples were taken at harvest : growth stage BBCH 87 (trial 08-2176-01) and BBCH 89 (trial 08-2176-02).



The field samples were stored deep-frozen within 24 hours after sampling and until dispatch. All field samples were shipped by deep-freeze lorry and arrived in good condition. The field samples were stored in a freezer at  $\leq$ -18°C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field samples were shredded with dry ice in a cutter. Representative parts of the shredded field samples and laboratory samples were transferred into polys rene boxes exparately for analysis or archiving and stored at  $\leq$ -18°C.

Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-prethyl sulfoxide), were determined by LC-MS/MS according to method 00984 (**1997**, 05/02/2007, **1997**, 283301-01-1, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues of these compounds were extracted from 0 g of sample material (5 g or wheat straw) by wo successive extractions using a high-speed blender with a mixture of a conitride: water (80:20, v:v). After centrifugation the extract volume was adjusted. Then, the extracts were different times by adding the internal standards:

- One dilution was performed under acidic conditions: this extract allowed the determination of FLU-PCA and FLU-methyl-sufficiency.
- In parallel, another dilution was performed under basic conditions: this extract allowed the determination of FLU, FLUybenzamide and FLU-7-OIL

An aliquot of the extracts was injected into LCMS/MS operated in Electrospray Onization mode:

- One injection in positive electrospear ionization for the determination of FLU, FLU-benzamide and FLU-7-OH.
- Another injection in negative electrospray ionization for the determination of FLU-PCA and FLU-methyl-sulfoxide under different conditions

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standardization using isotopically stable labelled internal standards.

The Limit of Quantification (LOQ), expressed as fluopyrath, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat straw and 0.01 mg/kg for all other matrices.

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

### Findings

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and treated samples from the study in each set of analyses. The overall means of the concurrent recoveries were within the acceptable range of 70 - 110 % except for FLU-PCA (65% at 0.01 fmg/kg spiking level). All overall mean recoveries are in the acceptable range of 70 - 110 %; therefore, the results are considered valid. Recovery results are presented in Table 6.6.2-26.

No residue of flue yram of related metabolites were found above the LOQ in any of the control samples of rotational crop matrices and ysed.

The residue levels of fluopyram and its relevant metabolites in the rotational crop matrices of tomato fruits are summarized in the Table 6.6.2-27.

The storage period of deep-frozen samples ranged between 259 and 348 days.

### Residues in tomato fruits



In trial 08-2176-01 (PBI 30 days), residues of fluopyram (AE C656948) and its metabolites (FLUbenzamide, FLU-PCA, FLU-7-OH, FLU-methyl-sulfoxide) were all < 0.01 mg/kg in tomato fruitoat

In trial 08-2176-02 (PBI 30 days) residues of fluopyram (AE C656948) and its metabolites (FLU) benzamide, FLU-PCA, FLU-7-OH, FLU-methyl-sulfoxide) were all < 0.01 harvest.

soil at a pile of , and is gridebolik of the of and is gridebolik of the Following one spray application conducted with fluopyram SC500 to fore soil at a face of by kg as /ha residues in succeeding crops were analysed for fluopyram (AE C65(948) and its metabolites fluopyram benzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLOPCA AE C657188) and fluopyram-7-hydroxy (BCS-AA10065) and fluopyram-method sulfoxide (AE 1344122) using a validated selective HPLC-MS/MS analytical method.

These data show that residues in tomato (fruit) as succeeding cropping covered by the current EU MRL.



111	uit	for fluopyram (AE C656)	948) and its metabol	lites in tomato,
Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD(%)
Fluopyram (AE C656	5948)		· <u>·</u> ···	
	0.01	84; 94; 90	89	5.6 × ×
Tomato, fruit	0.10	97; 106; 100 (5) Overall recovery (n=6)	101	× 457 67 0 ~ 1 × 1
Fluopyram-benzamid	le (AEF14881			
<u></u>	0.01	77; 80; 85	81.	5.00 0
Tomato, fruit	0.10	90; 85; 102	× 89 Q	0 4 <u>1</u>
		Overall recovery (n=6)	°° ² .°∕85 ≈ .	×6.7 ×
Fluopyram-pyridyl-ca	arboxilic-acid			
	0.01	68,66;61	D 65 O	£ 5.5 c°
Tomato, fruit	0.10	A 94; 90, 90 A	\$ 491 Q	
,		Overall recovery (p=6)		V , 18.8 S
Fluopyram-7-hydroxy	y (BCS-AA10			
	0.01	6 <b>98</b> ; 94; <b>92</b>	No & S	3,2
Tomato, fruit	0.10	<b>9</b> 01; 108; 99	N 0103 A	\$ 44.6
	~	Overall recovery (n=6)	99,0	<del>ک</del> کرچ
Fluopyram-methylsul	lfoxide (AP13	44122)		×
<u>1 100 pj 1 000 1000 1000 1000 1000 1000 </u>	0.04	\$\$73; 97¢ 95	1 <b>88</b>	0″ 15.1
Tomato, fruit	<b>0</b> 10	18; 109; 124 °	~~120 ~~	© 2.7
-		Orderall manayona (n=6)	104 9	197
inal determination as: EDU-n inal determination as FLU-P inal determination of FLU-P i	neth Bulfoxide Ro A Residue's calc H Residue's calc H Residue's calc A A A A A A A A A A A A A A A A A A A A A A A A A A A A A A A A A A A A A A A A A A A	Deviation		



Page 725 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Table 6.6.2- 2	27: Results of	of rotational cr	op trials co	nducted	with fluopy	ram		er B ^C	\$	ert	ATLO.	T. C.	og Ju ^e .	jð.
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application treatm <u>to bare soil</u> <u>cro</u>	ent or target	Dates of treatment or no. of treatments and last date_	Portion analysed	Growth stage at sampling	ec ^{tija}	L Prof	° Residues	(mg/kg)	CONTER CONTER CONTER CONTER CONTER CONTER	r O ^{fe}	PHI (days)
	(a)	(b)	kg a.s./ha (L/ha	r kg a.s./hL				LC656948	ex = 10.10	6 2 (0 1 9	0000000	as AE C656948	Total residue calc.	
08-2176-01 Spain 46230 Alginet Comunidad Valenciana Europe, South F 2008	Application to bare soil <b>PBI: 30 d</b> Rotational crop: Tomato Vilma	1) 18.07.2008 2) 01.09.2008 - 01.10.2008 3) 10.09.2008 - 10.10.2008	0.5 200 0.5 200 0.5 200 0.5 200 0.5 200 0.5 200			WACT UIDOCT					<0.01 NS	<0.01	<0.02	125
08-2176-02 Italy 00055 Ladispoli (RM) Lazio Europe, South F 2008	Application to bare soil PBI: 30 d Rotational crop: Tomato Perfect Peel PS 1296	1) 01.05.2008 2) 25.05.2008 - 24.07.2008 3) 15.07.2008 - 15.08.2008	0.5 5 300 D J C J C D D J C J C			CC Dailt BIROL	\$\$ ⁶⁸⁹	0 ³⁹¹	ALE E	<0.01	<0.01	<0.01	<0.02	114
<ul> <li>(a) According</li> <li>(b) Only if re</li> <li>(c) Year mus</li> <li>(d) Either group</li> <li>G greenhous</li> </ul>	g to CODEX Cossificat levant t be indicated wth stage description o se F	r BBCH Code	(e) Da Ster (f) Sudarsts Studarefe print da	last appflication nay in Pide: C nay line metab rence st treatment	n (Label preharve limatic conditions; solides are included	st interval, PHI. Reference to an	, underline) nalytical method	and	(i) Applic (j) Metho (k) LOQ	lation type ation method d information e in control	(l) (m) #	Method valida Storage (max) ! based on dat P based on pro no data availa	) e of analysis oduction date	
Total residue c	alculated : sum E ^{ULCELDEL} COLECT	tion / Guide r BBCH Code field field fie	Uzb <mark>en</mark> žamide U ^{DC} U ^T DC	Per di										725



Data Point:	KCA 6.6.2/14
Report Author:	
Report Year:	2009
Report Title:	Determination of the residues of AE C656948 in/on pea, after spraying of
	fluopyram SC 500 in the field in Germany and Netherlands
Report No:	08-2167
Document No:	<u>M-354235-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/41 EEC of July 16, 1991, Annex I, part A, section
study:	6 and Annex III, part A, section 8; Residues in Son Treated Products Food and
	Feed
Deviations from current	none A Q & A L
test guideline:	
Previous evaluation:	No, not previously submitted of a second sec
	rev. 1 to Vol.3 of DAR B7 Angust 2012 (references relied on)
GLP/Officially recognised	Yes, conducted under GLP Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes in the second secon

### **Materials and Methods**

The purpose of the study was to determine the magnitude of residues of fluopyrim (AE C656948) and its metabolites fluopyrim-ben amide (AE F148815), fluopyram ovridykearboxylic acid (FLU-PCA, AE C657188), fluopyram?/-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122), in/on pea, field (dry sees and green seed) harvested after one spray application with Fluopyram SC 500 on bare soil 30 days before sowing/planting of pea in northern Europe (the Netherlands and Germany). The investigated plant back interval was 30 days.

The formulation Fluopyram SC 300 is a suspension concentrate formulation containing 500 g/L of Fluopyram. In trial 08:2167-01 and 08-2167-02 the application was done on bare soil followed by incorporation into the soil ( 8 cm) 30 days (trial 08-2167-01) and 28 days (trial 08-2167-02) before sowing of pea, field

In both trials the application was done with 1% L test item per ha and 300 L water per ha, corresponding to a spray concentration of the test item of 0.33 % 0.17% of active substance in the spray liquid). The application rate was 0.50 ko fluopyram /ba.

For residue analysis samples of pea, field, green seed and dry seed, were taken from the treated and the control plots. In order to obtain representative samples of the raw commodity, samples were taken at random along the treated and the control plot.

Samples of pods were taken in both trials at gowth stage BBCH 79. Samples of pods were separated in pods and green seed. Samples taken at normal harvest (growth stage BBCH 89) were also separated in pods and dry seed.

The field samples and lab sample were stored deep-frozen within 24 hours after sampling and until dispatch. The field samples and lab samples of trial 08-2167-01 and trial 08-2167-02 were shipped by car with dry ice and arrived in good condition. The field samples and lab samples were stored in a freezer at  $\leq$ -18 °C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field samples and lab samples were shredded with dry ice in a cutter. Representative parts of the shredded field samples were transferred into polystyrene boxes separately for analysis or archiving and stored at  $\leq$ -18 °C.



Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (**1999**, 05/02/2007, <u>M-283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method, are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitrile:water (8030; v:) After centrifugation the extract volume was adjusted. Then, the extracts were diffuted ten times by adding the internal standards:

- One dilution was performed under acidic conditions: this extract allowed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed the determination of FLU, FLU-benzamide and FLU-7-Q.

An aliquot of the extracts was injected into LO-MS/MS operated in Electrospray anization mode:

- One injection in positive electrospiration for the determination of FLU, FLU benzamide and FLU-7-OH.
- Another injection in negative electrospray tonization for the determination of FLU-PCA and FLU-methyl-sulfoxide under different conditions

The linearity was demonstrated in each analytical batch with above the calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by Onternal standardization using isotopically stable labelled internal standards.

The Limit of Quantification (600), expressed as theopyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat shaw and 0.01 mg/kg for all other matrices.

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

### **Findings**

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and treated samples from the study in each set of analyses. The overall means of the concurrent recoveries were within the acceptable range of 70 - 110 % and all the results are considered valid. Recovery results are presented in Table 6.6.2-28.

No residue of uopytam or clated netabolites were found above the LOQ in any of the control samples of rotational crop matrices analysed.

The residue levels of floopyram and its relevant metabolites in the rotational crop matrices of pea, field are summarized in the Table 6.6.2 29.

The storage period of deep frozen samples is up to 362 days for green seeds and 335 days for dry seeds... Residues in pear field

In trial 08-2 67-01 (DBI 30 days), residues of fluopyram (AE C656948) and its metabolites (FLUbenzamide (FLU-FCA, FDU-7-QH, FLQ methyl-sulfoxide) were all < 0.01 mg/kg in pea, field matrices (both green seed and dry seed) at harvest and at BBCH 79.

In triat 08-2167-02 (PBI 28 days) residues of fluopyram (AE C656948) and its metabolites (FLUbenzamide, FLU-PCA, FLU-7-OH, FLU-methyl-sulfoxide) were all < 0.01 mg/kg in pea, field matrices (both green seed and dry seed) at harvest and at BBCH 79 except for FLU-PCA in dry pea seed in which the residues were at the level of 0.02 mg/kg at harvest.

### **Conclusions**



Following one spray application conducted with fluopyram SC500 to bare soil at a rate of 0.5 kg a.s./ha, residues in succeeding crops were analysed for fluopyram (AE C656948) and its metabolites fluopyrambenzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE C657188) and fluopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122) using a validated selective

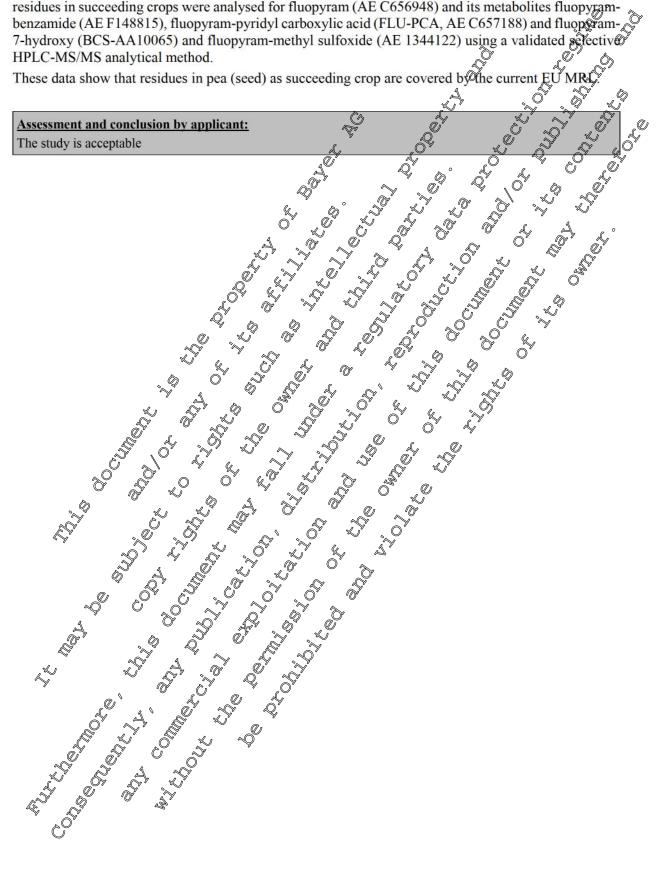




Table 6.6.2- 28:         R	Recovery data	for fluopyram (AE C6569	948) and its metabol	lites in pea, field
Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD*(%)
Fluopyram (AE C65			Ś	<u> </u>
	0.01	104	104	X
Pea, field	0.10	100	100	, 0 [°] 6 [°] , 1
Dry seed	1.0	93 🏠	98	
		Overall recovery (n🕉)	699	
	0.01	116 🔍	_O¥16 🐇	1 2 - S 1
Pea, field	0.10	109 de la companya de	^م 109 ⁰	<u> </u>
Green seed	1.0	99		
		Overall recovery (n=3)	× ×108	×7.9 ~
Fluopyram-benzami	ide (AEF14881			Ĵ, v ² k <u>r</u>
1.	0.01		<u> 840 0</u>	a 2
Pea, field	0.10	\$ 94°°, Ø	Q .94 ~	
Dry seed	1.0	84 ~ 7	84 0 3	
Diyseed	1.0	Overall recovery (n=3)	0 [×] 86 ×	8.4
	0.01			
Pea, field	0.10		N 896 N	
Green seed	1.0	<u>y 0 90,</u>		5 ×
Green seeu	1.0	.Overall recovery (n=3)		<u>%, 7.9</u>
Fluopyram-pyridyl-				1.9 0
r luopyrain-pyriuyi-	0.01	$1207 \circ 1207 \circ $		
D., C.L.	>0.01		99 ° *	<u> </u>
Pea, field				
Dry seed	1.0			
		≪Overall recovery (n=3)		15.9
	0.01			
Pea, field	00.10		94	
Green seed	<u> </u>			
- Ö		Overall recovery (n 3)	103 July 103	16.8
Fluopyram-7-hydro				
	×0.01 ×		<i>7</i> 0	
Pea, field	0.105	<u> </u>	<u> </u>	
Dry seed		U O 23 K	§¥ 93	
J.		Overall recovery@n=3)	94	4.9
Q	<u></u> →0.01	94	94	
Pea, fiel	» ⁰ 04,0 °C		105	
Green seed			95	
4		Overall recovery (n=3)	98	6.2
Fluopyram-methyls	ulfoxide (DE13			
	0.01	839	85	
🗸 Pea, field 🔍	Ø.10 ~	1 A 196	106	
Dry seed	01.0	Q105	105	
		Overa@ recovery (n=3)	99	12.0
	2 0691 ×	95	95	
Des Kil	0.10 w	×Q 115	115	
Pea, field	0.10	111	115	
Green seed				
	Relative Standard	Overall recovery (n=3)	107	9.9

Table 6.6.2- 28:	Recovery data for fluopyram (AE C656948) and its metabolites in pea, field, °

FL: fortification by El, RSD, Relative Standard Deviation * some RSDs when not calculated as there were only two individual recoveries given Final determination as: fluopyram Residues calculated as: fluopyram Final determination as: FLU-benzamide Residues calculated as: fluopyram Final determination as: FLU-methylsulfoxide Residues calculated as: fluopyram Final determination as: FLU-PCA Residues calculated as: fluopyram



Page 730 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Table 6.6.2- 2 Trial No./ Location/	29: Results Plot (commodity)	Date of 1. Sowing or planting 2. Flowering	rop trials conducted Application rate per treatment <u>to bare soil or target</u>	Dates of treatment or no. of treatments	Portion analysed	Growth stage at	Per A	) 1 PTOF	Régulues	office tection tection tection tection	DI DI DI DI DI DI DI DI DI DI DI DI DI D	and an and an	PHI (days)
Year	(a)	3. Harvest 4. Transplanting (b)	crop kg a.s./ha Water (L/ha) s.s.	and last C date	e offi	Sumpling	AE C656948 AE	FLU- benzamede	FLU- PCA as AE C656948*	C 556948	FLU- methyl- sulfoxide	Total residue calc.	(e)
08-2167-01 Netherlands 1681 ND Zwaagdijk- Oost Noord- Holland Europe, North F 2008	Application to bare soil <b>PBI: 30 d</b> <u>Rotational</u> <u>crop:</u> Pea, field Kelvedon	1) 14.05.2008 2) 01.07.2008 - 01.08.2008 3) 29.08.2008 - 05.09.2008			Seed de 1 JID	3795 89 1 1 0 1 0 1 0 1 0 5		7 7 1			<pre></pre> C656948 <pre></pre> <pr< td=""><td>&lt;0.02</td><td>121</td></pr<>	<0.02	121
08-2167-02 Germany 51399 Burscheid Nordrhein- Westfalen Europe, North F 2008	Application to bare soil PBI: 28 d Rotational crop: Pea, field Konto				seed area seed, dry b seed, dry	79 CF 0 89 0 2 2 t C	<0.01	<0.01	<0.01 0.02	<0.01 <0.01	<0.01	<0.02	90 117
(b) Only if rel		ation / Guide of BBCHCott field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field field f	Days after last application (f) Records may include ( information which meta Study reference prior clast treatment) LU-benzamide	Climatic conditions	: Reference to a	I, underline) inalytical method	l and	<ul> <li>(i) Applic</li> <li>(j) Method</li> <li>(k) LOQ</li> </ul>	lation type ation method 1 information in control	(l) (m) #	Method valida Storage (max) ! based on dat P based on pr no data availa	e of analysis oduction date	



Data Point:	KCA 6.6.2/15
Report Author:	
Report Year:	2009
Report Title:	Determination of the residues of AE C656948 in/on pea, other spraying of
	fluopyram SC 500 in the field in Italy and Spain
Report No:	08-2178
Document No:	<u>M-354237-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/41 (EEC of July 16, 1991, Annex II, part X, section 6 and Annex III, part A, section 8; Residues in S on Treated Products Pood and
study:	6 and Annex III, part A, section 8; Residues in Son Treated Products Pood and
	Feed
Deviations from current	none A & & A
test guideline:	
Previous evaluation:	No, not previously submitted Study was not found an DAR RAR and the Addenda
GLP/Officially recognised	Yes, conducted under GLP Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes in it is a si

### **Materials and Methods**

The purpose of the study was to determine the magnitude of residues of fluopytam (AE C656948) and its metabolites fluopytam-benzamide (AE F148815), fluopytam-pyridy carboxylic acid (FLU-PCA, AE C657188), fluopytam-7-hydroxy (BCS-AA 10065) and fluopytam-methyl sulfoxide (AE 1344122), in/on pea, field (dry seed and green seed) harvested after one spraying application with Fluopytam SC 500 on the bare soil 20 dates before sowing/planting of pea in southern Europe (Spain and Italy). The investigated plant back interval was 30 days.

The formulation Fluopyram SC 500 is a suspension concentrate formulation containing 500 g/L of Fluopyram. The application was done with 1.0 L of test item per ba and 300 L water per ha on bare soil followed by incorporation into the soil (< Scm) 39 days before the sowing of pea, fields.

In trial 08-2178-0, 330 L water per ha were used, corresponding to a spray concentration of 0.33 %. The application rate was 0.55 kg/ha of the active substance (a.s.) Fluopyram.

In trial 08-2178-02, 390 L water per hawere used, corresponding to a spray concentration of 0.33 %. The application rate was 650 kg/a of active substance (a.s.) Fluopyram.

In both torals the application was tone on bare soil followed by incorporation (08-2178-01: no information on incorporation depth, 08-2178-02; \$010 cm depth) 28 days before the sowing of pea, field. For tesidue analysis samples of pea, field, green seed and dry seed, were taken from the treated and the control plots. In order to obtain representative samples of the raw commodity, samples were taken all along the treated and the control plot trial (8-2178-01) and according to S-sampling (trial 08-2178-02).

Samples of pods were taken in both trial at growth stage BBCH 79. Samples of pods were separated in pods and green seed. Samples taken at normal harvest (growth stage BBCH 89) were also separated in pods and dry seed.

In trial 08-21-78-02 (by seeds were sampled in growth stage BBCH 87 because the pods were open very early and seeds dropped off, therefore, the plots had to be harvested earlier.

The field samples and laboratory samples were stored deep-frozen within 24 hours after sampling and until dispatch. All field samples and laboratory samples were shipped by deep-freeze lorry and arrived in good condition. The field samples and laboratory samples were stored in a freezer at  $\leq$ -18°C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen



field samples and laboratory samples were shredded with dry ice in a cutter. Representative parts of the shredded field samples and laboratory samples were transferred into polystyrene boxes separately for analysis or archiving and stored at  $\leq$ -18°C.

Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU methyl⁽²⁾ sulfoxide), were determined by LC-MS/MS according to method 00984 (**1999**), 05/02 2007, <u>283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements onlined within SANCO/3029/99 rev 4.

Residues of these compounds were extracted from 10 g of sample material (5 g for wheat staw) by two a successive extractions using a high-speed blender with a mixture of acetonitrile:water (80,20; v:v). After centrifugation the extract volume was adjusted. They, the extracts were diluted ten times by adding the internal standards:

- One dilution was performed under acidic conditions. This extract allowed the determination of FLU-PCA and FLU-methyl-sulfoxide
- FLU-PCA and FLU-methyl-sulfoxide
   In parallel, another dilution was performed under basic conditions; this extract aboved the determination of FLU, FLU-benzamide and FLU-7-QU.

An aliquot of the extracts was injected into LC-MS/MS operated in Electrospray 2000 mode:

- One injection in positive electrosphiry ionization for the determination of FLG, FLU-benzamide and FLU-7-OH.
- Another injection in negative electrospray prization for the determination of FLU-PCA and FLU-methyl-sulfoxide under different conditions.

The linearity was demonstrated in Each analytical batch with a 1/x weighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standardization using isotopically stable labelled internal standards.

The Limit of Quantification (LOQ), expressed as fluopyram, defined as the lowest validated fortification level, was 0.09 mg/kg for wheat straw and 0.01 mg/kg for all other matrices.

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU egulatory requirements outfined within SANCO/3029/99 rev 4.

### **Findings**

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and reated samples from the study in each set of analyses. The means of the concurrent recoveries were for all fortification levels within the acceptable range of 70 - 110 % except for FLU methyl sulfoxed at 122 % at 0.1 mg/kg. All overall mean recoveries are in the acceptable range of  $70^{-110}$  %, therefore, the results are considered valid. Recovery results are presented in Table 6.6.2- 30.

No residue of fluopyram or related metabolites were found above the LOQ in any of the control samples of rotational crop matrices analysed

The residue vers of fluor fluor ram and its relevant metabolites in the rotational crop matrices of pea, field are summarized in the Table 6.62-31.

The storage period of deep-frozen samples is up to 365 days for green seeds and 352 days for dry seeds.

# Residues in pea, field

In triat 08-2178-01 (PBI 28 days), residues of fluopyram (AE C656948) and its metabolites (FLU-benzamide, FLU-7-OH, FLU-methyl-sulfoxide) were all < 0.01 mg/kg in pea, field matrices (both green



seed and dry seed) at harvest and at BBCH 79. Residues of FLU-PCA were 0.02 mg/kg in green seeds and 0.03mg/kg at harvest in dry seeds.

In trial 08-2178-02 (PBI 28 days) residues of fluopyram (AE C656948) and its metabolites (FLUbenzamide, FLU-7-OH, FLU-methyl-sulfoxide) were all < 0.01 mg/kg in pea, field matrices (both green seed and dry seed) at harvest and at BBCH 79. Residues of FLU-PCA were 0.01 mg/kg in gree and 0.03mg/kg at harvest in dry seeds.

### Conclusions

Following one spray application conducted with fluo gram SC500 bare soil at Orate of 0.5 kga.s./hg A CONTROL OF CONTROL O residues in succeeding crops were analysed for fluopyram (AE C656948) and itometabolites fluopyrambenzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FCU-PCA, AE C657188) and fluopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl suffoxide (AE J344122) using a validated selective HPLC-MS/MS analytical method.

These data show that residues in pea (seed) as succeeding crop are covered by the current EC MRC



Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD*(0)
Fluopyram (AE C65	56948)			A A
	0.01	86; 92; 83	87 🔬	£5.3 ×
Pea, field	0.10	96; 99; 94	96	<u></u> 2.6 ¢
Dry seed	1.0	94 🖏	24	\$ ~ ~ ~
-		Overall recovery (n=7)	92	
	0.01	89; 95; 93 🗸	^{©%} 92 ×	3.3 5 4
Pea, field	0.10	109; 106; 105	0 [×] 107.	2.00
Green seed	1.0	97.	A 99 Q	
		Overall recovery (n=7)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	N
Fluopyram-benzam	ide (AEF14881		Y X A	$\gamma \sim \gamma \sim \gamma$
ruopyrum benzum	0.01	69,87;64	N B N	L 17 L . °
Pea, field	0.10	91; 89; <b>8</b> 7	Q 489 Q	
Dry seed	1.0	82	× 40, ×	
Dry seeu	1.0	Querally recovery (n=7)	81	13.50
	0.01			
D (* 11	0.01	98; 95; 96	27 89 <u>6</u> 27 896 62	3,5
Pea, field				<u>, 4.6</u>
Green seed	1.0		<u>90</u> <u>91</u>	J '¥
		•Overall recovery (n=7)		5.9
Fluopyram-pyridyl-				0
	0.01	84; <b>98</b> , 89 °	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Q 7.9
Pea, field	مُ	89 <b>59</b> 0; 925	× \$ 90 \$	1.7
Dry seed	1.0		& <u>80</u> 0	
		Óverall recovery (n∈7)	0° 389 2	6.4
	0,01	~ ~ 98; 83; 80 ~ . (	87	11.1
Pea, field 🔊	0.10	93,95;103	6 ⁴ 97	5.5
Green seed	≫ 1.0	91, 9	A W	
ð .		Overall recovery (p.7)	<b>\$</b> 092	8.8
Fluopyram,7-hydro	xv (BCS-AAfd		<u>v</u>	
	0.01	78; 81; 75, ~~	~ 78	3.8
Pea, field	0,10	26; 103,000 V	<u>∞</u> 0″ 100	3.5
Dry seed	1.0	90 [×] %, ,	\$ 90	
Dij seca		Overall recovery (n=7)	<u>89</u>	12.5
	0.01	₩ \$9,90; <b>\$</b>	89	1.1
Dec fol		Q3; 10 Q101	102	1.1
Pea, field Green seed		1805, 1819 101	95	
Green seed				
		Overall recovery (n=7)	95	6.7
Fluopycom-methyls			07	17.7
A I	© <u>0.01</u>	83; 104, 74	87	17.7
🕎 Pea, field 🏾 🎽	9.10 ×	Q 105; Q91; 107	104	2.9
Dry seed	1.0 C	<u>2</u> 102	102	
Dry seed		Overal recovery (n=7)	97	13.2
_0" ~	<b>1</b> 9901	<i>Q</i> , 73; 90; 77	80	11.1
Pea, field 🖉	0.10 🔬	[•] 113; 113; 109	112	2.1
Green seed	$010^{\circ}$	104	104	
19 N	A ~~	Overall recovery (n=7)	97	17.5
C forteffection lawal PSI	Palative Standard		21	1110

Table 6.6.2- 30:	Recovery data for fluopyram (AE C656948) and its metabolites in pea, field.	
------------------	-----------------------------------------------------------------------------	--

FL: for first cation (yel, RSL) Relative Standard Deviation * some RSDs were not calculated as there were only two individual recoveries given Final determination as: fluopyram Residues calculated as: fluopyram Final determination as: FLU-benzamide Residues calculated as: fluopyram Final determination as: FLU-methylsulfoxide Residues calculated as: fluopyram Final determination as: FLU-PCA Residues calculated as: fluopyram



Page 735 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram 4

Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application rate treatment <u>to bare soil or ta</u> <u>crop</u>	arget or no. of treatments and last	Portion analysed	Growth stage at sampling	ect va	L Prof	Residues		CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTERP CONTER	0 ⁷⁶	PHI (days)
	(a)	(b)	kg Water a.s./ha (L/ha)	kg a.s./hL	TU GE	d the constant	as AE C056948	(7656948	1/2656948	6658948	Costone States Sulfoxide as AE Costone States Costone States Costo	Total residue calc.	(e)
08-2178-01 Spain 08850 Gava - Barcelona Cataluña Europe, South F 2008	Application to bare soil PBI: 28 d Rotational crop: Pea, field Utrillo	1) 11.04.2008 2) 20.05.2008 - 30.06.2008 3) 20.06.2008 - 30.06.2008	apalor ocuralor		seed green Steed, dry JJD		+ Dil -			<0.01 ATO	<0.01	<0.02	105
08-2178-02 Italy 40128 Bologna Emilia - Romagna Europe, South F 2008	Application to bare soil PBI: 28 d Rotational crop: Pea, field Pepone	- 15.07.2008		(G)7 12.05 2008 TO 12.05 2008 0 1 0 0 0 1 0 0 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	sced (b) seed (b) b	87.CT	₹0.01 ₹	<0.01	0.01	<0.01 <0.01	<0.01	<0.02 <0.02	106 119
(a) According	g to CODEX Classifica levant t be indicated with stage description of se F alculated : Jim	or BB Code	(e)	Application (Lake Pre-harve ficlude: Clinatic conditions nich metabolites are included autent	est invertal, PHI, Reference to an	underline) nalytical methoc	d and	<ul><li>(i) Applica</li><li>(j) Method</li><li>(k) LOQ</li></ul>	ation type ation method 1 information in control	(l) (m) #	Method valida Storage (max) ! based on dat P based on pro no data availa	e of analysis oduction date	
	C	W. L.											73



Data Point:	KCA 6.6.2/16
Report Author:	
Report Year:	2009
Report Title:	Determination of the residues of AE C656948 in/on maizecorn after spraving of
-	fluopyram SC 500 in the field in France (North) and Germany
Report No:	08-2168
Document No:	<u>M-355324-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/41 EEC of July 16, 1991, Annex II, part X, section 6 and Annex III, part A, section 8 Residues in a con Treated Products, pood and
study:	6 and Annex III, part A, section 8 Residues in a con Treated Products, bood and
	Feed EC guidance working document 7029/X0/95 rev. 5 (1987-07-22)
Deviations from current	none A Q & A L
test guideline:	
Previous evaluation:	No, not previously submitted
	Study was not found in DAR AR and the Addenda Study was not found in DAR
GLP/Officially recognised	Yes, conducted under GLP Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes in the second secon

### Materials and Methods

The purpose of the study was to determine the magnitude of the relevant residues of fluopyram (AE C656948) and its metabolites fluopyram-benzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE C657188),fluopyram -hydroxy (BC S-AA10065) and fluopyram-methyl sulfoxide (AE 1344122), in/on maize corn (green material, kernel and immature kernel (milk ripe)) harvested after one spray application with Fluopyram 8C 500 on bare soil 30 days before sowing of maize/corn in northern Europe (northern France and Germany). The investigated plant back interval was 30 days.

The formulation Fluopyram SC 500 is a suspension concentrate formulation containing 500 g/L of Fluopyram. The application was done with 1.0 L test tem per ha and 300 L water per ha on bare soil followed by incorporation into the soil 5 cm, 32 days and 8 cm, 31 days before the planting of maize in trial 08-2168-01 and 08-2108-02 respectively.

In both trials the application was done with 4.0 L of test item/ha and a water rate of 300 L/ha, corresponding to spray concentration of the test item of 0.33% (0.17% of active substance in the spray liquid). The application rate was 0.50 kg fluopyram/ha.

For residue analysis samples of maize/corp (green material, kernel and immature kernel (milk ripe)) were taken from the treated and the control plots. In order to obtain representative samples of the raw commodity, samples were taken according to S-sampling (trial 08-2168-01) and at random (trial 08-2168-02) along the treated and the control plot.

Samples of green material were taken in both rials at growth stage BBCH 34. Samples of ear without husk were taken at BBCH 75 and then were used to generate laboratory samples of immature kernel (milk ripe). Samples of kernel were taken at harvest (BBCH 89).

The field samples from all trials were stored deep-frozen within 24 hours after sampling and until dispatch. All field and laboratory samples of trial 08-2168-01 were shipped by deep-freeze lorry, those of trial 08-2168 02 by car with dry ice and arrived in good condition. The field samples and laboratory samples were stored in a freezer at  $\leq$ -18°C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field and laboratory samples were shredded with dry ice in a cutter. Representative parts of the shredded field and laboratory samples were transferred into polystyrene boxes separately for analysis or archiving and stored at  $\leq$ -18°C.



Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (**1999**, 05/02/2007, <u>M-283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method, are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitatile:water (80,30; v:3). After centrifugation the extract volume was adjusted. Then, the extracts were diffuted ten times by adding the internal standards:

- One dilution was performed under acidic conditions: this extract allowed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed the determination of FLU, FLU-benzamide and FLU-7-Q.

An aliquot of the extracts was injected into LO-MS/MS operated in Electrospray donization mode:

- One injection in positive electrospiration for the determination of FLU, FLU benzamide and FLU-7-OH.
- Another injection in negative electrospray ionization for the determination of FLU-PCA and FLU-methyl-sulfoxide under different conditions

The linearity was demonstrated in each analytical batch with above the calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by Onternal standardization using isotopically stable labelled internal standards.

The Limit of Quantification (DOQ), expressed as theopyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat shaw and 0.01 mg/kg for all other matrices.

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

### Findings ~

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and treated samples from the study in each set of analyses. The means of the concurrent recoveries were for all fortification levels within the acceptable range of 70 - 110% and all the result are considered valid. Recovery results are presented in Table 6.6.2-32.

No residue of huopy cam or clated metabolites were found above the LOQ in any of the control samples of rotational crop matrices analysed.

The residue levels of fluopyram and its relevant metabolites in the rotational crop matrices of maize/corn are summarized in the Table 6.6.2-33.

The storage period of deep frozen samples is up to 279 days in immature kernels, 281 days in kernel and 352 days in green material.

# Residues in maize corn

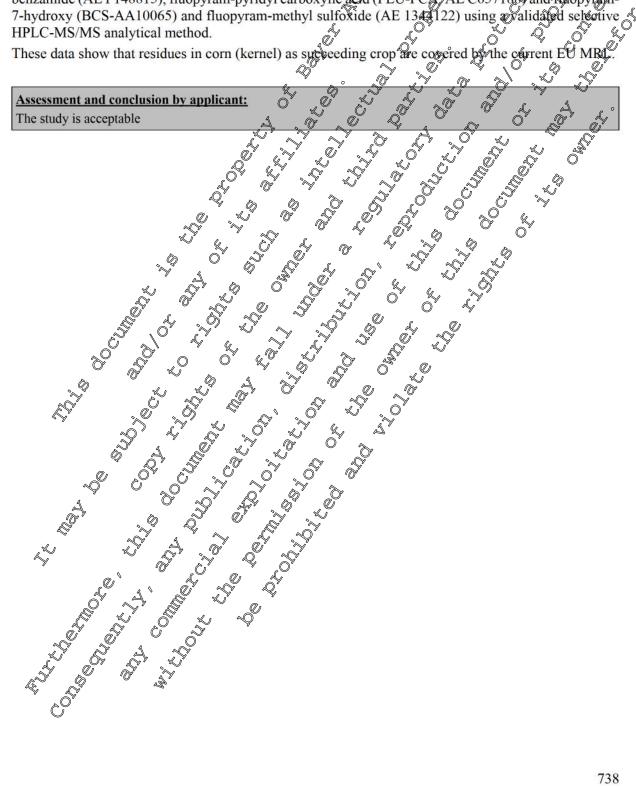
In trial 0, 2168 1 (PBF 32 do's), residues in corn green material (BBCH 34) were at the level of 0.07 mg/kg (Huopyram), 0.01 mg/kg (FLU-benzamide), 0.03 (FLU-7-OH) and <0.01 mg/kg (FLU-PCA and FLU) methy sulfoxate). The residues of fluopyram (AE C656948) and its metabolites in other corn matrices (Gernel & immature kernel) were all <0.01 mg/kg.



In trial 08-2168-02 (PBI 31 days), residues of fluopyram (AE C656948) and its metabolites were all < 0.01 mg/kg in corn matrices except for fluopyram (AE C656948) in corn green material (BBCH 34) de la constante de la constant in which the residues were at the level of 0.05 mg/kg.

### Conclusions

Following one spray application conducted with fluopyram SC500 to bare soil at a rate of 0.5 kg a.s./ha residues in succeeding crops were analysed for fluopyram (AE C656948) and its metabolites fluopyram benzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA AE C657188) and Avopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1349122) using availabed selective





Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD*(())
Fluopyram (AE C65	6948)		S	4.4
••/	0.01	80, 88, 67, 86	80 ,	Q11 X
Corn, green	0.10	92, 91, 96, 84	91	, 0° 5, 6° , 4°
material	1.0	97 🏷	2\$	
		Overall recovery (n=9)		
	0.01	93, 91, 79, 100	<u>۵</u> 91 ×	10 S a
Corn, immature	0.10	87, 108, 99, 86	95° 0	× 110 0
kernel	1.0	96		
		Overall recovery (n=9)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
	0.01	83, 88, 93, 89	88 %	$\gamma \gamma 4 \gamma \gamma 4$
	0.10	101, 92, 95, 92	<u></u>	L 52 0
Corn, kernel	1.0	A 940 A	Q 494 (N	
	1.0	Overall recovery (n=9)	97.0 [×]	6
luopyram-benzami	de (AFF14881			
Tuopyram-Denzami	0.01	91 95, 11 Q 80 V		13
Corn, green	0.01	<b>94</b> , 86, <b>89</b> , 84		
material	1.0	<u>× × × × × × × × × × × × × × × × × × × </u>		
material	1.0	• Overall recovery (n=9)	2 90 °	× 10
	0.04	98,97,110	<u> </u>	
C	<b>U</b>	\$4, 86@3, 88 °		÷
Corn, immature	0,10 ×1.0	98 L		<i>Q</i> 4
kernel	~1.0			
		@veralbrecovery (n=90)		8
Ő		91, 108, 97, 105 <u>9</u>		8
Corn, kernel 🖉	AU 10	× ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	79	12
	01.0	87 3	0 [×] 87	
	ð,	Øverall recovery (n=9)	57 <b>89</b>	14
luopyram-pyridyl-		(AE C6571886)		
. Q	0.01	A 78, HOS, 78, 79	86	18
Corn, green	0.10	78, 81, 77, 79	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	2
material .	01.00	<u>~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~</u>	<u> </u>	
		Overall recovery (n=9)	<u>ه گ</u>	12
, ST	<u> </u>	<u>م</u> 97, <b>98</b> , 88, 6	86	18
Corn, immature	0.10	93, 80, 79, 80	83	8
kernel		0 870 0	87	
		Overall recovery (0r=9)	85	12
	0.01	2 77, 84, 84, 96	85	9
Corn, kernel	0.16Q	84 82, 73 79	79	5
Corn, kernel	k0	X / 88	88	
		Oxerall recovery (n=9)	83	8
Fluopyram-7-hydrox	y (BCS-AA10			
<u> </u>	0.00	6 <b>Q</b> ,93, 95, 105	90	17
Corn, green	) <u>9</u> 90	@183, 85, 97, 84	87	8
material 👋		~ 88	88	
material		Overall recovery (n=9)	89	12
	A 07697	73, 95, 92, 101	90	13
Corn, immature	>0,10	83, 84, 96, 89	88	7
Lorpol	× 1.0	94	94	
& kernel	~ 1.0		94 90	
<u> </u>	0.01	Overall recovery (n=9)		<u>9</u>
	0.01	82, 94, 92, 100	92	8
Corn, kernel	0.10	87, 96, 94, 91 88	92 88	4

### Table 6.6.2- 32: Recovery data for fluopyram (AE C656948) and its metabolites in corn



Crop/Sample material       FL (mg/kg)         Fluopyram-methylsulfoxide (AE1344         Corn, green 0.10         material         1.0         Corn, green 0.10         material         1.0         Corn, green 0.10         material         1.0         Corn, immature 0.10         kernel         1.0         Corn, kernel         1.0         FL: fortification level, RSD - Relative Standard DA         * some RSDs were not calculated as there were on Final determination as: FLU-benzamide Residues calculated as there were on Final determination as: FLU-benzamide Residues calculated estimates calculated as there were on Final determination as: FLU-PCA Residues calculate Final determination as: FLU-PCA Residues calculate calculate estimates calculated estimation as: FLU-PCA Residues calculated estimates imat			,
Fluopyram-methylsulfoxide (AE1344         0.01         Corn, green         0.10         material         1.0         Corn, immature         0.01         Corn, immature         0.01         Corn, immature         0.01         Corn, immature         0.01         Corn, kernel         1.0         * some RSDs were not calculated as there were on         Final determination as: FLU-methylsulfoxide Registues calculate         Final determination as: FLU-TOH Residues calculate         Final determination as: FLU-TOH Residues calculated         Final determination as: FLU-TOH Residues calculated         Final determination as: FLU-TOH Residues calculated         Compute       Arther the	Single values (%)	Mean value (%)	RSD*(%)
Fluopyram-methylsulfoxide (AE1344 0.01 Corn, green material 1.0 0.01 Corn, immature 0.01 Corn, immature 0.01 Corn, kernel 1.0 FL: fortification level, RSD - Relative Standard Da * some RSDs were not calculated as there were on Final determination as: FLU-benzamide Residues calculated Final determination as: FLU-Denzamide Residues calculated Final determination as: FLU-PCA Residues calculated Final determination as: FLU-PCA Residues calculated Final determination as: FLU-TOH Residues cal	Overall recovery (n=9)	92	6 🔊 🛇
Corn, green material       0.01         Imaterial       1.0         Corn, immature double       0.01         Corn, kernel       1.0         FL: fortification level, RSD - Relative Standard Date         * some RSDs were not calculated as there were on         Final determination as: FLU-benzamide Residues calculated         Final determination as: FLU-PCA Residues calculated         Final determination as: final determination as: Flut         Final determination as: final determination as: f	122)		
Corn, green material       0.10         Imaterial       1.0         Corn, immature       0.01         Kernel       1.0         Imaterial       0.01         Corn, immature       0.01         Imaterial       0.01         Corn, immature       0.01         Imaterial       0.01         Corn, kernel       0.01         Imaterial       0.01         Corn, kernel       0.01         Imaterial       0.01         Corn, kernel       1.0         Imaterial       0.01         Corn, kernel       1.0         Imaterial       0.01         Corn, kernel       1.0         Imaterial       1.0         FL: fortification level, RSD - Relative Standard Do         * some RSDs were not calculated as there were on         Final determination as: FLU-benzamide Residues calculated as there were on         Final determination as: FLU-7OH Residues calculated as there were on         Imaterial       Imaterial         Imaterial       Imaterial         Imaterial       Imaterial         Imaterial       Imaterial         Imaterial       Imaterial         Imaterial       Imateri	95, 80, 90, 95	90	
material 1.0 0.01 Corn, immature 0.10 kernel 1.0 0.01 Corn, kernel 0.00 FL: fortification level, RSD - Relative Standard Do * some RSDs were not calculated as there were on Final determination as: FLU-methylsulfoxide Resi Final determination as: FLU-methylsulfoxide Resi Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determinat	82, 72, 78, 75	77 🐨	6 5
Corn, immature       0.01         Image: constraint of the second sec	80	80 🔬	
Corn, immature kernel       0.01         1.0       0.10         kernel       1.0         0.01       0.01         Corn, kernel       0.01         1.0       0.01         Corn, kernel       1.0         1.0       0.10         FL: fortification level, RSD - Relative Standard De * some RSDs were not calculated as there were on Final determination as: fLU-henzamide Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as the end on a s: FLU-PCA Residues calculated as the end on a s: FLU-PCA Residues calculated as the end on a s: FLU-PCA Residues calculated as the end on a s: FLU-PCA Residues calculated as the end on a s: FLU-PCA Residues calculated as the end on a s: FLU-PCA Residues calculated as the end on a s: FLU-PCA Residues calculated as the end on a s: FLU-PCA Residues calculated as the end on a s: FLU-PCA Residues calculated as the end on a s: FLU-PCA Residues calculated as the end on a s: FLU-PCA Residues calculated as the end on a s: FLU-PCA Residue calculated as the end on a s: FLU-PCA Residue calculated as the end on a s: FLU-PCA Residue calculated as the end on a s: FLU-PCA Residue calculated as the end on a s: FLU-PCA Residue calculated as the end on a s: FLU-PCA Residue calculated as the end on a s: FLU-PCA Residue calculated as the end on a s: FLU-PCA Residue calculated as the en	Overall recovery (n=9)	83	× 10 ×
Corn, immature kernel       0.10         1.0       1.0         Corn, kernel       0.01         0.10       0.10         FL: fortification level, RSD - Relative Standard Determination as: fluopyram Residues calculated as there were on Final determination as: fluopyram Residues calculated as there were on Final determination as: FLU-benzamide Residues calculated as there were on Final determination as: FLU-benzamide Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as the ever on Standard Determination as: FLU-PCA Residues calculated as the ever on Final determination as: FLU-PCA Residues calculated as the ever on the event of the	103, 89, 88, 85	Ô.	
kernel     1.0       Corn, kernel     0.01       Image: the standard process of the standard pr	87, 80, 76, 69 [°]	~78	
Corn, kernel       0.01         FL: fortification level, RSD - Relative Standard Determination as: fluopyram Residues calculated as there were on Final determination as: fLU-benzamide Residues calculated as there were on Final determination as: FLU-benzamide Residues calculated as there were on Final determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-benzamide Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as there were on Sinal determination as: FLU-PCA Residue calculated as there were on Sinal determination as	84	<u> </u>	
Corn, kernel     0.01       FL: fortification level, RSD - Relative Standard De* some RSDs were not calculated as there were on Final determination as: fLU-benzamide Residues calculated as there were on Final determination as: FLU-methylsulfoxide Residues calculated as there were on Sinal determination as: FLU-PCA Residues calculated as the event on as: FLU-PCA Residues calculated as the event on as: FLU-roth Residues calculated as the event on a set of the event of t	Overall recovery (n=9)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u> 11</u>
Corn, kernel	89, 88, 27, 82	$\sim$ $\otimes$ $\circ$	
FL: fortification level, RSD - Relative Standard Do * some RSDs were not calculated as there were on Final determination as: FLU-benzamide Residues calculated final determination as: FLU-benzamide Residues calculated Final determination as: FLU-PCA Residues calculated Final determination as: FLU-PCA Residues calculated Final determination as: FLU-7OH Residues calculated Final determination as: FILI-7OH Residues calculated Final de	<u> </u>	82 0	
FL: fortification level, RSD - Relative Standard De * some RSDs were not calculated as there were on Final determination as: FLU-benzamide Residues of Final determination as: FLU-benzamide Residues calcula Final determination as: FLU-PCA Residues calcula Final determination as: FLU-PCA Residues calcula Final determination as: FLU-PCA Residues calcula Final determination as: FLU-7OH Residues calcula Final determination calculation	<u> </u>	<u> </u>	
FL: fortification level, RSD - Relative Standard Da * some RSDs were not calculated as there were on Final determination as: FLU-benzamide Residues Final determination as: FLU-DCA Residues calculated Final determination as: FLU-7OH Residues calculated Final determination as: FL	Overall recovery (n=9)		
$\bigcirc$	Ades calculated as fluopyram ited as fluopyram it		
			740



Page 741 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram 3 @ °

Table 6.6.2- Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application rate per treatment <u>to bare soil or target</u> <u>crop</u>	Dates of treatment or no. of	Portion apartysed	Growte stage at sampling		arties	ReQuirues	ر (mg/kg) (************************************	DID TEODIC CONTER CONTER CONTER CONTER CONTER	, t ^{\$}	PHI (days)
	(a)	(b)	kg a.s./ha (L/ha)			OTU C(d) C.U.	AE C656948 às AE 2656948	FLU- benzamide MAE Ve656948	FLU- PCA as ME C656948		FLU- methyl- sulfoxide as AE C656948	Total residue calc.	(e)
08-2168-01 France, north 71570 Saint Symphorien	Application to bare soil PBI: 32 d	1) 10.05.2008 2) 30.07.2008 - 10.08.2008 3) 15.10.2008		08.04.206	græn material kernel immiture	34 0 75 10 1	0.07 0.01 <0.01	0.01 30 <0.01 30	<0.01 5 T	0.03 ⁴⁰¹⁴ 5 <0.01	<0.01 <0.01	0.08 <0.02	93 141
d'Ancelles Bourgogne Europe, North F 2008	<u>Rotational</u> <u>crop:</u> Maize / Corn, field PR37Y12	- 21.10.2008		of fall	Vremel	1 2 85° of	J.O.L	D. D	Q.01	<0.01	<0.01	<0.02	192
08-2168-02 Germany 51399 Burscheid	Application to bare soil PBI: 31 d	1) 05.05.2008 2) 15.07.2008 - 30.07.2008 3) 16.09 2008			100 1	34 CS 0595	0.05	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0.06 <0.02	67 140
Nordrhein- Westfalen Europe, North F 2008	<u>Rotational</u> <u>crop:</u> Maize / Corn, field		dor Julie cat		ketture ketture	0.75 0.180 [°] [°]	<0.01	<0.01	<0.01	<0.01	<0.01	<0.02	165
(b) Only if re (c) Year mus	t be indicated	0.2	(f) Reparks may include	aion (Label pre-file) Climatic conditions etabolite are included	; Reference to a	I, underline) analytical methoc	1 and	<ul> <li>(i) Applica</li> <li>(j) Method</li> <li>(k) LOQ</li> </ul>	ation type ation method 1 information in control	(l) (m) #	Method valida Storage (max) ! based on dat P based on pro no data availal	e of analysis oduction date	
	$C_{O_{P_n}}$	W The											741



Data Point:	KCA 6.6.2/17
Report Author:	
Report Year:	2009
Report Title:	Determination of the residues of AE C656948 in/on maize corn after spraying of
	fluopyram SC 500 in the field in Italy and Spain
Report No:	08-2179
Document No:	<u>M-355327-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/41 (EEC of July 16, 1991, Annex II, part 4, section 6 and Annex III, part A, section 8 Residues in Son Treated Products, Food and
study:	6 and Annex III, part A, section 8 Residues in or on Treated Products Food and
	EC guidance working document 7029/VI/9 Prev. 5 (1997-67-22)
Deviations from current	none $Q^{\prime} \rightarrow Q^{\prime} \rightarrow Q^{\prime} \rightarrow Q^{\prime}$
test guideline:	
Previous evaluation:	No, not previously submitted
	No, not previously submitted Study was not found in DAW/RAR and the Addenda
GLP/Officially recognised	Yes, conducted under GLP/Offreially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes a win win win win of a company of a company with the second s
	Yes V V V V V V V V V

### Materials and Methods

The purpose of the study was to determine the magnitude of the relevant residues of fluopyram (AE C656948) and its metabolites thopyram-ben amide (AE F1488 5), fluopyram pyridyl carboxylic acid (FLU-PCA, AE C657788), fluopyram-7-hodroxy BCS-AA10065) and Duopyram-methyl sulfoxide (AE 1344122), in/on maze/confr (green material, kernel and immadure kernel (milk ripe)) harvested after one spray application with Puopyram SC 500 on bare soil 30 days before sowing of maize/corn in southern Europe (Spain and Italy). The investigated plant back interval was 30 days.

The formulation Fluopyram SC 500 is a suspension concentrate formulation containing 500 g/L of Fluopyram. The application was done with 1.0 L test item per ha and 300 L water per ha on bare soil followed by incorporation into the soil < 8 cm. 32 days and 5-90 cm, 28 days before the planting of maize in trial 08-21/9 01 and 08-21/9-02 respectively.

In both trials the application was depe with 1.0  $L^{\circ}$  of test item/ha and a water rate of 300 L/ha, corresponding to a spray concentration of the test item of (233% (0.17% of active substance in the spray liquid). The application rate was 250 kg through the spray liquid.

For residue analysis samples of maize/corn, green material, kernel and kernel, immature (milk ripe) were taken from the treated and the control plots. In order to obtain representative samples of the raw commodity, samples were taken according to different sampling procedures from various parts of each treated and control plot.

Samples of green material were taken in both trials at growth stage BBCH 34. Samples of ear without husk were taken at BBCH 75 and then were used to generate laboratory samples of immature kernel (milk ripe). Samples of kernel were taken at harvest (BBCH 89).

The field samples from all trials were stored deep-frozen within 24 hours after sampling and until dispatch All field and laboratory samples of trial 08-2168-01 were shipped by deep-freeze lorry, those of trial 08-2168-02 by car with dry ice and arrived in good condition. The field samples and laboratory samples were stored in a freezer at  $\leq$ -18°C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field and laboratory samples were shredded with dry ice in a cutter. Representative parts of the shredded field and laboratory samples were transferred into polystyrene boxes separately for analysis or archiving and stored at  $\leq$ -18°C.



Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (**1998**, 05/02/2007, <u>M-283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitatile:water (80,30; v:3). After centrifugation the extract volume was adjusted. Then, the extracts were diffuted ten times by adding the internal standards:

- One dilution was performed under acidic conditions: this extract allowed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed the determination of FLU, FLU-benzamide and FLU-7-Q.

An aliquot of the extracts was injected into LO-MS/MS operated in Electrospray donization mode:

- One injection in positive electrospiration for the determination of FLU, FLU benzamide and FLU-7-OH.
- Another injection in negative electrospray ionization for the determination of FLU-PCA and FLU-methyl-sulfoxide under different conditions

The linearity was demonstrated in each analytical batch with above weighted Calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by Onternal standardization using isotopically stable labelled internal standards.

The Limit of Quantification (FOQ), expressed as theopyrain, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat shaw and 0.01 mg/kg for all other matrices.

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

### Findings

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and reated samples from the study in each set of analyses. The means of the concurrent recoveries were for all fortification levels within the acceptable range of 70 - 110% and all the results are considered valid. Recovery results are presented in Table 6.6.2-34.

No residue of huopy cam or clated metabolites were found above the LOQ in any of the control samples of rotational crop matrices analysed.

The residue levels of fluopyram and its relevant metabolites in the rotational crop matrices of maize/corn are summarized in the Table 6.6.2-3/5.

The storage period of deep frozen samples is up to 318 days in immature kernels, 264 days in kernel and 353 days in green material.

# Residues in maize corn

In trial 0 217901 (PBI 34 days), residues of fluopyram (AE C656948) and its metabolites were all < 0.01 mg/kg/m correspondences except for fluopyram (AE C656948) in corn green material (BBCH 34) in which the residues were at the level of 0.03 mg/kg.

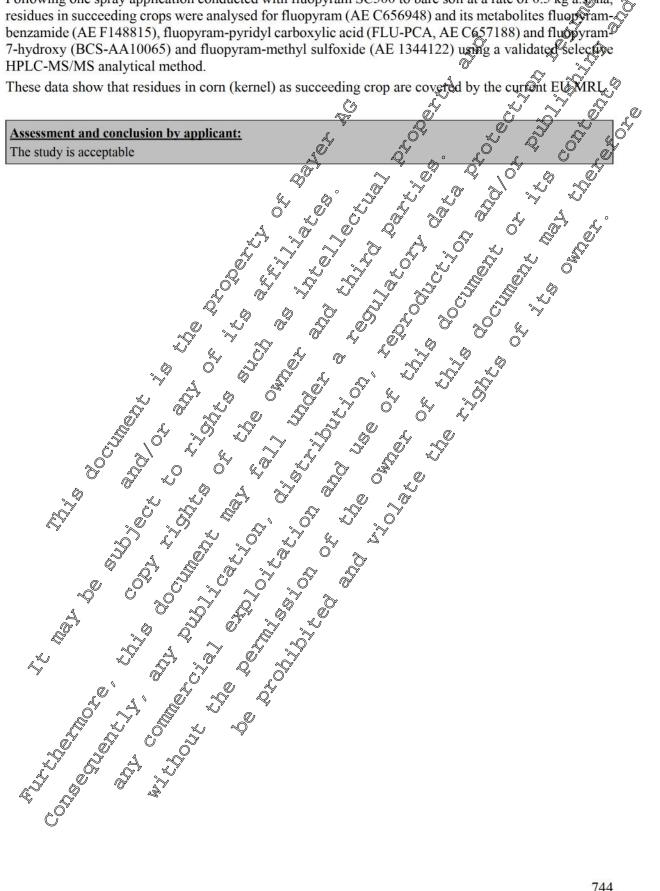
In trial 68-2179-02 (PBI 28 days), residues of fluopyram (AE C656948) and its metabolites were all < 0.01 mg/kg in all corn matrices (green material BBCH 34, immature kernel and kernel).



### Conclusions

Following one spray application conducted with fluopyram SC500 to bare soil at a rate of 0.5 kg a.s. ha, residues in succeeding crops were analysed for fluopyram (AE C656948) and its metabolites fluopyram benzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE C657188) and fluopyram 7-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122) using a validated selective HPLC-MS/MS analytical method.

These data show that residues in corn (kernel) as succeeding crop are covered by the current EUMR





Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD*(25)
Fluopyram (AE C650				4.5
Corn, green	0.01	84	84	
material	0.10	85; 87	86	<u> </u>
material		Overall recovery (n=3)	85	L' 2 S
	0.01	89 🚿	89	
Corn, immature	0.10	92	<u>0[™]92</u> ×	
kernel	1.0	79	Q ^Y 79 .	<u> </u>
		Overall recovery (n=3)	~~~~ <b>8</b> 9 ~Q`	
	0.01	85	Q ⁷ ~85 ~ 4	
Corn, kernel	0.10	×86	86 %	ý Ý [×]
	1.0	97 2 0	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
		Overall recovery (n=3)	89 2	
Fluopyram-benzamio				<u>V</u>
Corn, green	0.01	V10 2		<u> </u>
material	0.10	<u>6</u> 492; 87 5	~ <u>\$</u>	<u> </u>
		Overall recovery (n=3)	<b>3 39</b> 6 8	J
	0.01		2 93 °C	ŷ *>
Corn, immature	0.10	× ¹⁰ 93 × 0	<u>93</u> 6	Y
kernel	1.0	85	L	
	<u> </u>	[✓] Overall recovery (n ² 3)	88	<u>©</u> 5
	\$0.01		<u> </u>	
Corn, kernel	0.10	<u>\$ 0³ 96 } 0'</u>	<u> </u>	
	× 1.0°			
		Overall recovery (n=3)	<u>94</u>	3
Fluopyram-pyridŷl-c			<u>6</u> 89	
	0.01			
Corn, gran		<u> </u>	× 90	
material		Qverall recovery (n=3)	86	
			× 80	4
Coming the second secon	0,00) 20,10		87 81	
Corn, immature kernel	× 0.10		77	
		Overall recovery (n=2)	82	6
 			82	
~~ Ĉ			74	
Corn, kernel	1.0		89	
E .		Overal recovery (n=3)	81	
Fluopyram-7-hydrox			01	7
<u>riuopyram-7-nyurox</u>		065) <u>(</u> ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	78	
Corn, green	0.10	91; 79	85	
material 🖉 🔪	0.10	Overall recovery (n=3)	83	9
	× 0\$51		80	
Corn, inimature		<u> </u>	96	
kernel	1.0	<u>90</u> 75	75	
		Overall recovery (n=3)	84	13
- Ž – Č	>0.01	78	84 78	
NO O	×0.01 ×0.10	87	87	
Corn Kernel	1.0	87	87	
ĉ	1.0			7
	lforido (AE12	Overall recovery (n=3)	84	1
Fluopyram-methylsu			00	
	0.01	80	80	

### Table 6.6.2- 34: Recovery data for fluopyram (AE C656948) and its metabolites in corn



Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD*(%) °
Corn, green	0.10	79	79	, 🗳 🥳
material	1.0	80	80	5
material		Overall recovery (n=3)	80 80	1° O
	0.01	87	87 🔊	\$
Corn, immature	0.10	77	77 🔊	
kernel	1.0	76	76	
Ker ner	1.0	Overall recovery (n	80	
	0.01			
	0.01	73	0 72	
Corn, kernel	0.10	73	73	
,	1.0	76	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
		Overall recovery (n=3)		
* some RSDs were not calcula Final determination as: fluopy Final determination as: FLU-F Final determination as: FLU-F Final determination as: FLU-F	ated as there were tram Residues calco benzamide Residues calco benzamide Residues calco benzamide Residues calco to the residues ca	83 73 76 Overall recovery (n=3) Deviation only two individual recoveries given usuated as: fluopyram sulated as: fluopyram pulated as: fluopyram pulate		
				746



Page 747 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Fable 6.6.2- (	35: Results		rop trials conducto	ed with fluopy	yram		ler PC	3	ert	alda .	10 10 10	⁷ 0 ¹ 0 ¹ 0 6 °	
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application rate per treatment <u>to bare soil or target</u> <u>crop</u>	treatments	Portion analysed	Growth stage of sampling	) · · · ·	J Pros	Residues		CONTER CONTER CONTER CONTER	,¢\$ 0 ^{¶€}	PHI (days)
	(a)	(b)	kg a.s./ha (L/ha) kg		10 2.5 6 2.5	(d) : C =	as AE C056948	as AB	AE	AF C656948	as AE	Total residue calc.	(e)
08-2179-01 Spain 46230 Alginet Comunidad	<u>Application to</u> <u>bare soil</u> <b>PBI:34 d</b>	1) 13.05.2008 2) 10.07.2008 - 25.07.2008 3) 15.09.2008		09.04.2008 09.04.2008	green machial Kernel, immatu@.		0.03	<0.01 0.01 0.01	<0.01 <0.01 0.01 0.01 0.01 0.01 0.01 0.01	<0.01 5 50.01	<0.01 <0.01	0.04 <0.02	78 113
Valenciana Europe, South F 2008	<u>Rotational</u> <u>crop:</u> Maize / Corn, field DKC 6418	- 15.10.2008		et the	vkennel		(\$0.01 \$0.94 \$ \$ \$ \$ 0.01		Ster .	<0.01	<0.01	<0.02	156
08-2179-02 Italy 40128 Bologna Emilia -	Application to bare soil PBI: 28 d	1) 09.04.2008 2) 20.06.2008 - 30.06.2008 3) 20.08.2008			green material kennel, immature	ONTROP I	<0.01	<0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.02 <0.02	86 121
Romagna Europe, South F 2008	Rotational crop: Maize / Corn, field pr33a46	- 10.09.2008				10 ¹⁸⁸⁷	<0.01	<0.01	<0.01	<0.01	<0.01	<0.02	175
(a) According (b) Only if rel (c) Year must (d) Either gro G greenhous Total residue c	to CODEX Classific levant be indicated wth stage description e alculated? Sum	ation / Guide	Remarks may includ	ation Cabel pre-barv Chinatic conditions etabolites are include t	ewinterval, PH ;; Reference to d	I, underline) analytical method	l and	<ul> <li>(i) Applica</li> <li>(j) Method</li> <li>(k) LOQ</li> </ul>	ation type ation method l information in control	(l) (m) #	Method valida Storage (max) ! based on data P based on pro no data availal	e of analysis oduction date	
	CODA	all's hit he	J Y										74



Data Point:	KCA 6.6.2/18
Report Author:	
Report Year:	
Report Title:	Determination of the residues of AE C656948 in/on leek after spraying of
	Determination of the residues of AE C656948 in/on leek other spraying of fluopyram SC 500 in the field in France (North) and Germany
Report No:	08-2164
Document No:	<u>M-357777-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/41 EEC of July 16, 1991, Annex I, part X, section
study:	6 and Annex III, part A, section 8; Residues in P on Treated P oducts Food and
	EC guidance working document 7029/VI/9 Prev. 5 (1997-67-22)
Deviations from current	none
test guideline:	
Previous evaluation:	No, not previously submitted
GLP/Officially recognised	Yes, conducted under OLP Offregally recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes X X X X X X X
	Yes y y y y y y y y y y y y y y y y y y y

I. Materials and Methods

The purpose of the study 08-2164 was to determine the magnitude of residies of fluopyram (AE C656948) and its metabolites fluopyram-benzamide (AE 148865), fluopyram pyridyl carboxylic acid (FLU-PCA, AE C652188), fluopyram-benzamide (AE 148865), and fluopyram-methyl sulfoxide (AE 1344122), in/on leck (whole plant without root) har ested after one spray application with Fluopyram SC 500 on bare soil 30 days before planting of leek in northern Encope (Northern France and Germany). The investigated plant back (nterval was 30 days)

For application the formulation Pluopyram SC 500 was used, a suspension concentrate formulation containing 500 g/L of Finopyran. The application was done on bare soil followed by incorporation into the soil 8 cm) 30 days (trial 08-2164-01) and 3 days (trial 08-2164-02) before the planting of leeks. In both trials the application was done with 4.0 L of test item/ha and a water rate of 300 L/ha, corresponding to spray concentration of the test item of 0.33% (0.17% of active substance in the spray liquid). The application rate was 0.50 kg flappyram/ha.

For residue analysis samples of leeks were taken from the treated and the control plots. In order to obtain representative samples of the raw commodity samples were taken at random along the treated and the control plot.

In both trials, samples were taken from the treated and untreated plot in both trials 14 days before harvest and at harvest.

The field samples were stored deep frozen within 24 hours after sampling and until dispatch. The field samples were shipped by deep-freeze larry (08-2164-01) and by car with dry ice (08-2164-02) and arrived in sood condition. The field samples and lab samples were stored in a freezer at  $\leq$ -18°C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field samples were shredded with dry ice in a cutter. Representative parts of the shredded field samples were dransferred into polystyrene boxes separately for analysis or archiving and stored at  $\leq$ -18°C.

Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (**1997**, 05/02/2007, <u>M-283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method



are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.  $Q_p^{\circ}$ 

Residues of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitrile: water (80:20; v). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

- One dilution was performed under acidic conditions: this extract allowed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed the determination of fluopyram, FLU-benzamide and FLU-7-QU.

An aliquot of the extracts was injected into LC-MSMS operated in Electrosprov Ionization mode:

- One injection in positive electrospray ionization for the determination of fluopyram FLUbenzamide and FLU-7-OH.
- Another injection in negative electrospray ionization for the determination of FLUPCA and FLU-methyl-sulfoxide under different conditions.

The linearity was demonstrated in each malyfical batch with a 1/x weighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient Rayas above 0.99.

The quantification was done by internal standard ation Using Sotopically stable kabelled internal standards.

The Limit of Quantification (LOO), expressed as fluopyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat straw and 0.01 mg/kg for all other matrices.

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANÇO/3029/99 rev 4.

### **Findings**

In order to the ket the performance of the analysical method, pecovery determinations were concurrently performed to the analysis of control and treated samples from the study in each set of analyses. The means of the concurrent recoveries were for all fortification levels within the acceptable range of 70 - 110 % except for FU-methyl-sufficient at 118 % 8 at 9.1 mg/kg. All overall mean recoveries are in the acceptable range of 70 - 110 % therefore, the tesults are considered valid. Recovery results are presented in Table 6.6.2–26.

No residue of fluopyram or related metabolites are found above the LOQ in any of the control samples of rotational crop matrices analysed.

The restrice levels of Duopyram and its relevant metabolites in the rotational crop matrices of leeks are summarized in the in Table 0.6.2-37.

The maximum storage period of deep frozen samples was 363 days.

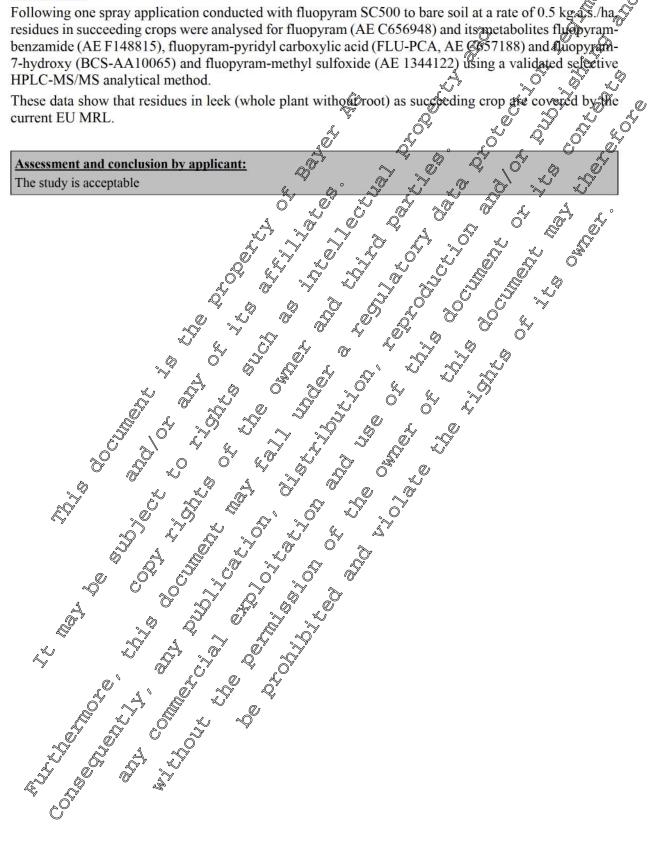
# Residues in Teek (whole fant without poots)

In trial 0 216401 (PB 30 days), residues of fluopyram (AE C656948) were at 0.04 mg/kg in leeks 14 days before harvest and at harvest. The residues of the metabolites (FLU-benzamide, FLU-PCA, FLU-7-OFF FLU-methyl sulfoxide) were < 0.01 mg/kg 14 days before harvest and at harvest.

In trial 08 2164-02 (PBI 31 days) residues of fluopyram (AE C656948) were 0.02 mg/kg and 0.03 mg/kg in potato tubers 14 days before harvest and at harvest, respectively. The residues of the metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methyl-sulfoxide) were < 0.01 mg/kg 14 days before harvest and at harvest.



<u>Conclusions</u> Following one spray application conducted with fluopyram SC500 to bare soil at a rate of 0.5 kg as./ha residues in succeeding crops were analysed for fluopyram (AE C656948) and its metabolites fluopyrambenzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE (\$57188) and Quopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122) using a validated selective HPLC-MS/MS analytical method.





a 10 -	Fortification			
Crop/Sample	level	Single values (%)	Mean value (%)	RSD* (%)
material	(mg/kg)		4	
Fluopyram (AE C65	, ,	60	"Ø"	
Leek	0.01	69		
(whole plant	0.10	96, 100 💍	<b>9</b> 89	× - ~ ~
without root)		all recovery (n=3)	288	
Fluopyram-benzami		4		
Leek	0.01			<u> </u>
(whole plant	0.10	85086	× × 86	$\lambda$ $\vec{x}$ $\vec{y}$
without root)		all recovery (n=3)	<u>بر 81 مر م</u>	S 8.9 V
Fluopyram-pyridyl-o				
Leek	0.01	100 ~ »	× <u>A</u> - S	-& &
(whole plant	0.10	9 <b>2</b> , 95	<u>94</u> ~	
without root)	Over	affrecovery (n=3)	× 96 &	¢ 4.2
Fluopyram-7-hydrox			Y <del>X</del> A	S.J.
Leek	0.01			
(whole plant	0.10	¹ / ₂ / ₂ ¹ / ₂ / ₉ 0, 90 ² / ₂ ¹ / ₂	<u> </u>	<u>~</u> -
without root)		all recovery (4=3)	× ×84 Q	11.6
Fluopyram-methylsu	Ifoxide (AE194	4122		К ^У
Leek	0.01	6 6 96 O	<u> </u>	-
(whole plant	S 0.200	116ST20 2	O' M8 X	-
without root)		all recovery (n=3)		11.6
.: fortification level, RSD -	Relative Standard D	eviation y y y y y y y y y y y y y y y y y y y		
nal determination as: fluon	mam Residues calcu	ated as Aluopyram		
nal determination as: FLUG nal determination as: FLU-	Benzamide Residues methylsulfoxide Res	calculated as: fluopyram	× ×	
nal determination as: FLU-	PCA Residuce calcul	lated as: fluopyram	$\sim$	
nal determination as: FLU-	70 A Resides calcul	eviation wytwo individual receiveries given lated as: fluopyram idues calculated as: fluopyram idues calculated as: fluopyram lated as: fluopyram lated as: fluopyram		
Ş				
Ę,	A			
Q,	, ⁶ * 6 ³ . (			
	n J			
, and a second s				
	× A . o			
	T S			
Ű,				
	Ň.	~Ģ		



Page 752 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram 3 @ °

Table 6.6.2-	37: Results	of rotational c Date of	rop trials conducte			- B ^Q	lez Þ.	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	erti		) ^{IL} (L ² )	29 35	
Trial No./ Location/ Year	Plot (commodity)	1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application rate per treatment <u>to bare soil or target</u> <u>crop</u>	Dates of treatment or no. of treatments and last date	Portion analysed	Growth stage at sampling		arties	Restrice	s (mg/kg)	Legi Di Gui Oli Gui Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Conter Con	, ^{to}	PHI (days)
	(a)	(b)	kg a.s./ha (L/ha) s the			J. A. J. A. J. D.	AE C656948 as AE C656948	102656948	CC656948	C050948	© C656948		
08-2164-01 France, north 78410 Bouafle Ile-de-France Europe, North F 2008	Application to bare soil PBI: 30 d Rotational crop: Leek Saint victor	1) 18.07.2008 3) 28.10.2008 - 30.11.2008	500 300 1795 20 ^{C1} 1200 7 ¹	Se Elle	where Winner without JD	485 249				\$0.01 \$0.01	<0.01 <0.01	0.05 0.05	124 138
08-2164-02 Germany 51399 Burscheid Nordrhein- Westfalen Europe, North F 2008	Application to bare soil PBI: 31 d Rotational crop: Leek Axima	1) 05.05.2008 3) 24.07.2008	opy Juneat			1018 ^{te}	£ JA	<0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0.03 0.04	97 111
<ul> <li>(a) According</li> <li>(b) Only if re</li> <li>(c) Year mus</li> <li>(d) Either grad</li> </ul>	t be indicated		(e) Pays after to tapplica (f) Remarks may include internation which for (g) Study reference * prior to las Ocalment U-benzanardle	tabolites are laciude	e Onterval, PHI ; Reference to a d	, underline) nalytical method	and	<ul> <li>(i) Applica</li> <li>(j) Method</li> <li>(k) LOQ</li> </ul>	ation type ation method 1 information in control	(l) (m) #	Method valida Storage (max) ! based on dat P based on pro no data availa	e of analysis oduction date	
	C°	W L											75



Data Point:	KCA 6.6.2/19
Report Author:	
Report Year:	2009
Report Title:	Determination of the residues of AE C656948 in/on leek after spraying of
	fluopyram SC 500 in the field in Italy and Spain
Report No:	08-2175
Document No:	<u>M-357762-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/41 EEC of July 16, 1991, Annex T, part X, section
study:	6 and Annex III, part A, section 8; Residues in or on Treated Products Food and
	EC guidance working document 7029/VI/9Qrev. 5 (1997-67-22)
Deviations from current	none $Q_{ij}^{(0)}$ $Q_{ij}^{(0)}$ $Q_{ij}^{(0)}$ $Q_{ij}^{(0)}$ $Q_{ij}^{(0)}$
test guideline:	
Previous evaluation:	No, not previously submitted 2 2 2 2 2 2
	Study was not found in DAR/RAB and the Adden a
GLP/Officially recognised	Yes, conducted under GLP/Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes a way way way way of a construction of the

### Materials and Methods

The purpose of the study was to determine the magnitude of residues of fluopyram (AE C656948) and its metabolites fluopyram-benzample (AE (148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE C657188),fluopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl suffoxide (AE 1344122), in/on leek (whole plant without root) harvested after one spraying application with Fluopyram SC 500 on bare soil 30 days before planting of leek in Southern Furope Italy and Spain). The investigated plant back interval was 30 days.

For application the formulation Fluopyram SC 500 was used, a suspension concentrate formulation containing 500 g/L of Fluopyram. The application was done on bare soil followed by incorporation into the soil 29 days before the planting of leeks in the two trials.

In both trials the application was done with 1.0 L of test item/ha and a water rate of 300 L/ha, corresponding to a spray concentration of the test item of 0.33% (0.17% of active substance in the spray liquid). The application rate was 0.30 kg fluopy an /ha

For residue analysis samples of beek were taken from the treated and the control plots. In order to obtain representative samples of the taw commodity, samples were taken at random along the treated and the control plot.

In both trials, samples were taken from the treated and untreated plot in both trials 14 days before harvest and at harvest.

The field samples were stored deep-frozen within 24 hours after sampling and until dispatch. All field samples were shirped by deep-freeze forry and arrived in good condition. The field samples and lab samples were stored in a freezer at  $\leq$ -18°C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field samples and lab samples were shredded with dry ice in a outer. Representative parts of the shredded field samples were transferred into polystyrene boxes separately for analysis or archiving and stored at  $\leq$ -18°C.

Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (**1997**, 05/02/2007, <u>M-283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method



are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.  $Q_n^{\circ}$ 

Residues of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitrile:water (80:20; v:6). After centrifugation the extract volume was adjusted. Then, the extracts were diluted for times by adding the internal standards:

- One dilution was performed under acidic conditions: this extract aboved the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract plowed the determination of FLU, FLU-benzamide and FAU-7-OH.

An aliquot of the extracts was injected into LC-MSTMS operated in Elegrospray Ionization mode:

- One injection in positive electrospray ionization for the determination of FDU, FLU-benzamide and FLU-7-OH.
- Another injection in negative electrospration for the determination of FLUPCA and FLU-methyl-sulfoxide under different conditions.

The linearity was demonstrated in each analytical batch with a /x weighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standardization using isotopically stable labelled internal standards.

The Limit of Quantification (LOQ) expressed as fluopyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat shaw and 0.01 mg/kg for all other matrices

Full details and acceptable validation data to support this nothod are presented within document M-CA 4, which comply with the EU/regulatory requirements outfined within SANCO/3029/99 rev 4.

### **Findings**

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and treated samples from the study in each set of analyses. The means of the concurrent recoveries were for all fortification levels within the acceptable range of 70 - 110 % scept for FLUe methods sulfoxide at 111 % at 0.1 mg/kg. All overall mean recoveries are in the acceptable range of 70 - 110 %; therefore the results are considered valid. Recovery results are presented in Table 6.6.2-38

No residue of fluopyrane or related metabolites were found above the LOQ in any of the control samples of rotational coop matrices analysed, except for trial 08-2175-02 in which FLU-PCA was at the level of 0.02 mg/kg in leek whole plant of thour poot 14 days before harvest.

The residue levels of floopyram and its relevant metabolites in the rotational crop matrices of leek are summarized in the Fable 6.6.2-39

The storage period of deep frozen samples ranged between 273 and 369 days.

### Residues in leek

In trial 08-205-01 (DBI 29 days), residues of fluopyram (AE C656948) and its metabolites (FLUbenzamide, FLU-PCA, FDU-7-OH, FEQ-methyl-sulfoxide) in leek whole plant without root were all <0.01 mg/kg 14 days before harvest and at harvest.

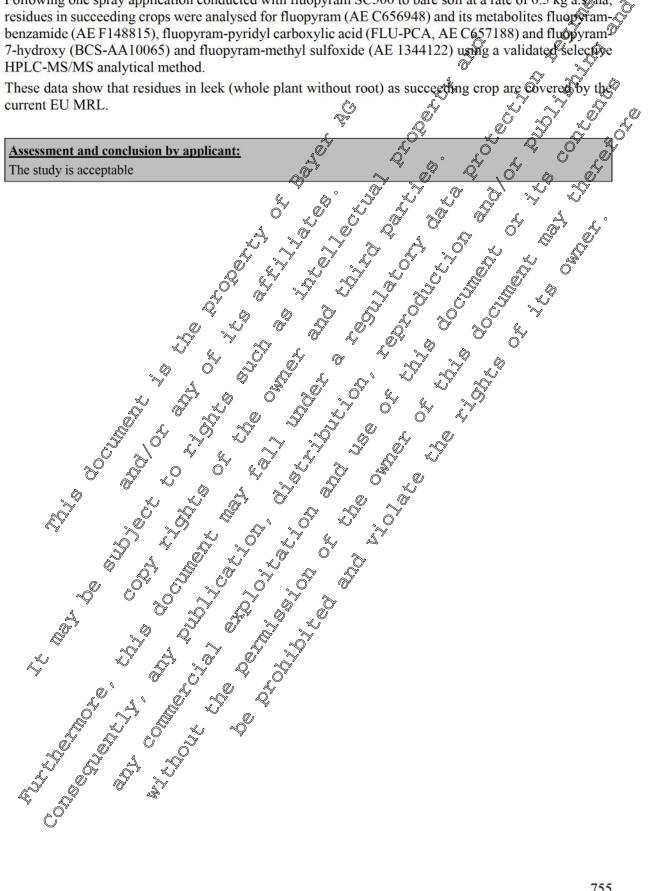
In triat 08-21 5-02 (PBI 29 days), residues of fluopyram (AE C656948) were at the level of 0.02 mg/kg 14 days before harvest and at harvest. Residues of fluopyram metabolites (FLU-benzamide, FLU-PCA, FLU-7-OE), FLU-methyl-sulfoxide) were < 0.01 mg/kg in leek whole plant without root 14 days before harvest and at harvest except for FLU-PCA for which the level was 0.02 mg/kg 14 days before harvest.



### **Conclusions**

Following one spray application conducted with fluopyram SC500 to bare soil at a rate of 0.5 kg a.s. ha, residues in succeeding crops were analysed for fluopyram (AE C656948) and its metabolites fluopyram benzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE C657188) and fluopyram 7-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122) using a validated selective HPLC-MS/MS analytical method.

These data show that residues in leek (whole plant without root) as succeeding crop are ow current EU MRL.





Crop/Sample	FL	Single values (%)	Mean value (%)	RSD*(20)
material	(mg/kg)	Shigle values (78)	Wiean value (70	KSD (CO)
Fluopyram (AE C650	6948)			4.5
	0.01	78; 87; 84; 77; 68	79 🦿	\$ ^{9.3}
Leek, whole plant without root	0.10	103; 94; 92; 90; 92	94 ⁶	× 5.4 ×
		Overall recovery (n=10)	87	Č 13.6 V
Fluopyram-benzamic	de (AEF14881	5)	, Ô¥ k	
	0.01	84; 83; 79; 76, 88	82 0	م [∞] 5.7¢ ¢
Leek, whole plant without root	0.10	82; 89; 89; 89; 82		10× 44
Without 100t		Overall recovery (n=10) ▲	° ~84 ° 1	5.4
Fluopyram-pyridyl-c	arboxilic-acid			
<b>.</b>	0.01	85; <u>1</u> 21; 92; 6; 107	Q 98 ~	O 1806 A
Leek, whole plant without root	0.10	110; 97, 88; 98, 88	کہ ² 96 ⁰	ý.4 s
without 100t		Overall recovery (n=10)		13.90
Fluopyram-7-hydrox	y (BCS-AA10			
<b></b> .	0.01 🔍	81; 78; 80; 80; 70	5 ⁷ 678 C	\$.8 \$.8
Leek, whole plant without root	0.10	92; 98 <del>0</del> 88; 89€91		4.3
		Overal recovery (n=10)	, O ^V , <b>85</b>	$0^{\nu}$ 9.8
Fluopyram-methylsu	lfoxide (AE13	44122) ³ ³ ³		Ôj
	°>Ø.01	108; 96 88; 102; 72		15.0
Leek, whole plant without root	≪ 0.10 [°]	\$15; 129, 100; M1; 198		6.8
() ninout 100t		Overall recovery (n€10)	Q ₀₂	13.8

### . . ... . . - -. ______

FL: fortification level, RSP- Relative Standard Deviation * some RSDs were not actualized as there are only two individual recoveries given Final determination as fLU-Bonzamide Residues calculated as fluopyram Final determination as: FLU-Bonzamide Residues calculated as fluopyram Final determination as: FLU-PCA.Residues calc



Page 757 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram 3 @ °

Trial No./ Location/ Year	39: Results Plot (commodity)	Of rotational of Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	crop trials conduc Application rate po treatment <u>to bare soil or targ</u> <u>crop</u>	er Dates of treatment or no. of	Portion	Growthe stage at Nampling	yer ectur	partices	Resulties (r Resulties (r FLU-PON #SAE 20056948	e ^{CT} mg/kgP ^{UL}	plienten jonten	07 ⁶ 79	PHI (days)
	(a)	(b)	kg a.s./ha Water ki (L/ha)			ALL BL	C656948	FLU- benzannde as AE 0656948	FLU-PON 85 AE 0656948	FLU- 704 as AE C656948	FLU- methyl- sulfoxide as AE C656948	Total residue calc.	(e)
08-2175-01 Spain 41310 Brenes Sevilla Andalucia Europe, South F 2008	Application to bare soil PBI:29 d Rotational crop: Leek Shelton	1) 15.05.2008 3) 01.09.2008 - 31.10.2008	0.47 0.1 0.0 ^{C1} 201911 0.1 0.0 ^{C1} 201911 0.1 0.1 0 ^{C1} 201911 0.1 0 ^{C1} 201911 0.1	JE 32	wheer Without Toope UID		CONT TON			<0.01	<0.01 <0.01	<0.02 <0.02	145 159
08-2175-02 Italy 40128 Bologna Emilia - Romagna Europe, South F 2008	Application to bare soil PBI: 29 d Rotational crop: Leek Linx	1) 10.04.2008 3) 10.07.2008 - 25.07.2008				202200	* The	€0.01	0.02/0.02** <0.01	<0.01 <0.01	<0.01 <0.01	<0.03 <0.03	107 121
(a) Accordin	ng to CODEX Classific elevant st be indicated owth stage description ise calculated Sum	cation / Guide Char of Puepyram	(c) Pays after payap (b) Remarks may inc integration which (g) Study references * Oprior to last reading (g) Denzanticle	plication (Cabel pre-har lude: Carnatic condition before a condition hent before a condition of the second second second second of the second	vesenterval, PH is; Reference to ed	H, underline) analytical metho	od and	(i) Appli (j) Metho (k) LOQ	ilation type cation method d information e in control	(l) (m) #	Method valida Storage (max) ! based on date P based on pro no data availab	e of analysis duction date	
	Ŭ	L BU											75



Data Point:	KCA 6.6.2/20
Report Author:	
Report Year:	
Report Title:	2009 Determination of the residues of AE C656948 in/on stravberry after spraying of fluonyram SC 500 in the field in France (North) and Gemany
Report The.	fluopyram SC 500 in the field in France (North) and Germany
Report No:	08-2166
Document No:	M-357953-01-1
Guideline(s) followed in	EU-Ref: Council Directive 91/41 EEC of July 10, 1991, Annex II, part X, section
study:	6 and Annex III, part A, section 8 Residues in Ron Treated Products, Food and
5	EU-Ref: Council Directive 91/41 (EEC of July 16, 1991, Annex II, part X, section 6 and Annex III, part A, section 8 Residues in a con Treated Products, food and Feed EC guidance working document 7029/XU/95 rev. 5 (1987-07-22)
Deviations from current	none A Q & A Q
test guideline:	
Previous evaluation:	No, not previously submitted
	Study was not tound any DA VAP AV and the Addenda ~
GLP/Officially recognised	Yes, conducted under GLP Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes in the second secon
	Yes y y y y y y y y y y y y y y y y y y y
Materials and Methods	

#### **Materials and Methods**

The purpose of the study was to determine the magnitude of residues of Huopyram (AE C656948) and its metabolites fluopyram-ben amide (AE F148815), fluopyram oyridykearboxylic acid (FLU-PCA, AE C657188), fluopyran@7-hydroxy (BCS-A#10065) and thiopyram-methyl sulfoxide (AE 1344122), in/on strawberry (fruits) parvested after one spraying application with Fluopyrands C 500 on bare soil 30 days before sowing/planting of strawberry in northern Europe (France and Germany). The investigated plant back interval was 30 days. X Ô Õ

For application the formulation PluopAram \$\$ 500 was used, a suspension concentrate formulation containing 300 g/L of Foropyrum. The application was done with 20 L test item per ha and 300 L water per ha on bare soil followed by incorporation into the soil (< 8 cm) 31 days (trial 08-2166-01) and 32 days (trial 08-2166 92) before the planting of strawberries. Documentation of the incorporation in trial 08-2166-02 is missing. 🔬 Ľ

In both trials the appreation was done with 10°L of test item/ha and a water rate of 300 L/ha, corresponding to a spray concentration of the test item of 0.33% (0.17% of active substance in the spray liquid). The application rate was 9.50 kg fluoppram /ka.

For residue analysis samples of strawberries (fruit) were taken from the treated and the control plots. In order to obtain representative samples of the row commodity, samples were taken according to Ssampling (trial 08-2166-01) and at random (trial 08-2166-02) along the treated and the control plot. Samples of strawberries (fruit) were taken from the treated and untreated plot in both trials at harvest (BBCH 87). \$

The field samples were stored deep-from within 24 hours after sampling and until dispatch. The field samples were shipped by deep treeze lorry (trial 08-2166-01) and by car with dry ice (trial 08-2166-02) and arrived in good condition. The field samples were stored in a freezer at  $\leq$ -18 °C or below until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field samples were shredded with dry ice in a cutter. Representative parts of the shredded field samples were transferred into polystyrene boxes separately for analysis or archiving and stored at  $\leq$ -18°C.

Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (**1997**, 05/02/2007, M-



<u>283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues of these compounds were extracted from 10 g of sample material (5 g for wheat strawby two successive extractions using a high-speed blender with a mixture of acetonitrile water (80:20; v). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

- One dilution was performed under acidic conditions: this extract allowed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed the determination of FLU, FLU-benzamide and FLU-7-OH.

An aliquot of the extracts was injected into LC-MS/MS operated in Electrospray Ionization mode

- One injection in positive electrospray onization for the determination of FLU, FLU-benzamide and FLU-7-OH.
- Another injection in negative electrospray ionization for the determination of FLO-PCA and FLU-methyl-sulfoxide under different conditions.

The linearity was demonstrated in each analytical batch with a 1/x reighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standard zation using sotopically stable babelled internal standards.

The Limit of Quantification (LOO), expressed as fluopyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat straw and 0.01 mg/kg for all other matrices.

Full details and acceptable varidation data to support this method are presented within document M-CA 4, which comply with the EU regulatory equirements outlined within SANCO/3029/99 rev 4.

#### Findings

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and treated samples from the study in each set of analyses. The means of the concurrent recoveries were for all fortification levels within the acceptable range of 70 - 110 % except for FbU-methyl-subtoxide at 61 % at 0.01 mg/kg. All overall mean recoveries are in the acceptable range of 70 - 110 %: therefore, the results are considered valid. Recovery results are presented in Table 6.6.2-40.

No residue of luopy cam or clated metabolites were found above the LOQ in any of the control samples of rotational crop matrices analysed.

The residue levels of floopyram and its relevant metabolites in the rotational crop matrices of strawberry fruits are summarized in the Table 6.6.2-4.

The storage period of deep frozen samples ranged between 328 and 349 days.

A new storage stability study of fluopyram byridyl-acetic-acid in acidic matrix (strawberry) is ongoing and will be something by Japaary 2022 to support a storage longer than 6 months.

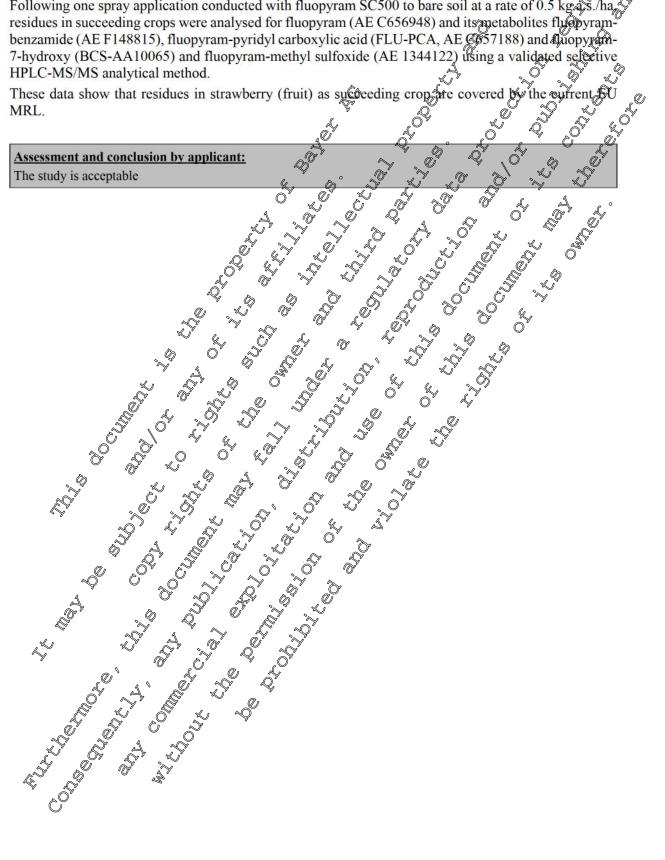
## Residues in strawberry fruits

In trial 08-2,66-01  $PBI_{3}$  days), residues of fluopyram (AE C656948) and its metabolites (FLU-bergamide FLU-PCA, EU-7-OH, FLU-methyl-sulfoxide) were all < 0.01 mg/kg in strawberry fruit at harves

In trial 08-2166-02 (PBI 32 days) residues of fluopyram (AE C656948) and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methyl-sulfoxide) were all < 0.01 mg/kg in strawberry fruit at harvest.



<u>Conclusions</u> Following one spray application conducted with fluopyram SC500 to bare soil at a rate of 0.5 kg as./ha residues in succeeding crops were analysed for fluopyram (AE C656948) and its metabolites fluopyrambenzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE (\$57188) and Quopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122) using a validated selective HPLC-MS/MS analytical method.





Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD*(25)
Fluopyram (AE C656	5948)			×
	0.01	87	87 3	\$ \$
Strawberry, fruit	0.10	107	107	<u>`~</u> - <u>~</u> ?` <u>~</u>
Strawberry, ir un	1.0	99 🚫	£9	
		Overall recovery (n=3)	<b>Q</b> 98	0 <b>30.3</b> ×
Fluopyram-benzamic	<u>`</u>			
	0.01	80	<u>Q' 89 °</u>	<u> </u>
Strawberry, fruit	0.10	104	<u>∼y</u> <u>004</u> ~ √	
	1.0	<u>95</u> °°	Ø <u>1</u> 95 Ø	
		Overall @cover@(n=3)		
Fluopyram-pyridyl-c		(AE C63/188)		
	0.01			
Strawberry, fruit	0.10	$\sqrt{\frac{91}{102}}$	100	
•	1.0	Overal recovery (n≥3)		
Fluopyram-7-hydrox				<u>~</u> 4.7.0
riuopyram-7-nyurox	0.01		Q, 85° °	<u> </u>
	0.10	× × 100	1. 190 A	
Strawberry, fruit	0. NU 1.0	<u>96</u> 97 0	<u> </u>	 Ø
		Overall recovery (n=3)	93	8.2
Fluopyram-methylsu	1			1 0.2
ruopyrum meenyisu			0° 061 4	
	AQ.10 . O	101	V 101 0	
Strawberry, fruit	1.0 2	132 2 2	13\$\$``	
~0°		Overall recovery (n=3)	98	36.3
L: fortification level, RSD	Relative Standard	Deviation S		<u> </u>
some RSDs were not calculation as: fluopy	ated as there were	Deviation view of the second s	, O	
Final determination as: FLU-b	penzamide Residu	ulated as: fluopyram	^o y	
inal determination as: FLU	nethylsultoxide R	esidues calculated as: fluopyram	ÂN .	
· · · · · · · · · · · · · · · · · · ·		ulated as: fluopyman O		
Ŵ.	A S			
	Ö ^v õ ^v i			
~Q (				
A				
Å.	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			
4, ⁵	X A 0			
× ·	A N			
S , t				
A L				
inal determination as: FD9-,				
19 D 1	1 ~~			
A PA S				
B. S. Q. W	N. N			
× ⁴ ^y				
Ű				

#### data far fl d its motobolitos in strawb Table ( ( ) 10 ъ (AE C(E(040))



Page 762 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram 4

Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application r treatme <u>to bare soil or</u> <u>crop</u>	nt	Dates of treatment or no. of treatments and last date	Portion analysed	Growth stage of sampling	ectula	1 Prof	Residues	ECT F	COLLER COLLER COLLER COLLER COLLER COLLER COLLER Sulfoxide	r ^{\$}	PHI (days)
	(a)	(b)	kg a.s./ha Water (L/ha)	kg a.s./hL	(c) 50 05	ajta Seza		1 0,90940	00000	G	CO ON IN	QLU- methyl- sulfoxide as AE C656948	Total residue calc.	(e)
08-2166-01 France, north 80700 Cremery Picardie Europe, North F 2008	Application to bare soil PBI: 31 d Rotational crop: Strawberry Isadora	1) 26.05.2008 2) 05.07.2008 - 24.07.2008 3) 10.08.2008 - 20.08.2008	0.5 390 8.0 CURRENT 8.0 CURREN			WART UTAGE?			2001 JU 3.0 C JU 2.1 S 3.0 2.1 S 3.0 2.0 2.0 3.0 3.0 3.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5	L J	<0.01, 10 0 5	<0.01	<0.02	91
08-2166-02 Germany 51399 Burscheid Nordrhein- Westfalen Europe, North F 2008	Application to bare soil <b>PBI: 32 d</b> Rotational crop: Strawberry Elsanta	1) 19.05.2008 2) 01.06.2008 - 20.06.2008 3) 01.07.2008 - 15.07.2008	OPI LURE		17.04.2008	f the	US ^{®7} OW ^{ILEI}	BOH TIDE		<0.01	<0.01	<0.01	<0.02	78
(a) According (b) Only if re (c) Year mus (d) Either gro G greenhous Total residue c	to CODEX Classifica levant be indicated wth stage description of e F alculated :	or BP Code	(e) after l (f) Remarks m	ast apprication of hicfude: C which metal ence	on (Laber Pre-harv Linear conditions whites are in Object	est interval, PH georetrence to a	I, underline) Inalytical method	l and	<ul> <li>(i) Applic</li> <li>(j) Method</li> <li>(k) LOQ</li> </ul>	lation type ation method 1 information in control	(l) (m) #	Method valida Storage (max) ! based on dat P based on pro no data availa	e of analysis oduction date	
	EUIT THE OF	or BB Code	ut pe	S _{TOr}										76



Data Point:	KCA 6.6.2/21
Report Author:	
Report Year:	2009
Report Title:	Determination of the residues of AE C656948 in/on strawberry after spraying of
-	fluopyram SC 500 in the field in Italy and Spain
Report No:	08-2177
Document No:	<u>M-357930-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/41 (EEC of July 16, 1991, Annex II, part X, section 6 and Annex III, part A, section 8 Residues in Fon Treated Products, Food and
study:	6 and Annex III, part A, section 8 Residues in Fon Treated Products Food and
	Feed EC guidance working document 7029/X0/95 rev. 5 (1987-07-22)
Deviations from current	none A Q & A L
test guideline:	
Previous evaluation:	No, not previously submitted
	Study was not found and DAR AR and the Addenda
GLP/Officially recognised	Yes, conducted under GLP Officially recognised testing facilities
testing facilities:	Yes, conducted under GLP officially recognised testing facilities
Acceptability/Reliability:	Yes A A A A A A

### **Materials and Methods**

The purpose of the study was to determine the magnitude of the relevant residues of fluopyram (AE C656948) and its metabolites fluopyram-benzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE C657188), fluopyram 7-hydroxy (BC S-AA10065) and fluopyram-methyl sulfoxide (AE 1344122), in/on strawberry (fruits) harvested after one spraying application with Fluopyram SC 500 on bare soil 30 days before sowing planting of strawberry in southern Europe (Spain and Italy). The investigated plant back interval was 30 days

For application the formulation Fluopyram SC 500 was used a suspension concentrate formulation containing 500 g/L of Fluopyram The application was none with 1.6 L test item per ha and 300 L water per ha on bare soil followed by incorporation into the soil 25 before the planting of strawberries. In trial 08-217% of the incorporation was done by rotovator (the depth of incorporation is unknown) and in trial 08-2177-02 the incorporation was done by rotary tiller at 5 - 40 cm depth.

In both trials the application was done with 1.0 L of test item/ha and a water rate of 300 L/ha, corresponding to a spray concentration of the test item of 0.33% (0.17% of active substance in the spray liquid). The application rate was 0.50 kg fluopyram /ha

For residue analysis, samples were taken from the treated and the control plots. In order to obtain representative samples of the raw commodity, samples were taken according to different sampling procedures from various parts of each treated and control plot. Samples of strawberries (fruit) were taken from the treated and untreated plot in both triats at harvest (BBCH 87) and 14 days before harvest trial 08-2177-01 only.

In trial 08-2179-01 the sample weight at harvest was only 794g instead of 1 kg; mostly all fruits were lightly affected by diseases

The field samples from all trives were stored deep-frozen within 24 hours after sampling and until dispatch All field samples were shipped by deep-freeze lorry and arrived in good condition. The field samples were stored in a freezer at  $\leq$ -18°C until preparation of the examination samples. For the preparation of the shredded field samples were shredded with dry ice in a cutter. Representative parts of the shredded field samples were transferred into polystyrene boxes separately for analysis or archiving and stored at  $\leq$ -18°C.



Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (**1998**, 05/02/2007, <u>M-283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitible:water (80,30; v:) After centrifugation the extract volume was adjusted. Then, the extracts were diffuted ten times by adding the internal standards:

- One dilution was performed under acidic conditions: this extract allowed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed the determination of FLU, FLU-benzamide and FLU-7-Q.

An aliquot of the extracts was injected into LO-MS/MS operated in Electrospray donization mode:

- One injection in positive electrospiration for the determination of FLU, FLU benzamide and FLU-7-OH.
- Another injection in negative electrospray ionization for the determination of FLU-PCA and FLU-methyl-sulfoxide under different conditions

The linearity was demonstrated in each analytical batch with above weighted Calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by Onternal standardization using isotopically stable labelled internal standards.

The Limit of Quantification (600), expressed as theopyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat shaw and 0.01 mg/kg for all other matrices.

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

### Findings ~

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and treated samples from the study in each set of analyses. The means of the concurrent recoveries were for all fortification levels within the acceptable range of 70 - 110 % except for FLUPCA at 63 % at 0.01 mg/kg. All overall mean recoveries are in the acceptable range of 70 - 510 % therefore, the results are considered valid. Recovery results are presented in Table 6.6.2-42.

No residue of fluopyram or related metabolites were found above the LOQ in any of the control samples of rotational crop matrices analysed

The residue levels of fluory ram and its relevant metabolites in the rotational crop matrices of strawberry fruits are summarized in the Table 6.62-43

The storage period of deep-frozen samples ranged between 319 and 393 days.

A new storage stability study of thuopytam-pyridyl-acetic-acid in acidic matrix (strawberry) is ongoing and will be submitted by January 2022 to support a storage longer than 6 months.

#### Resideres in strawberry fruits

In trial 08/2177-012 (PBK 28 days), residues of fluopyram (AE C656948) and its metabolites (FLUbenzamide, FLU-PCA, FLU-7-OH, FLU-methyl-sulfoxide) were all < 0.01 mg/kg in strawberry fruit 14 days before harvest and at harvest.



In trial 08-2177-02 (PBI 28 days) residues of fluopyram (AE C656948) and its metabolites (FLUbenzamide, FLU-PCA, FLU-7-OH, FLU-methyl-sulfoxide) were all < 0.01 mg/kg in strawberry fruit at de la constante de la constant harvest.

#### Conclusions

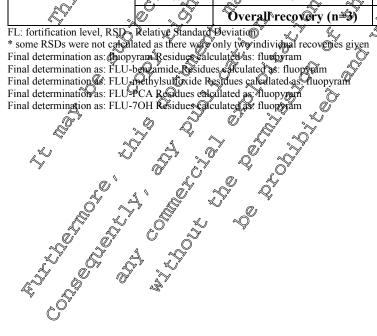
Following one spray application conducted with fluopyram SC500 to bare soil at a rate of 0.5 kg a.s./ha residues in succeeding crops were analysed for fluopyram (AE C656948) and its metabolites fluopyram benzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA/AE COS/100/ and recopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1340122) using availabled selective HPLC-MS/MS analytical method. These data show that residues in strawberry (fruit) as succeeding erop are copyred by the current EU MRL. benzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA AE C657188) and Avopyram-

And set of the current of the curren Entremone with and with the state of the sta the periodicities and window the art of the



Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD*((%))
Fluopyram (AE C65				
	0.01	92	92 4	
	0.10	100	100	
Strawberry, fruit	1.0	89		
	1.0	¥		
<b>F</b> I I I		Overall recovery (n=3)	0 ³ 94 x	
Fluopyram-benzami				
	0.01	90.00		
Strawberry, fruit	0.10	<u>94</u> °	0 × 94 0	$\gamma \sim \gamma \sim \gamma$
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	1.0	<u> </u>	<u> </u>	<u> </u>
		Overall recovery (n=3)	Q 489 🔊	O' 😥 🖓
Fluopyram-pyridyl-o	carboxilic-acid	(AE (657188) ~ ~		
	0.01	63 2 2		Ş Õ
64	0.10	95 95	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
Strawberry, fruit	1.0 4		D 80 0	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
	Ø	.Overall recovery (n=3)		<u>لار</u> 20.2
Fluopyram-7-hydrox	y (BCSAA10			0 [°]
	0 01		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Q
	*0 .10 A	Q Q 09 4 5	1090 20	
Strawberry, fruit	L 1.05	92 0 32	8 92 m	
		Overall recovery (0=3)	». ⁰ 96 [~]	11.6
Fluopyram-methors	ılfoxûle (AE¥3			
<u>~</u>	0.01	× 6 84,5 %	\$ ⁵ 84	
		109 - 409	0 v 101	
Strawberry, fruit	\$ 1.0 €		101	
je St		Överall recovery (n=3)	<u></u>	10.3

Recovery data for fluopyram (AE C656948) and its metabolites in strawberry Table 6 6 7- 47.





Page 767 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	treat to bare so	on rate per ment il or target op	Dates of treatment or no. of treatments and last date	Portion analysed	Growth stage at sampling	ect vo	L PTOP	Residues		CONTER CONTER CONTER CONTER CONTER	OT ^E	PHI (days)
	(a)	(b)		ha) kg		0. ⁹		C656948 as AE C656948	67556948	6656948	6656948	as AE	Total residue calc.	(e)
08-2177-01 Spain 08850 Gava - Barcelona Cataluña Europe, South F 2008	Application to bare soil PBI: 28 d Rotational crop: Strawberry Albion	This	JOCURTE.	*0		JUL CL	a socor				<0.01 <0.00 \$	<0.01 <0.01	<0.02 <0.02	126 140
08-2177-02 Italy 40128 Bologna Emilia - Romagna Europe, South F 2008	Application to bare soil PBI: 28 d Rotational crop: Strawberry Clery	1) 28.03.2008 1) 28.03.2008 2) 25.04.2008 3) 15.05.2008					0.6 ⁰⁷	STAN ARE	ALS ES	<0.01	<0.01	<0.01	<0.02	80
 (a) According (b) Only if rel (c) Year must (d) Either gro G greenhous 	to CODEX Cossifica evant be indicated wth stage description o e F	tion / Guide	(e) Dava (f) Barnari vaform (f) Studar prizete	ther last application cs may implied to ation which meta reference Mast treatments	on (Label preparve Climatic conditions bolitics are included	est interval, PHI ; Reference to a	, underline) nalytical method	and	 (h) Formula (i) Applica (j) Method (k) LOQ ** residue 	ation type tion method information in control	(l) (m) #	Method valida Storage (max) ! based on dat P based on pro no data availa	e of analysis oduction date	
Γotal residue ca	alculated : sumo EUIT ^{TUEI} COILE	s) 15.05.2008 G be a field of the field of	U- b ênzami E ^D Enzami	dep ^{ert}	101									76



Data Point:	KCA 6.6.2/22
Report Author:	
Report Year:	2009
Report Title:	Determination of the residues of AE C656948 in/on spinach after spraying of
	fluopyram SC 500 in the field in France (North) and Germany
Report No:	08-2071
Document No:	<u>M-357943-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/41 EEC of July 16, 1991, Annex II, part X, section
study:	6 and Annex III, part A, section 8 Residues in a con Treated Products, bood and
	Feed EC guidance working document 7029/XC/95 rev. 5 (1987-07-22)
Deviations from current	none A Q & A A
test guideline:	
Previous evaluation:	No, not previously submitted
	Study was not found and DAR AR and the Addenda
GLP/Officially recognised	Yes, conducted under GLP Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes A Y Y Y Y Y Y Y Y
	$\frac{\operatorname{Yes}}{\operatorname{Q}} \xrightarrow{\mathcal{A}} \xrightarrow{\mathcal{A}} \mathcal$

Materials and Methods

The purpose of the study was to determine the magnitude of residues of fluopyram (AE C656948) and its metabolites fluopyram-benzamide (AE F148815), thiopyram-pyridyl carboxyle acid (FLU-PCA, AE C657188), fluopyram-7 hydroxy (BCS-AA10065) and fluopyram methol sulfox de (AE 1344122), in/on spinach (leaf) harvested after one spray application with Pluopyram SO 500 on bare soil 30 days before sowing of spinach in northern Europe (northern France and Germany). The investigated plant back interval was 30 days.

In both trials the application was done with 10° L of test dem/ha and a water rate of 300 L/ha, corresponding to a spray concentration of the test item of 0.33% (0.14%) of active substance in the spray liquid). The application rate was 0.50 kg fluopyram ha.

In both trials the application was done on pare soft (followed by incorporation to 5-6 cm depth in trial 08-2071-01; incorporation tepth was not documented by trial 08-2071-02).

The applications were done 29 days (trial 08 - 2071 - 01) and 28 days (trial 08 - 2071 - 02) before sowing of spinach

For residue analysis samples of spinach were taken from the treated and the control plots. In order to obtain representative samples of the raw commodity, samples were taken according to S-sampling (trial 08-2071.91) and at random alkalong the treated and the control plot (trial 08-2071-02).

In both trials, samples were taken from the treated and untreated plot in both trials 14 days before harvest and at harvest (BBCH 49).

The field samples were stored deep bozen within 24 hours after sampling and until dispatch. All field samples were shipped by deep-freeze lorry (08-2071-01) or by car with dry ice (08-2071-02) and arrived in good condition. The field samples were stored in a freezer at \leq -18°C or below until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field samples were shredded with dry ice in a cutter.

Representative parts of the shredded field samples and laboratory samples were transferred into polystyre boxes separately for analysis or archiving and stored at $\leq -18^{\circ}$ C.

Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (**1997**, 05/02/2007, <u>M-283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method



are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4. Q_n°

Residues of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitrile:water (80:20; v:6). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

- One dilution was performed under acidic conditions: this extractationed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed determination of FLU, FLU-benzamide and FLU-7-OH.

An aliquot of the extracts was injected into LC-MSTMS operated in Electrospray Ionization mode:

- One injection in positive electrospray ionization for the determination of FDU, FLU-benzamide and FLU-7-OH.
- Another injection in negative electrospration for the determination of FLUPCA and FLU-Methyl-sulfoxide under different conditions.

The linearity was demonstrated in each analytical batch with a /x weighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standardization wing isotopically stable labelled internal standards.

The Limit of Quantification (LOQ) expressed as fluopyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat shaw and 0.01 mg/kg for all other matrices

Full details and acceptable validation data to support this nothod are presented within document M-CA 4, which comply with the EU/regulatory requirements outfined within SANCO/3029/99 rev 4.

Findings

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and treated samples from the study in each set of analyses. The means of the concurrent recoveries were for all fortification levels within the acceptable range of 70 - 110 %. All the recovery results are considered valid. Recovery results are presented in Table 6.6.2- 44. No residue of fluor and or related metabolites were found above the LOQ in any of the control samples of rotational croppinatrices analysed.

The residue levels of the propyram and its reprivant metabolities in the rotational crop matrices of spinach leaves are summarized in the Table 6.6.245.

The storage period of deep-frozen samples ranged between 280 and 417 days.

Residues in spinach leaves

In trial 08-2071-01 and 08-2071-02 (PBI 29 days),

14 days before harvest .

- residues of fluopyfam (AE C656948) were at 0.03 mg/kg
- residues of FLU benzapride range between 0.02 mg/kg and 0.07 mg/kg.
- Desidues of FAU-7-OM range between 0.08 mg/kg and 0.26 mg/kg.

residues of FLU-PCA and FLU-methyl-sulfoxide were < 0.01 mg/kg.

At harvest?

- Gresidues of fluopyram (AE C656948) range between <0.01 mg/kg and 0.01 mg/kg
- residues of FLU-benzamide range between 0.02 mg/kg and 0.08 mg/kg.
- residues of FLU-7-OH range between 0.05 mg/kg and 0.10 mg/kg.



residues of FLU-PCA and FLU-methyl-sulfoxide were < 0.01 mg/kg.

Conclusions

de la constante de la constant A consistence STR89 ppt. Strange of the form and the coverage of the form and Following one spray application conducted with fluopyram SC500 to bare soil and rate of 0.5 kg a.s./ha. residues in succeeding crops were analysed for fluopyram (AE C656948) and is metabolites fluopyram-



Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD*((25))
Fluopyram (AE C	656948)			4 . Q
	0.01	80; 82; 87; 83	83	\$3.5
Sector ask loof	0.10	93; 99; 95	96 [°] ×	× 3.2 ×
Spinach, leaf	1.0	81	®1	
		Overall recovery (n=8)	0 ⁸ 88 ×	8.3 2
Fluopyram-benzai	mide (AEF14881	5) 3		
	0.01	86; 76; 84, 69	~ 78 ~	<u></u> 83 m
Spinach, leaf	0.10	82; 81; 80; 103 。	or ~787 or (↓ <u>↓</u> <u>1</u> .8 <u>↓</u> <u>1</u> .8
Spinaen, iear	1.0	<u>879 03 x</u>	<u> </u>	
		Overall recovery (n=9)	Q 82	
Fluopyram-pyridy	l-carboxilic-acid		$\rightarrow A \delta^{\gamma}$	
	0.01	67; 1 2, 63; 79	0 ⁷ 72, 7	v 🔬 10.8 🕉 🖉
Spinach loof	0.10	87; 87; 87 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		4.2 5
Spinach, leaf	1.0		N 288 E	
	<i>a</i>	Qverall recovery n=8)	م ج 78 م	11.4
Fluopyram-7-hydi		065		
	0.01	8 1; 80; 8 0; 84	× ×81 . Q	2.3
	\$ 0.10	ي 93; 9 2 , 94; 1 1 1	\$\$\$ 98.~~ ×	9.3
Spinach, leaf	1.0	\$ 0 ⁸ 86 \$. 0 ⁸	& <u>86</u> 5	
		Overall receivery (n=9)	88 4	11.2
Fluopyram-methy	Sulfoxide (AEIS	44122		
Ľ.	0.01	68, 75; 72, 79 S	A TAS	6.3
	. O. O	0 \$ 88; 94 94 0	<u>92</u>	3.8
Spinach, leaf		A 36 0	× 96	
		Overall recovery (n=89)	83	13.3

Recovery data for fluonyram (AF C656948) and its metabolites in spinach leaf Table 6 6 7 14.

FL: fortification level, RSD - Kelative Standard Deviation * some RSDs were not calculated as there were only two individual, recoveries given. Final determination as: fLU-methylsulfayide Residues calculated as rhiopyram Final determination as: FLU-methylsulfayide Residues calculated as rhiopyram Final determination as: FLU-MCA Residues calculated as: thiopyram Fi

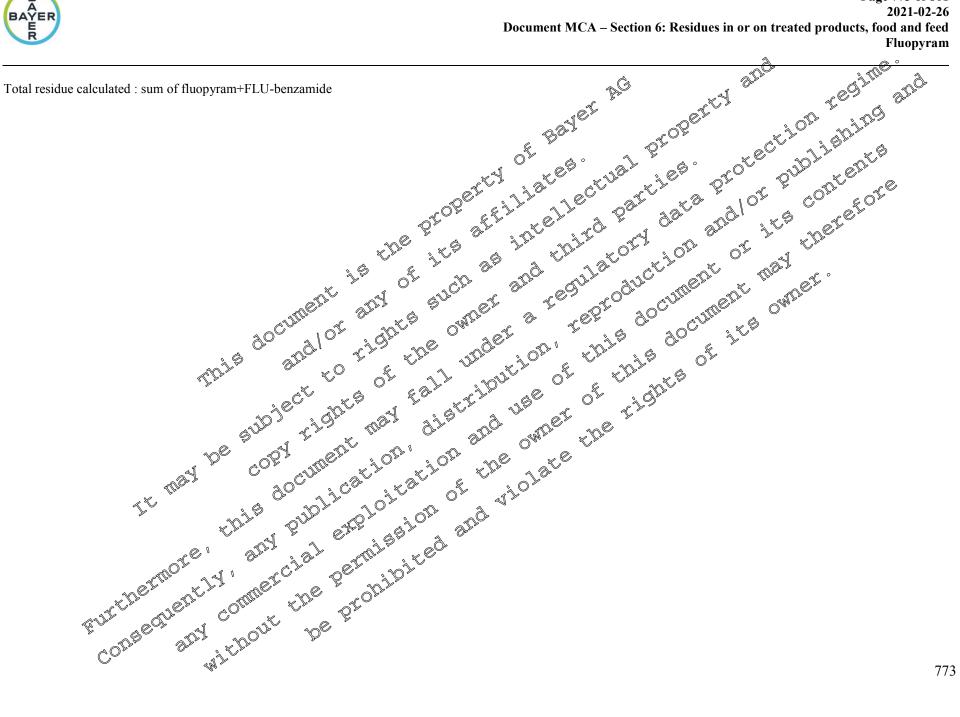


Page 772 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Location/ Year	Plot (commodity)	planting 2. Flowering 3. Harvest 4. Transplanting	tı tı	cation ra reatmen <u>e soil or</u> <u>crop</u>	it -	Dates of treatment or no. of treatments and last date		Growth stage at sampling	ec ^{tur}	al pro	Residence		COLLER COLLER COLLER X methyl-	t ^{\$} 0 ^{t€}	PHI (days)
	(a)	(b)	kg a.s./ha	Water (L/ha)	kg a.s./hL	date P ^T C) O ^T	\$ 10		as AF C656948	as AE	AE	AE C65N948	sulfoxide as	Total residue calc.	(e)
3-2071-01- rance, north 3410 ouafle Ile-	Application to bare soil PBI: 29 d <u>Rotational</u> <u>crop :</u> Spinach, Samos F1	1) 19.06.2008 3) 28.07.2008 - 12.08.2008	mje	C N Ø	0.17 01 0 0 0 0 0	1.05.2008 975 975 576 576 576 576 576 576 576 5				right,		0.26 M	≥<0.01 <0.01	0.1	64 78
3-2071-02 3-2071-02- ermany (399 urscheid ordrhein- /estfalen urope, orth 008	Application to bare soil PBI: 28 d Rotational crop: Spinach Cezanne	1) 02.05.2008 3) 10.06.2008 - 25.06.2008 - 2	BIDI I	131 DUDI	0.17 V Cat		legger	1012t	0.03	0.02 0.02	<0.01 <0.01	0.08 0.05	<0.01 <0.01	0.05 0.03	60 74



Page 773 of 801 2021-02-26 Document MCA - Section 6: Residues in or on treated products, food and feed Fluopyram





Data Point:	KCA 6.6.2/23
Report Author:	je standard and a standard and a standard a s
Report Year:	2009
Report Title:	Determination of the residues of AE C656948 in/on spinach after spraying of fluonyram SC 500 in the field in Italy and Spain
	fluopyram SC 500 in the field in Italy and Spain
Report No:	08-2170
Document No:	<u>M-357959-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/41 EEC of July 16, 1991, Annex II, part 4, section 6 and Annex III, part A, section 8 Residues in Ron Treated Products, pood and
study:	6 and Annex III, part A, section 8 Residues in Fron Treated Products, Food and
	Feed EC guidance working document 7029/X0795 rev. 5 (1987-07-22)
Deviations from current	none A Q & A A
test guideline:	
Previous evaluation:	No, not previously submitted or a straight of the straight of
GLP/Officially recognised	Yes, conducted under GLP Officially recognised testing facilities
testing facilities:	Yes, conducted under GLP Officially recognised testing facilities *
Acceptability/Reliability:	Yes to y y y y y y

Materials and Methods

The purpose of the study was to determine the magnitude of residues of fluopytam (AE C656948) and its metabolites fluopytam-ben amide (AE F148815), fluopytam pyridy carbox vic acid (FLU-PCA, AE C657188), fluopytam 7-hydroxy (BCS-AC10065) and fluopytam-methyl sulfoxide (AE 1344122), in/on spinach (leaf) have sted after one spray application with Fluopytam SC 500 on bare soil 30 days before sowing of spinach in Southern Europe (Spain and Italy). The investigated plant back interval was 30 days.

For application the formulation Fluopytam St 500 Was used, a suspension concentrate formulation containing 500 g/L of Fluopytam.

In both trials the application was done with 1.0 L of test item/ha and a water rate of 300 L/ha, corresponding to a spray concentration of the test item of 0.33% (0.17% of active substance in the spray liquid). The application are was 0.50 g fluopyram/ha.

The applications were done on bare soil 28 hays (trial 08-2170-01) and 29 days (trial 08-2170-02) before sowing of spinach.

For residue analysis, samples were taken from the treated and the control plots. In order to obtain representative samples of the raw commodity, samples were taken according to different sampling procedures from various parts of each treated and control plot.

In both trials, samples were taken from the treated and untreated plot in both trials 14 (or 12) days before harvest and at harvest at harvest and at harvest at ha

The field samples from at trials were stored deep-frozen within 24 hours after sampling and until dispatch. All field samples were shipped by deep-freeze lorry and arrived in good condition. The field samples were stored in a freezer at $\leq -18^{\circ}$ C until preparation of the examination samples. For the preparation of examination samples, the deep-frozen field samples were shredded with dry ice in a cutter. Representative parts of the shredded field samples were transferred into polystyrene boxes separately for analysis of archiving and stored at $\leq -18^{\circ}$ C.

Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (**1997**, 05/02/2007, <u>M-283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method



are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4. Q_n°

Residues of these compounds were extracted from 10 g of sample material (5 g for wheat straw) by two successive extractions using a high-speed blender with a mixture of acetonitrile:water (80:20; v:6). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

- One dilution was performed under acidic conditions: this extract allowed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed determination of FLU, FLU-benzamide and FLU-7-OH.

An aliquot of the extracts was injected into LC-MSMS operated in Elegrospray Ionization mode:

- One injection in positive electrospray ionization for the determination of FDU, FLU-benzamide and FLU-7-OH.
- Another injection in negative electrospration for the determination of FLUPCA and FLU-Methyl-sulfoxide under different conditions.

The linearity was demonstrated in each analytical batch with a /x weighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standardization using isotopically stable labelled internal standards.

The Limit of Quantification (LOQ) expressed as fluopyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat shaw and 0.01 mg/kg for all other matrices

Full details and acceptable validation data to support this nothod are presented within document M-CA 4, which comply with the EU/regulatory requirements outfined within SANCO/3029/99 rev 4.

Findings

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and treated samples from the study in each set of analyses. All overall average recoveries were within the acceptable range of 70 110 %. All the recovery results are considered valid. Recovery results are presented in Table 6.6.2.46.

No residue of fluop am or related metabolites were found above the LOQ in any of the control samples of rotational cropp natrices analysed.

The residue levels of Dropycan and its refevant metabolites in the rotational crop matrices of spinach leaves are summarized in the Table 6.6.2 47.

The storage period of deep-frozen samples ranged between 356 and 380 days.

Residues in spinach leaves

In trial 08-2070-01 and 08-2070-02 (BBI 28-29 days),

14 days before harvest .

- residues of fluopyfam (AE C656948) range between 0.02 mg/kg and 0.09 mg/kg.
- reductor FLUbenzamide range between 0.04 mg/kg and 0.05 mg/kg.
- Desidues of FAU-7-OM range between 0.08 mg/kg and 0.22 mg/kg.

residues of LU-PCA and FLU-methyl-sulfoxide were < 0.01 mg/kg.

At harves

- Gresidues of fluopyram (AE C656948) range between <0.01 mg/kg and 0.07 mg/kg
- residues of FLU-benzamide range between 0.01 mg/kg and 0.02 mg/kg.
- residues of FLU-7-OH range between 0.045 mg/kg and 0.08 mg/kg.

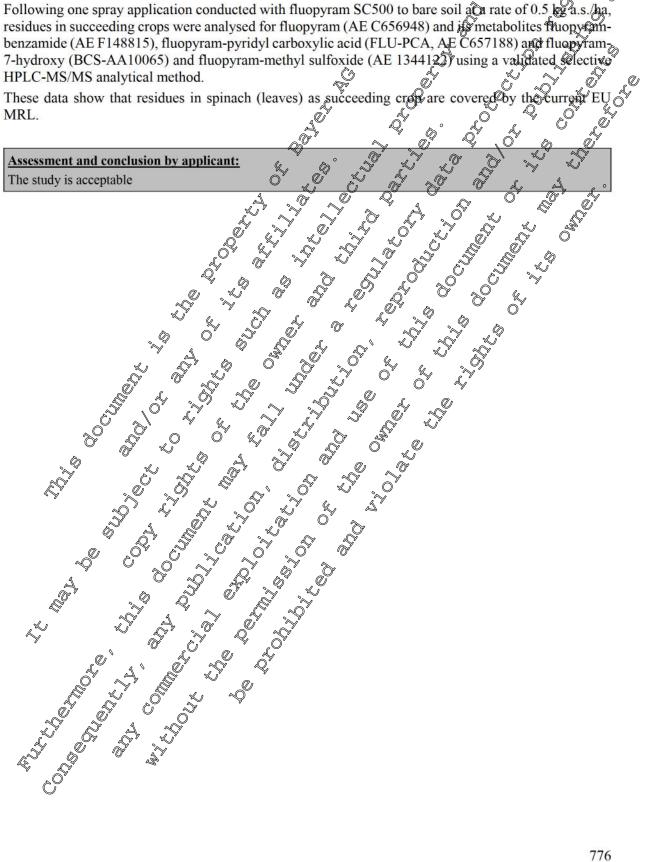


residues of FLU-PCA and FLU-methyl-sulfoxide were < 0.01 mg/kg.

Conclusions

Following one spray application conducted with fluopyram SC500 to bare soil and rate of 0.5 gas./ha, residues in succeeding crops were analysed for fluopyram (AE C656948) and is metabolites fluopyrambenzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE C657188) and fluopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122) using a valuated selective

HPLC-MS/MS analytical method. These data show that residues in spinach (leaves) as succeeding cropp are covered by MRL.



Ů



Crop/Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD*(())
Fluopyram (AE C650	5948)			<u> </u>
	0.01	98	98	\$ \$
Spinach, leaf	0.10	67	67	
Spinacii, icai	1.0	91	Ð	
		Overall recovery (n=3)	85	Ø 39.1 ×
Fluopyram-benzamic	de (AEF14881	5)	ý "Ô	
	0.01	91	. ~~ 99°° (~~	
Spinach loof	0.10	610	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	$\sqrt{\sqrt{2}}$
Spinach, leaf	1.0	\$\$6 Q	86 2 2), [*] [*]
		Overall recovery (n=30)	N 10 N	ي 20 ج
Fluopyram-pyridyl-c	arboxilic-acid	(AE C657188)		
	0.01	× 83 × 1	P √83 √ 2	
Solarah lasf	0.10	0 490 2 3	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	- Q O
Spinach, leaf	1.0	N 86 V		Å, Å
	Â	Overall recovery (n=3)	S 086 0	^ ≫ • √ 4.1
Fluopyram-7-hydrox	y (BCS-AA)0	065X 0 5 0		×.
	0.01	× ~ 89 ~ ~		
Spinach, leaf	0.10		× × × × × ×	õ
Spinacii, ieai	°∼1.0	\$ \$ \$6 \$ \$	× × 86, 7 ×	. —
	*	Øverallorecovery (n=3)	× 79 5	19.5
Fluopyram-methylsy	Øoxide (ÅE13	122) <i>(1</i> 22) (1) (1) (1) (1) (1) (1) (1) (1) (1) (1		
Į.	Q 01 0		61	
Spinach look	0.10	109 N N	0 1 99	
Spinach, leaf	© 1,0	0 40 102 S	102	
, ^o ô		Overall recovery (n≠3)	O _≪ 091	28.6
L: fortification level, RSD -	Relative Standard	Deviation O	<u> </u>	
some RSDs were not calculation as: fluopy	ated as there were	only two individual recoveries given	. O [¥]	
inal determination as: FLU4	onzamide/Residu	es calculated as: fluopyram	S S S S S S S S S S S S S S S S S S S	
inal determination as: FLY1	nethylsulfoxide®	ésidues calculated as: fluopyram	-	
inal determination as: FLU-3	700 Residues cal	culated as: fheopyram		
	or or a			
ÂŶ C				
A				
	~~~~~			
A 4	XA			
N° N				
_@`	. 4	e é		
		culated as: fhoopyram		
		3		
inal determination as: FU- inal determination as: FU- inal determination as: FLU- Control of the second sec	PCAResidues data 700 Residues calo 100 Residues c	culated as: fluor)fram		

#### atahalitas in spinach loof Table 6 6 7 16 ъ data for fl 1 • /



Page 778 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram 9

Image: constraining (a)         Transplanting (b)         date (b)         constraining (c)         date (c)         constraining (c)         for (c)         fo	Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application rate per treatment <u>to bare soil or target</u> <u>crop</u>	treatments and and last	ortion alvsed stage al sampling		arties	Residues (r	ec ^t i ng/kgj ^{ij}	olisiten conten	t ^{\$} O ^{TC}	PHI (days)
08-2170-01       Application to bare soil       1) 11.04.2008       0.5       300       0.17       14.03.2008       1eaves       47       0.02       0.05       0.05       0.06       0.00       <0.01       0.07         Spain       3) 25.05.2008       3) 25.05.2008       -15.06.2008       -15.06.2008       0.01       0.01       0.03       0.00       <0.01       0.03       <0.01       0.03         Barcelona       crop: Spinach       -15.06.2008       0.01       0.01       0.01       0.01       0.03         Barcelona       crop: Spinach       -15.06.2008       0.01       0.01       0.01       0.03         Barcelona       crop: Spinach       -15.06.2008       0.01       0.02       0.05       0.01       0.03         South       Application to F       10.04.04.2008       0.5       300       0.717       0603.2008       0.01       0.01       0.02       <0.01       0.02       <0.01       0.02       <0.01       0.02       <0.01       0.02       <0.01       0.03         08-2170-02       Application to F       1) 04.04.2008       0.5       300       0.717       0603.2008       Vereves       0.01       <0.01       0.02       <0.01       0.08		(a)		kg a.s./ha Water (L/ha) kg a.s./hL			C656948 as Af C656948	benzamide as AE C (36948	PCA as	70H as	methyl- sulfoxide as AE	residue	(e)
Veneto Europe, <u>Rotational</u> South <u>crop:</u> F Spinach 2008 Seven R	Spain 08850 Gava - Barcelona Cataluña Europe, South F	bare soil <b>PBI: 28 d</b> <u>Rotational</u> <u>crop :</u> Spinach	3) 25.05.2008 - 15.06.2008	900010102 23	BUTS OW			3.9	4	0.08 0.00 3	<0.01 <0.01		67 81
<ul> <li>(a) According to CODEX Classification / Guide</li> <li>(b) Only if relevant</li> <li>(c) Year must be indicated</li> <li>(d) Either growth stage description or BBC Code</li> <li>(g) Stage (free conditions)</li> <li>(h) Formulation type</li> <li>(h) Formulation type</li> <li>(i) Application method</li> <li>(j) Method information</li> <li>(k) LOQ</li> <li>(k) LOQ</li> <li>(k) LOQ</li> <li>(k) Total residue calculated : Sum of fluopyram+FLC benzamide</li> </ul>	Italy 37050 Albaro Veneto Europe, South F 2008	bare soil PBI: 29 d Rotational crop: Spinach Seven R	May De	copy cument	JOR ' JOR	and ⁴⁹ er	£.b.b	0.01	<0.01 <0.01				65 77
FUT COMPANY CONTRACTOR	<ul> <li>(a) Accordin</li> <li>(b) Only if n</li> <li>(c) Year mu</li> <li>(d) Either gr</li> <li>G greenhou</li> </ul>	ng to CODEX Classifielevant st be indicated owth stage description ise calculated :	ication / Guide	(c) Bays after last applic (f) Remarks m@ ficlude information which m (g) Study reference (h) Buor to last trastbent (h) buor to last trastbent (h) buor to last trastbent	ation (Laber Pre-harvest id :: Climate conditions; Cel autorites are included	whal, PHI, underline) erence to analytical metho	od and	<ul><li>(i) Applica</li><li>(j) Method</li><li>(k) LOQ</li></ul>	ation method d information	(m)	Storage (max) ! based on date P based on pro	e of analysis duction date	



Data Point:	KCA 6.6.2/24
Report Author:	
Report Year:	
Report Title:	Determination of the residues of AE C656948 in/on summer rape after spraving of Fluopyram SC 500 in the field in northern France
Report No:	08-2169
Document No:	<u>M-350532-02-1</u>
Guideline(s) followed in study: Deviations from current	EU-Ref: Council Directive 914414/EEC of Jul 015, 1991, Annex II, part A, section 6 and Annex III, part A, section 8 Residues in or on Treated broducts, Food and Feed EC guidance working document 7029/VJ95 rev 5 (1997-07-22) OECD Guideline for testing of Chemicals; Residues to rotational crops (limited field studies), No. 504, 8 Jan. 2007
test guideline: Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes a way of a go and a go
8	

<u>Methods</u> The purpose of the study 08-2169 was to determine the magnifude of residues of fluopyram (AE C656948) and is metabolites fluopyram-benzamide (AE F148845), fluopyram-pyridyl carboxylic acid (FLU-PCA, APC65 \$88), floopyram-7-hydroxy BCS A10065) and fluopyram-methyl sulfoxide (AE 1344122), in/on rape (pod and seed). One spray application with Fluopyram SC 500, a suspension concentrate (SC) formulation containing 500 g/L thropyrain was done to bare soil followed by sowing of summer rape with plant back interval of 30 days. The crop was sowed 33 days instead of 30 days after application on bare soil due to bad weather conditions

0

One supervised asiductrial as conducted in northern Durope (northern France) during the 2008 growing season, Ó" Ô

One spray application of Quopyram S6 500 was done to bare soil at an application rate of 1 L/ha (equivalent to 0.50 kg/ha fluopyram), with a water, rate of 300 L/ha. The application procedure was followed by incorporation of the test item into the soil to a depth of 6 cm 33 days after application. The treatment was made at the scheduled rate

For residue analysis, samples of rape (pod and seed) were taken from the treated and the control plots. Samples of podewere taken 29 days prior barvest at a growth stage BBCH 79 and at harvest maturity growth stage BBCH &9.

The field samples were stored deep-frozen within 24 hours after sampling and until dispatch. All field samples were shipped by deep freeze lorry and arrived in good condition. The field samples were stored in a freezer at 18°C until preparation of the examination samples. For the preparation of examination samples, the deep for zen field samples were shredded with dry ice in a cutter. Representative parts of the shredded field samples were transferred into polystyrene boxes separately for analysis (examination samples Q and archiving (retain samples) and stored for analysis or archiving at  $\leq$ -18°C until analysis.

Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (1997), 05/02/2007, M-



<u>283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues were extracted from 10 g of sample material by two successive extractions using a high-speed blender with a mixture of acetonitrile:water (80:20; v:v). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

- One dilution was performed under acidic conditions: this extractationed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed the determination of fluopyram, FLU-benzamide and FLU-7-QP.

An aliquot of the extracts was injected into LC-MSTMS operated in Electrospray Ionization mode:

- One injection in positive electrospray ionization for the determination of fluopyram FLUbenzamide and FLU-7-OH.
- Another injection in negative electrosprationization for the determination of FLUPCA and FLU-methyl-sulfoxide under different conditions.

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standardization using isotopically stable labelled internal standards.

The Limit of Quantification (LOQ) expressed as fluopyram, defined as the lowest validated fortification level, was 0.05 mg/kg for wheat shaw and 0.01 mg/kg for all other matrices

Full details and acceptable validation data to support this nothod are presented within document M-CA 4, which comply with the EU/regulatory requirements outlined within SANCO/3029/99 rev 4.

#### **Findings**

In order to check the performance of the analytical method, receivery determinations were concurrently performed to the analyses of control and treated samples from the study in each set of analyses. The means of the concurrent recoveries were for all fortification levels within the acceptable range of 70 - 110 % even for FLU method sulfoxide at 111 % at 0.1 mg/kg in rape pod. All overall mean recoveries are in the acceptable range of 70 - 110 % therefore, the results are considered valid. Recovery results are presented in Table 6 6.2- 48

No residues above the 2005 were found in the control samples. The detailed results obtained in the rotational crop of rape are summarized in Table 6.6.2-49. The results were not corrected for concurrent recoveries

The maximum storage period of deep-frozen samples was 313 days for pods and 284 for seeds.

### Residues in rape 🦼

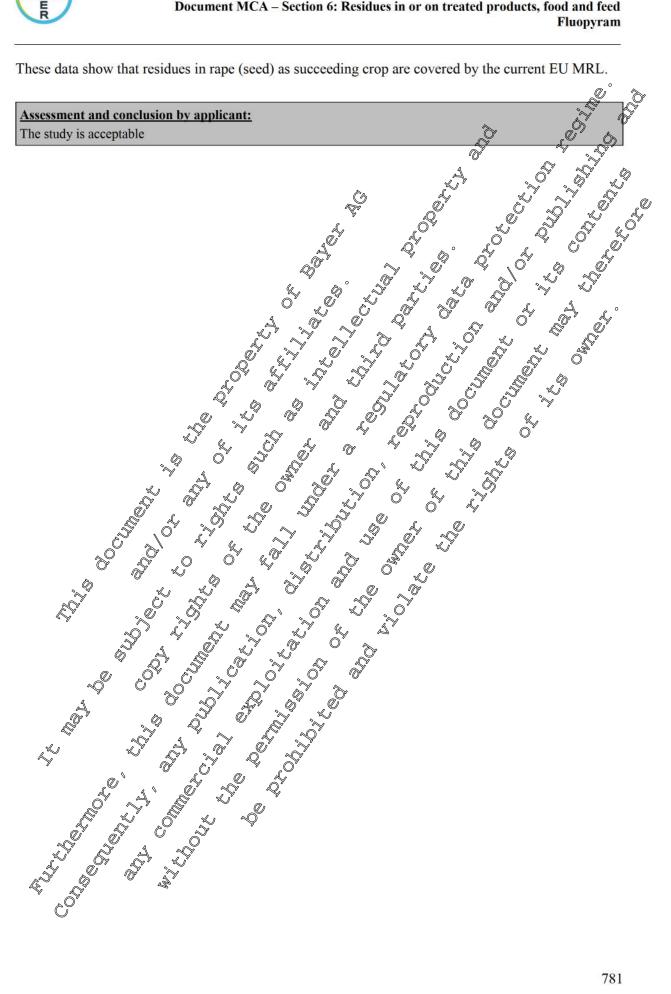
In trial 08-2169-01 (PBI) 3 days), residues of fluopyram (AE C656948) in pods were 0.02 mg/kg at BBCH 79 and 0001 mg/kg in seeds at flarves!

Residues of the metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methyl-sulfoxide) in pods were <0.01/mg/kg at BBOP 79 and <0.01 mg/kg in seeds at harvest.

## Conclusions

Following one spray application conducted with fluopyram SC500 to bare soil at a rate of 0.5 kg a.s./ha, residues of succeeding crops were analysed for fluopyram (AE C656948) and its metabolites fluopyrambenzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE C657188) and fluopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122) using a validated selective HPLC-MS/MS analytical method.







ble 6.6.2-48: R	Recovery data f	or fluopyram and its meta	abolites in rape	
Crop/Sample material	Fortification level (mg/kg)	Single values (%)	Mean value (%)	RSD* (%)
luopyram (AE C65			O.	
	0.01	94, 101	98,	<u>, 0² , 6³</u>
Rape (pod)	0.10	100, 102 💍	164	× - ~
	Over	all recovery (n=4)	Q99	0 3a ×
	0.01	72	- 4 -	<u> </u>
Rape (seed)	0.10	70		Å -
	Over	all recovery (n=2)	× ×71 ~	
luopyram-benzami	ide (AEF148815)			y y v
	0.005	86, 92	0 0 0	ð - Å
Rape (pod)	0.05	× 100x 96 ~ ~	A98 6	4 <u>-</u> A
	Over	all recovery (n=4)	0 [°] 94	8.4
	0.005	6° 4° 7.5° ,5°	0.5 \$	Q - 6
Rape (seed)	0.05	70 2	7 8- 0	
	Qver	all recovery (n=2)	× 73	) ₍ -
Fluopyram-pyridyl-	carboxilic acid (	AE C657188)		0×
	0.006	106,104 0	× 104 ×	jūj -
Rape (pod)	°∕>∕0.06	\$04, 104 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	104	-
	🖉 🖉 Över	all recovery (n 🗗 💊	× 404 ×	0
	0.006		0-4	-
Rape (seed)	0.06	103 × 103 ×		-
	ð Över	all recovery (n=2)	£ <b>190</b>	-
luopyram-79ñydro	() 👻 🔈			
	0.01	A 02, 100 0	<b>96</b>	-
Rape (pod)	0.10	ح [∞] م 98, 190 م	<b>○</b> [♥] 99	-
× * .	Ó "Ó Oyer	all recovery (n=4) 🔬 🔬	98	3.9
, S	0.01	× 0°62 °	-	-
Rape (seed)	Q 0.10		-	-
~~ (	Ovêr	all recovery (n=2)	65	-
Fluopyra <u>m</u> -methyls	ulfoxide (AF934	41 <b>22</b> )	•	
	0.000	86,99	88	-
Rape (pod)	\$ \$06	0 1 M 111	111	-
× ×		all recovery (n=4)	100	13.4
"Ø [°]	0.000	× 115	-	-
Rape (secol)	<b>€</b> 06 √	98	-	-
	Øver	all becovery (n=2)	107	-
fortification level @SD	- Relative Standard D	eviation		I.

Recovery data for fluonyram and its metabolites in rane Table 6 6 7- 48.

FL: fortification level@SD - Relative Standard Deviation * some RDS were not calculated as there were only two individual recoveries given Final determination as: Fl@-benzativde Residues calculated as: fluopyram Final determination as: Fl@-benzativde Residues calculated as: fluopyram Final determination as: FLU-methylsulfoxide Residues calculated as: fluopyram Final determination as: FLU-PCA Residues calculated as: fluopyram Final determination as: FLU-PCA Residues calculated as: fluopyram Final determination as: FLU-PCA Residues calculated as: fluopyram



Page 783 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Table 6.6.2- 4	49: Results o	f rotational cro	op trial conducted wi	th fluopyram		r BC	art I	3.D.J.	N. N.	9 ¹ Me.	Ĵ.	
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	Application rate per treatment <u>to bare soil or target</u> <u>crop</u>	Dates of treatment or no. of treatments and last date	rtion dysed c	tual F	FLU- bergamide C656948	Residues (		ants ants		PHI (days)
	(a)	(b)	kg a.s./ha (L/ha) a.s./hL	f of a		AE C656948 X#S AE C656948¢	FLU- benzamide as AE C656948	FLE-PCA Oas AE C656948	FK1-70H as AE C656948	FLU- methyl- sulfoxide as AE C656948	Total residue calc.	
08-2169-01 France, north 37310 Chambourg sur Indre Centre Europe, North F 2008	Application to bare soil <b>PBI:33 d</b> Rotational crop: Rape, summer Olindigo	1) 16.04.2008 2) 04.07.2008 - 15.07.2008 3) 29.08.2008	0.5 OCULINE 100 OCULINE 100 OCULINE 100 CULINE 100		od Je	222000 (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2001) (2		\$9.01 ₹\$ <0.01	<0.01	<0.01	0.03	139 168
<ul> <li>(a) According</li> <li>(b) Only if re</li> <li>(c) Year must</li> <li>(d) Either gro</li> <li>G greenhous</li> </ul> Total residue c	g to CODEX Classificati levant t be indicated wth stage description or se F f alculated : sum	on / Guide	Days affe last application (f) Rebarks may include: Clim information, disch metabol Study referre prior to ast treatment	Label pro-flurvest interva atic conditions; Reference tes are included	OHI, underline e to analytical method and the off of the off off off off off off off off off of	(h) (i) (j) (k) **	Formulation type Application method Method informatio LOQ residue in control	d (	P based o	max) 1 date of analysis n production date		
·	FUITTHERM	orat LAL.	Days affectives application of the second se	Billing and								
	COIL	de witter									783	



Data Point:	KCA 6.6.2/25
Report Author:	
Report Year:	2009
Report Title:	Determination of the residues of AE C656948 in/on winter rape after spraying of
	Fluopyram SC 500 in the field in Italy and Spain
Report No:	08-2180
Document No:	<u>M-359808-01-1</u>
Guideline(s) followed in	EU-Ref: Council Directive 91/41 (EEC of July 16, 1991, Annex II, part A, section 6 and Annex III, part A, section 8
study:	Annex II, part A, section 6 and Annex III, part & section 8
	Residues in or on Treated Products, Food and Feed
	EC guidance working document 7029/VI/9 Prev. 5 (1997-07-22) 2
Deviations from current	none
test guideline:	
Previous evaluation:	No, not previously submitted
GLP/Officially recognised	Yes, conducted under OLP Officially recognised testing facilities
testing facilities:	
Acceptability/Reliability:	Yes $\mathcal{A}$
	Yes 47 45 77 45 77 67 0

#### **Materials and Methods**

The purpose of the study 08-2180 was to determine the magnitude of residues of fluopyram (AE C656948) and its metabolites thiopyram-benzamide (AE F14885), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE C657188), fluopyram-7-h edroxy (BCS-AA10065) and luopyram-methyl sulfoxide (AE 1344122), in/on rape (pod and seed). One spray application with Fluopyram SC 500, a suspension concentrate (SC) formulation containing 500 g/L fluopyram was done to bare soil followed by sowing of summer rape with plant back interval of 29-30 days.

Two supervised residue trial was conducted in southern Europe (Italy and Spain) during the 2008 growing season.

In trial \$-2180-01, the application of Fluopyram \$C 500 was done to bare soil at an application rate of 0.88 L/ha (equivalent to 0.44 kg/ha fluopyram) with a water rate of 265 L/ha. The application procedure was followed by incorporation of the test item into the soil (using a rotovator three hours after the application) 29 days before solving of winter rape. The treatment was 12% underdosed due to clogging of one nozzle

In trial 08-2180-02, the application of Favopyram SC 500 was done to bare soil at an application rate of 1 L/ha (equivalent to 050 kg/ha fluopyram) with a water rate of 300 L/ha. The application procedure was followed by incorporation of the test item into the soil to a depth < 8 cm and 30 days before sowing of winter rape. The treatment was made at the cheduled rate.

For residue analysis, samples of raper pod and seed) were taken from the treated and the control plots. Samples of pod were taken 39-37 days prior harvest at a growth stage BBCH 79 and at harvest (BBCH 89).

The field samples from both toals were stored deep-frozen within 24 hours after sampling and until dispatch All field samples were shipped by deep-freeze lorry and arrived in good condition. The field samples were stored in a treezer at  $\leq$ -18°C until preparation of the examination samples. For the preparation of the shredded field samples were transferred into polystyrene boxes separately for analysis (examination samples) and archiving (retain samples) and stored for analysis or archiving at  $\leq$ -18°C until analysis.



Residues of fluopyram and its metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methylsulfoxide), were determined by LC-MS/MS according to method 00984 (**1999**, 05/02/2007, <u>M-283301-01-1</u>, see MCA section 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Residues were extracted from 10 g of sample material by two successive extractions using a high-speed blender with a mixture of acetonitrile:water (80:20; v:v). After centrifugation the extract volume was adjusted. Then, the extracts were diluted ten times by adding the internal standards:

- One dilution was performed under acidic conditions: this extract allowed the determination of FLU-PCA and FLU-methyl-sulfoxide.
- In parallel, another dilution was performed under basic conditions: this extract allowed the determination of fluopyram, FLU-benzamde and FLU-7-OH.

An aliquot of the extracts was injected into LCMS/MS operated in Electrospray Ionization mode:

- One injection in positive electrospray ionization for the determination of duopycam, FJUbenzamide and FLU-7-OH.
- Another injection in negative electrospray ionization for the determination of FLU-PCA and FLU-methyl-sulfoxide under afferent conditions

The linearity was demonstrated in each analytical batch with a 1-X weighted calibration curve established with at least 5 concentration levels. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standardization using isotopically stable labelled internal standards.

The Limit of Quantification (LOQ), expressed as fluoryranOdefixed as the lowes validated fortification level, was 0.05 mg/kg for wheat straw and 0.01 mg/kg for all other matrices.

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

#### Findings 🔊

The method performance could have been checked by concurrent recoveries. Unfortunately, the recovery samples which were extracted the same day as the examination samples were invalid, because of a dilution error. Therefore, the concurrent recoveries were extracted and analysed three days later. This deviation was accepted because the method 00984 was fully validated on rape seed. Details on concurrent recovery data are shown in Table 6.62- 50 No mean of recoveries and no RSD can be calculated because only on individual recovery was performed by level. The overall average recoveries (n=2) ranged between 92 1280

No residues above the COQs overe found in the control samples. The detailed results obtained in the rotational crop of rape are summarized in Pable 66.2-51. The results were not corrected for concurrent recoveries.

The maximum storage period of deep@frozer/samples was 158 days for pods and 123 for seeds.

#### Residues in rape 🔍

In pods, in trial the two trials (PBI 29-30 days), residues of fluopyram (AE C656948) were between 0.01 and 0.06 mg/kg at BBCH 79.

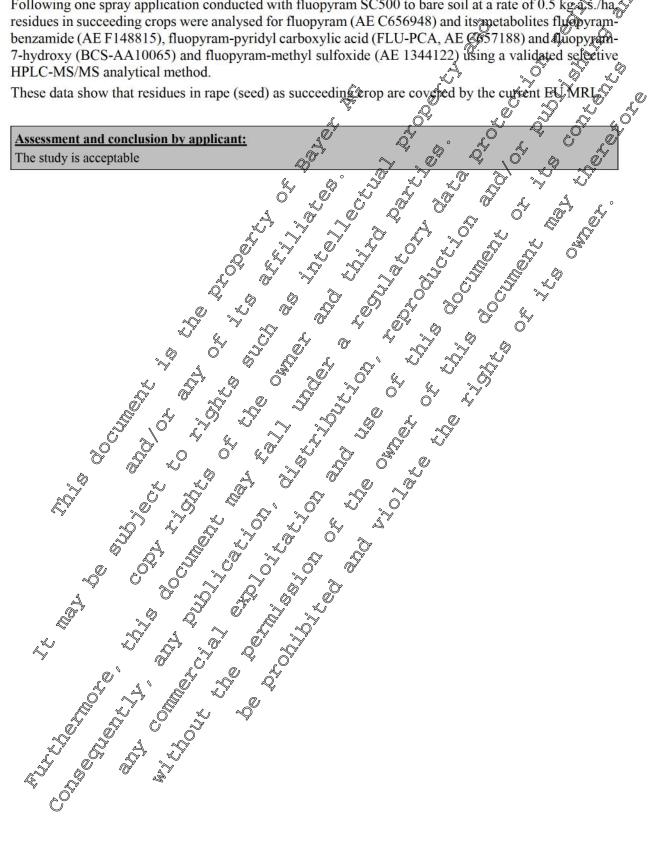
Residues of the metabolites FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methyl-sulfoxide) in pods were 0.01 mg/kg at BBCM 79.

In seeds of trial the two trials (PBI 29-30 days), residues of fluopyram (AE C656948) were between <0.01 and 0.01 mg/kg at BBCH 89.

Residues of the metabolites (FLU-benzamide, FLU-PCA, FLU-7-OH, FLU-methyl-sulfoxide) in seeds were <0.01 mg/kg at BBCH 89.



<u>Conclusions</u> Following one spray application conducted with fluopyram SC500 to bare soil at a rate of 0.5 kg as./ha residues in succeeding crops were analysed for fluopyram (AE C656948) and its metabolites fluopyrambenzamide (AE F148815), fluopyram-pyridyl carboxylic acid (FLU-PCA, AE (\$57188) and Quopyram-7-hydroxy (BCS-AA10065) and fluopyram-methyl sulfoxide (AE 1344122) using a validated selective HPLC-MS/MS analytical method.





Crop/Sample material	Fortification level (mg/kg)	Single values (%)	Mean value (%)	RSD* (%) - (%) - - - - - - - - - - - - -
luopyram (AE C65			- Q	P ²
	0.01	156	- 4	(
Rape (seed)	0.10	100 🖏	-4	- 🔊
1 ( )		all recovery (n=2)	428	<del>R</del>
luopyram-benzam			¥	
1 0	0.005	91	-0°	5-5
Rape (seed)	0.05			<u>∛ _\O`</u>
.F. ()		all recovery (n=2)	× 95 ×	
luopyram-pyridyl-				N K
	0.006	x 97 × 3		
Rape (seed)	0.06	07 , °~ 97 . O . ~		<u>S</u> - 1
1 ( )		antrecokery (n=2) ,S	970	<u> </u>
luopyram-7-hydro				y St
	0.01	L @ 85 L	× - ~	a 0 - 7
Rape (seed)	0,10	× 99 0 4	0 ⁴ -6	<u>0</u> - 0
	Over	all recovery (n=2)	× 32 ~	Ô
luopyram-methyls	ulfoxide (AE134	41220		
	L 0.000			<u>9</u> -
Rape (seed)	2 0.06			-
J.		all recovery (n=2)	× 101	-
al determination as: fluo al determination as: FLU al determination as: FLU al determination as: FLU	Jaced as there were of yram Resulues calcul -benzamide Resilfaes -methylsulfoxide Resi -PCA Resides calcul	viation by two and vidual secoverics given lated as: fluopyrand calculated as: fluopyrand iduo calculated as: fluopyran and as: fluopyran		
al determination as: FLU	H Residues calcul	lated as Anopyran		

Table 6 6 2- 50. Recovery data for fluonyram and its metabolites in rane



Page 788 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

Fable 6.6.2- :	51: Results	of rotational	crop trial c	onducted v	vith fluopyr	am		Þ	,	e e e e e e e e e e e e e e e e e e e	J.D.J.	reos)	TUC .	Ĵ.
Trial No./ Location/ Year	Plot (commodity)	Date of 1. Sowing or planting 2. Flowering 3. Harvest 4. Transplanting	treat to bare so	on rate per ment <u>il or target</u> op	Dates of treatment or no. of treatments and last date	Portion analysed	Growth Ostage at sampling	CEUR	Prop ^e	Residues	(mg/kg) ²	COLICE FLUE	, C ^{\$}	PHI (days)
	(a)	(b)	a.s./ha (L	ater g (ha) a.s./hL	De (c)	0.5£7		C656948 C656948 as AE C656948	as AE (). C656948	AE C656948	AE C656948	as AE	calc.	(e)
08-2180-01 Spain 41310 Brenes Sevilla Andalucia Europe, South F 2008	Application to bare soil <b>PBI:29 d</b> <u>Rotational</u> <u>crop:</u> Rape, winter Jura	MAIS	3.0CUM.C		t D	ND pod	01 7 0 9 0 89 7 0 1 1	0.06 0.06 0.001 0.001			5-0.01	<0.01	0.07	200
08-2180-01 Spain 41310 Brenes Sevilla Andalucia Europe, South F 2008	Application to bare soil <b>PBI:30 d</b> <u>Rotational</u> <u>crop:</u> Rape, winter Livius	a.	a l			Jelle L	OWNER T	~0.0E	<0.01	<0.01	<0.01	<0.01	0.02	240 275
(a) According (b) Only if re (c) Year must (d) Either gro G greenhous `otal residue c	to CODEX Constitution levant to indicated wth stage description to alculated : support BULL CORE	ation / Guide to r BBCH Code Frield Coff fluopytam+F UCAT COTO COTO COTO COTO COTO COTO COTO COTO COTO COTO COTO COTO	Ge Dave (1) Genar (1) Genar (1	ther last applicant ks may include: C lation which metal reference Mast treatment ideo	n (Label pro harve limatic conditions; offer are included	st interal, PHI Reference to a	, underline) nalytical method	and		ion method information	(l) (m) #	Method valida Storage (max) ! based on date P based on pro no data availal	e of analysis duction date	
	Ċ ^O [*]	W.L.												78



#### CA 6.7 **Proposed residue definitions and maximum residue levels**

#### CA 6.7.1 **Proposed residue definitions**

#### **Plants**

During the development and very first inclusion submission of fluopyram (data generation), for the selection of the metabolites possibly relevant for risk assessment, consideration was given to the relative levels found in the available metabolism studies (see MCA 6.2). Metabolites were envisaged for inclusion into the residue definition for risk assessment, if they were major metabolites.

The metabolism studies were conducted with two different radio beled test items (phenyl label and pyridyl label) to cover both sides of the molecule after cleavage. Considering that all metabolites which were not previously excluded from the assessment are covered by the toxicological profile of parent, the TRR is considered to give a good overview of the toxfoological exposure.

#### Metabolism in primary crops

- Phenyl label : the two main compounds fluopyram and fluopyram benzamide) represent more than 75% of the TRR in grapes, patato, bean, rice (all toliar applications), or pepper (drip application) and 54-68% in Wheat (seed treatment). , Ô
- Pyridyl label : parent fluopyram is the most abundant compound in most of the studies but fluopyram-pyridyl-aceter acid (M40) and fluopyram-pyrolyl-carboxyle acid (M43) are also major metabolites after cleavage of the parent in some matrices (potato tuber, succulent, dry bean, wheat straw and pepper fruit).

#### Metabolism in rotational crops

O The metabolic pathway in the rotational grop studies was shown to be similar than in primary crops. However, fluopyram-7-OH (M08) and its conjugates occurred in much higher proportions (swiss chard, wheat stow and hay), and metabolit fluopyram-methyl-surfoxide (M45) occurred in significant ×, amounts in wheat matrices

Based on the available metabolism data, for the first inclusion dossier (please refer to DAR Vol. 3, B-7); fluopyram and fluopyram-benzamide (M23), as well as fluopyram-pyridyl-acetic acid (M40) and fluopyram-pyridyl-carboxylic acid (M43) were measured in residue trials (primary crops). For rotational crops, fluopyram and fluopyram-benzamide (M25), Fluopyram-7-hydroxy (M08), Fluopyram-p@ridyl_Carboxylic acif (M4D and fluopyram-methyl-sulfoxide (M45) were determined.

Subsequent to the generation and evaluation of this data, low residue levels were observed for fluopyrampyridyl-acetic acid (M40), fluop ram-pyridyl-carboxylic acid (M43) and (for rotational crops), fluopyram-7-hydroxy (M02) and fluopyram-methyl-sulfoxide (M45). The respective contribution to the livestock dietary burden and to the consumer risk assessment turned out to be relatively low to very low (please refer to revised DAR Nol. 3B-7, August 2012, from p130).

As a result, FSA did not included these spetabolites in the residue definition for risk assessment (EFSA Journal 2013;11(4):3052) both for primary and rotational crops and defined it as parent fluopyram and fluopyram-benzamide.

Moreover, locause fluopyram-benzamide is expressed as parent and included in the definition of residue for risk assessment, it covers also the pyridine side when the dietary risk assessment is made and expositive compared to the toxicological endpoints of parent. For these reasons, there is no need to amend the DoR for risk assessment.

For monitoring purposes, **parent fluopyram** is a good marker and the following residue definition is proposed : Fluopyram.



#### Processed products

The radiolabeled high temperature hydrolysis studies for fluopyram and its metabolites fluopyrambenzamide, fluopyram-7-hydroxy (M08), fluopyram-pyridyl carboxylic acid (M43) and fluopyrampyridyl-acetic-acid (M40), which simulate the conditions associated with baking, brewing and boiling, showed that all compounds remained stable following the processing procedures except fluopyrampyridyl-acetic-acid. As residues of fluopyram-pyridyl-acetic-acid in raw agricultural commodities are expected to be very low (revised DAR, Vol. 3, B-7, p133-134), it is considered appropriate to maintain the current residue definitions (risk assessment and monitoring) for processed commodities, which are aligned with the residue definitions defined for the primary crops.

#### Animal commodities

Fluopyram, fluopyram-benzamide and fluopyram of this are the major metabolites identified from the poultry and ruminant metabolism studies with labeled fluopyram on the phenyl group. Fragments identified from the pyridyl labeled fluopyram show also the major preserve of parent fluopyram and fluopyram-olefins. Additionally, hydroxylated metabolites and onjugates are measured in tuminant liver and kidney but those compounds are considered to be covered by the toxicological profile of the parent and are not proposed to be included in the residue definition.

For these reasons, the proposed residue definition for risk assessment in mimal commonties is

• The sum of fluopyram, fluopyram-benzamide, and fluopyram-befins@xpressed as fluopyram.

For monitoring purposes, fluopyram benzamide appears to be a good marker anothe following residue definition is proposed :

• The sum of fluopyram and fluopyram bozzamide expressed as fluopyram

Ĉ

This conclusion is in the with the 2020 review of the EU existing MRL according to Art. 12 of the Regulation (EC) No 396/2005. Phase see below the extract of the document "Review of the existing maximum residue levels for fluopyram according to Article 12 of Regulation (EC) No 396/2005" (EFSA Journal 2020;18(4):60(59):

A wide range of growing conditions and crop groups has investigated (spraying in fruits, pulses, and tuber crops, drip irrigation in Huits; is well as cereals, row crops and leafy crops grown in rotation). Fluopyrom is also authorised as primary seed treatment on oil seeds and as a local treatment (preforcing) on chicory roots (withorts). A othe metabolite pattern is essentially the same in all crop categories even under different application systems, the above studies are considered to cover also the latter uses. Overall, the studies experimental designs were pepresentative of the authorized uses and no further study if required.

As the parent compound was found to be a sufficient marker in all crops investigated, the residue definition for enforcement is proposed as 'furpyrem' only.

An analytical method for the enforcement of the proposed residue definition at the LOQ of 0.01 mg/kg in all/four main plant matrices is available (EFSA, 2013a). According to the EURLs, the LOQ of 0.002 mg/kg in high water content and high acid content commodities and the LOQ of 0.01 mg/kg in high oil content and dev commodities is achievable by using the QuEChERS method in routine analyses (EURL, 2018).

The metabolic pathway of fluopyram in plants can be regarded as essentially the same in all crops investigated, with the parent compound being one of the major constituents of the residues. The metabolic pathway priminally consists of the hydroxylation of parent compound (M08), followed by cleavage of the hydroxylated parent compound leading to metabolite M25 (fluopyram-benzamide) from the phenyl moiety and metabolites M40 (primary crops only, including its hexose-conjugate M42), M45 (rotational crop only) and M43 from the pyridyl moiety of the active substance.



In the supervised field trials assessed in the current review M25 was detected only in a few commodities (up to a level of 0.16 mg/kg in rape seed) (see Section 1.2.1). In rotational crop field trials, solely M25 and M08 were found in significant amounts, and only in straw (see Section 1.2.2). However, as the relative contribution of M08 is little and would have very limited impact on the animal burden of at all its inclusion in the residue definition for risk assessment that would be specify to rotation  $\mathfrak{A}$  cereals (straw) is not proposed. The peer review concluded that metabolite M40 does not need to be included in the residue definition as is of no toxicological concern at the levels detected in supervised field trials and it may be covered by the concurrently detected phenyl specific M25, included in the residue definition (Germany, 2011).

M08, M25, M40 and its conjugate M42 were considered covered by the foxicological profile of the parent compound (EFSA, 2013a). M43 and M45, are common metabolites with active substance flugnicolide In the light of their levels in food and feed items and the conclusion for fluopecolide the peer review considered these metabolites as toxicologically not relevant (Germany, 201)

Altogether, the residue definition for risk assessment is proposed to remain with of fluopy am and fluopyram-benzamide (M25), expressed as fluopyram' as set by the peer review (EFSD, 2013a).

Note :

- •
- •

ration of all the above, leads to the follows Consideration of all the above, leads to the following proposed residue definitions for fluopyram: 

Table 6.7.1-1	ð	Resid	lue defin	uitions for	fluopyram	Ĩ
---------------	---	-------	-----------	-------------	-----------	---

Category O S C Category	Restrue definition
Enforcement (post-registration) residue definition in plant commodities	Fhiopyræm ở
Enforcement (post-registration) residue defortion for products of livestock origin:	Som of flyopyram and fluopyram-benzamide expressed as fluopyram
	Sum of flyopyram and fluopyram-benzamide expressed as fluopyram
Risk assessment residue definition for producte of livestock origin	Sum of flyopyram, fluopyram-benzamide and fluopyram-E/Z-olefins expressed as fluopyram
Riskassessment residue definition for processed plant commodities	Sum of flyopyram and fluopyram-benzamide expressed as fluopyram
Riskassessment residue definition for processed plant commodities	



Data Point:	KCA 6.7.1/01
Report Author:	
Report Year:	2008
Report Title:	U.S. plant residue definition for AE C656948: Communication with U.S. ECA
Report No:	201868
Document No:	<u>M-299913-01-1</u>
Guideline(s) followed in	OPPTS 860.1300 (Supplemental)
study:	
Deviations from current test guideline:	
Previous evaluation:	
GLP/Officially recognised	not applicable
testing facilities:	
Acceptability/Reliability:	

## CA 6.7.2 Proposed maximum residue levels (MRLs) and justification of the acceptability of the levels proposed 8

No MRL are proposed in the frame of this active substance renewar application.

## CA 6.7.3 Proposed maximum residue levels (MRLs) and justification of the acceptability of the levels proposed for imported products (import tolerance)

No MRL for imported products are proposed in the frame of this active substance renewal application.

## CA 6.8 Proposed safety intervals

There is no meed to propose safet intervals.

## CA 6.9 Estimation of the potential and actual exposure through diet and other

In order to evaluate the potential chronic and acute exponents to fluopyram residues through the diet, calculations were done using the EPSA PRIMo model (revision 3.1) and the following toxicological endpoints.

## Acceptable Daily Intake (ADI) and Dietary Exposure Calculation

According to the first EU inclusion peer review (EFSA, 2013), the ADI is at the level of 0.012 mg/kg bw/day.

## Acute Reference Dose (ARff) and Dietary Exposure Calculation

According to the first EU inclusion peer feview (EFSA, 2013), the ARfD is at the level of 0.5 mg/kg bw.

A risk based on MDI is not presented as it overpasses the 100% of ADI contribution. A more pertinent IEDI calculation is proposed in the frame of this renewal the consumer risk is evaluated regarding the contribution of the submitted data presented in Table 6.9-1 :

- Residues from representative uses according to the residue definition for risk assessment (RA)
- Residues in succeeding crops taken at the plant back interval showing the most critical values



- Residues in animal commodities from the submitted feeding studies at the worst-case feeding dose (tissues) or at a more realistic dose (milk)
- Residues in honey as presented in MCA 6.10.1 ٠

	Chronic	exposure assessment 😞	Acute	exposure assessment
Commodity	Input (mg/kg)	Comment 💎	Input (mg/kg)	Comment
Apple ¹⁾	0.07	STMR _{RA} rep. use	0.22	HRR rep. use
Table grape	0.025	STMR _{RA} rep use	0.05	ې HRRA rep. ase
Wine grape	0.025	STMR _{RA} Rep. use	0.05	HRRA rep. use
Strawberry	<loq< td=""><td>STMRevrotational</td><td>LOQ[®]</td><td>HRRACHAtional</td></loq<>	STMRevrotational	LOQ [®]	HRRACHAtional
Potato	0.03	STMR _{RA} rotational	0,69	HRRArotational
Carrot	0.05	STMR _{RA} rotational >	~0.06 £	HRRArotational HRRArotational HRRAROtational
Bulbs (onion. garlic)	0.02	TMRevrotational	√y 0.03 O	HRRAGIAtional
Tomato	<loq< td=""><td>STMRRA rotational</td><td></td><td>HRGX rotational</td></loq<>	STMRRA rotational		HRGX rotational
Sweet corn	<loq< td=""><td>STMR_{RA} rotational</td><td>SLOO C</td><td>ARRA rotational</td></loq<>	STMR _{RA} rotational	SLOO C	ARRA rotational
Lettuces	1.64	STMRA rep. 100		HRR Oep. use
Spinaches	<b>20,018</b>	STMRRA rotational	0.00	HRRA rotational
Pea(without pods)	<loq td="" ×<=""><td>SIMR_{RA} Forational</td><td><loq< td=""><td>HRRA rotational</td></loq<></td></loq>	SIMR _{RA} Forational	<loq< td=""><td>HRRA rotational</td></loq<>	HRRA rotational
Leek	y 0.03	STMR rotational	0.05 ×	HRRANStational
Pulses (dry)	< COQ	STMRRA rotational	[™] <l⊗q< td=""><td>HRRArotational</td></l⊗q<>	HRRArotational
Rape seed	0.02	SOMR _{RA} corational	0.02	<b>FR</b> RA rotational
Barley	0.02	STMRRA rep. use	\$ 0.09	HR _{RA} rep. use
Wheat C S Maize S	0.02	STMR _{RA} rotational	0,02	$\overset{\checkmark}{\swarrow}$ HR _{RA} rotational
Maize	LOQ C	STMR _{RA} totational	DOQ @	HR _{RA} rotational
Mammalian Maeat 🍡 🏑	0.32	Cow CedingRA	0.32	Cow feeding _{RA} *
Mammabar fat	<b>ð</b> 31 4	Cow feeding A*	0.31	Cow feeding _{RA} *
Mammalian liver	e ≫1.95 ≪J	ow feedingrat	1.95	Cow feeding _{RA} *
Mammalian kidney	0.30	Cow foedingra	0.31	Cow feeding _{RA} *
Poultry meat	6,694	Poutty feedingra*	0.04	Poultry feeding _{RA} *
Poultry meat	0.06	Poultry fécgingra*	0.06	Poultry feeding _{RA} *
Poultry liver	O″0. <b>≵</b> Q″	Poultry Geeding Co*	0.18	Poultry feeding _{RA} *
Poultry kieney	Q18	Pouttry feedingRA*	0.18	Poultry feeding _{RA} *
Milk	A 0.04	ow feeding _{RA} *	0.04	Cow feeding _{RA} *
Eggs	0.097	Poultry FeedingRA*	0.09	Poultry feeding _{RA} *
Honey 🖉	Story ~	TMR _{RA}	<loq< td=""><td>HR_{RA}</td></loq<>	HR _{RA}

Table 6 9- 1. Input values for the consumer risk assessme

RA Crops : sum of fluopyram and fluopyram-benzamide expressed as fluopyram

RA Animal commodifies : sun i fluogytam, fluogytam-benzamide and fluopyram-olefins expressed as fluopyram

*In tissues a worke case the resider results from the 1X group is used as input data to calculate the risk assessment.

*In milk the dietay burden of 0.07 mg/kg bw/day in dairy cattle is close to the 0.1 X dose value of 0.04 mg/kg bw/day. Values in milk from the 0.1 X dose group are considered to calculate the dietary risk assessment.

As shown in Table 6.9-2, the highest chronic risk is calculated for the NL toddler diet and represents 40% of the ADI. The highest contributors are cattle milk (20%) and apples (6%).



The results indicate that there is no unacceptable chronic risk to human health from the consumption of commodities treated with fluopyram according to the representative intended uses/GAPs. di di

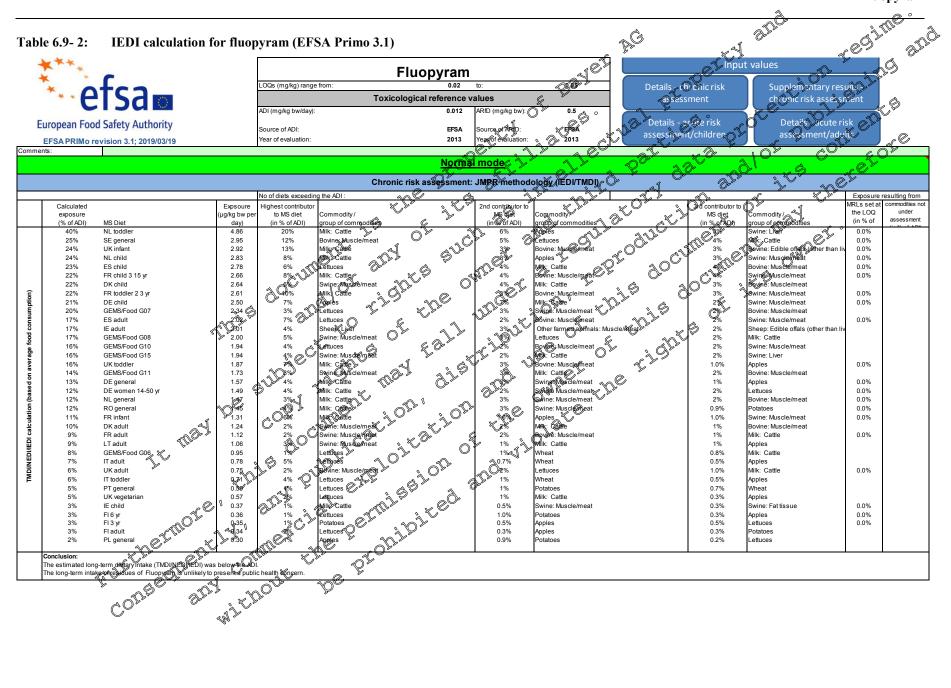
The short term exposure show the following acute risk according to the EFSA point 3.1 calculation

- for children, risk is below 100% of ARfD, lettuce being the highest contributor (76% of ARfD). •
- for adults, risk is below 100% of ARfD, lettuce being the highest contributor (24% of SRfD) •
- Acute risk from processed commodities remain below 1% of ARTD, in all population categories

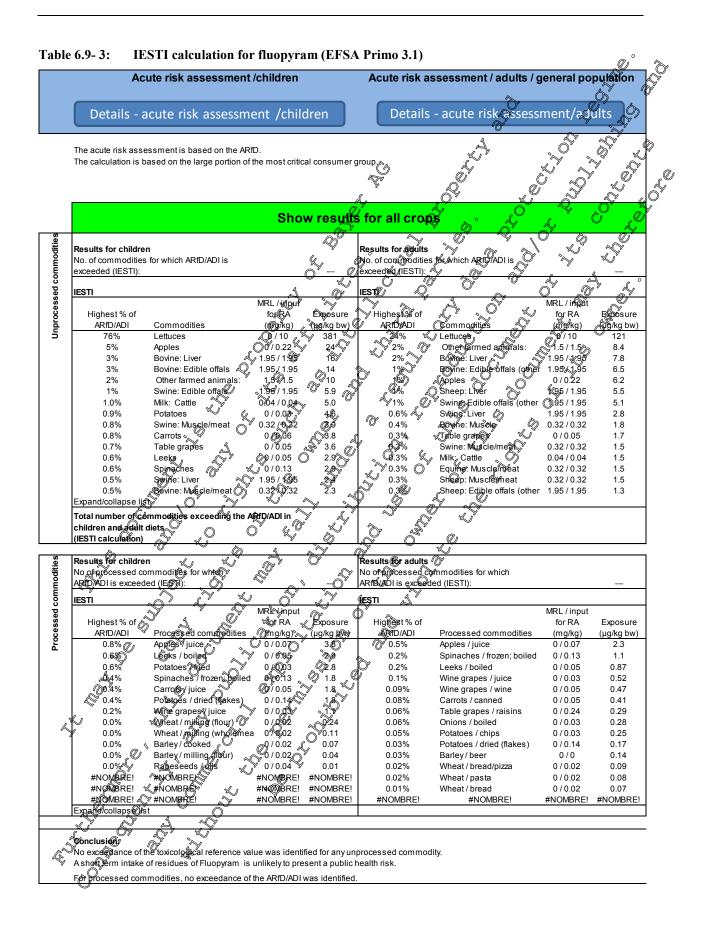
but in all population representation repres And and a second a se A short-term intake of residues of fluopyram according to the presented representative uses is therefore unlikely to present a public health concern.



Page 795 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram









### CA 6.10 Other studies

#### CA 6.10.1 Effect on the residue level in pollen and bee products

Following the publication of the guideline for setting MRLs in honey SANTE 1956 2016 record tunnel residue trials on the surrogate crop Phacelia tanacetifolia followed by honey analysis.

Data Point:	KCA 6.10.1/01
Report Author:	
Report Year:	
Report Title:	Determination of residues of the opyram and its metabolites in honey after the applications of FLU SC 250 in Phacelia tanaeetifolia at 4 stress in Northern and
Damant Mari	Southern Europe in 2019
Report No:	
Document No:	<u>M-681608-01-1</u> O' O' Z' A'
Guideline(s) followed in	OECD Guideline for the Testing of Chemicals on Crop Field Trian (TG 509) published in September 2009) EC (2018) Technical guidelines for determining the magnitude of pesticide residues in honey and setting Maximum Residue Levels in Coney
study:	published in September 2009) $\sim$ $\Delta$ $\Delta$
5	EC (2018) Technical guidelines for determining the magnitude of pesticide
	residues in honey and setting Maximum Residue Levels in Koney &
	(SANTE/10056/2016 ray by
	(SANTE/10)56/2016 rev 9 Commission Regulation (EU) 283/2013 and 280 2013 implementing Regulation
	Commission Regulation (EU) 283/2013 and 284/2013 unplementing Regulation
	(EC) 1107/2009 (Oct 2009)
Deviations from current	
test guideline:	
Previous evaluation:	
GLP/Officially recognised	
testing facilities:	
Acceptability/Reliability:	
Test sustam	

#### Test system

In order to support the intended and most critical ases of Huopyram or melliferous crops and in order to determine the resulting residues of fluopyram in honey, four GLP honey trials were conducted on *Phacelia anacetifolia* in northern and southern European zones under semi-field conditions during the 2019 season.

The trials were performed in Gennany (2), southern Foance and Spain.

Two spray applications of the formulation FLU SC 250 a suspension concentrate containing 250 g fluopyram/L were applied at 1 L/ra during flowering (BBCH 62-65) with an interval of 6-7 days, representing the most critical GCP of the crops intended for authorisation in EU MSs and covering the whole flowering period

## Table 5.10.1-1: Use pattern applied for the honey residue trials after spray application of fluopyram under semi_field conditions

Description		Förmulation	No. of appl.	Growth stage at last application	Application rate per treatment (g a.s./ha)	Interval (days)
Phacehia tanacetifolia (Honey tunnel trais)	Semi-field	SC 250*	2	62-65 (flowering)	250	6-7

* Suspension Concentrate containing 250 g fluopyram/L



On each trial site one tunnel confining the bees was established on the control and the treated plot. One bee hive was set up per tunnel for the control and treated plot, each. Colony assessments were performed before set-up of the hives in the tunnels and after sampling of the honey.

Honey was collected from initially empty combs which were introduced in the bives shortly before the last application. Honey was collected once mature at the end of flowering or  $3^{\circ}$  the water content was < 20% or after comb closure – whatever occurred first - for subsequent residue analysis. In case the water content was >20% at the end of flowering a subsample was dried in a compartment dryer at the laboratory at conditions simulating the bee hive conditions.

In one trial (S19-01064-04) honey was sampled before end of flowering and with a water content  $\sim 20\%$  C as rainy weather was forecasted, and new honey was only available at low amounts in the colonies. In order not to risk losing the produced honey, the honey was sampled already before the end of flowering. An additional honey sample was collected in this trial at the end of flowering to obtain honey with water content of < 20%.

Honey samples were taken 2 to 10 days after the last application

All honey samples were transported on dry ice from the field to the test facility, with exception of samples destinated for further drying which were transported at ambient temperature. Samples were stored deep frozen within 24 hours after sampling, or after end of drying, respectively. The field samples were stored in a freezer at -18 °C to below until preparation of the examination samples.

The samples were analysed for Huopyram (AE C656948) and its netabolites fluoryram benzamide (AE F148815, FLU-benzamide), Huopyram-pyredyl-carboxylic-acid (AE C637188, FLU-PCA), fluopyram-pyridyl-acetic-acid (BCS-AA 10/39, FLU-PCA), fluopyram-7-hydroxy (BCS-AA10065, FLU-7-OH)with the analytical method 01594 (Roth A, 20/02/2020, <u>M-681002-02-2</u>, see section MCA 4.1.2). Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements optimed within SANCO/3029/99 rev 4.

The samples were failly didated with an actionitrile/water mixture (1/1, v/v/An aliquot was analysed by high performance liquid chromatography, chromatographed under reversed phase gradient conditions and detected by Tandem Mass Spectrometry with electrospray ionisation.

The Limit of Quantification (LOQ) incon honey was 0.01 mg/kg for fluopyram and its metabolites, expressed as fluopyram?

The linearity was demonstrated in each analytical batch with a 1/x weighted calibration curve established with at least 5 concentration levely. For each calibration curve, the correlation coefficient R was above 0.99.

The quantification was done by internal standardization using isotopically stable labelled internal standards.

## Finding

In order to check the performance of the analytical method, recovery determinations were concurrently performed to the analyses of control and treated samples from the study in each set of analyses. For control material honey from local market was used for concurrent recoveries. The means of the concurrent recoveries were for all fortification levels within the acceptable range of 70 - 110 % and RSD values were <20%. All overall mean recoveries are in the acceptable range of 70 - 110 %; therefore, the results are considered valid. Recovery results are presented in Table 6.10.1- 2. The storage periods of deep trozen samples interded for the analysis of fluopyram and its metabolites was 28 to 104 days.

-<u>Résidue results</u>: After two spray applications of Fluopyram SC 250 to Phacelia tanacetifolia, the residues of fluopyram and its metabolites were determined in honey sampled 2-10 days after the last application to the flowering Phacelia tanacetifolia.



byram and its five metabolites (FLU-benzamide, FLU-PCA, FLU-PAA, FLU-70n and FLU-methylsulfoxide) were found above the LOQ in any of the control and treated samples of the second second above the LOQ in any of the control and treated samples of the second secon No residues of fluopyram and its five metabolites (FLU-benzamide, FLU-PCA, FLU-PAA, FLU-70H the

Table 6.10.1-3.

Conclusion

Following two fluopyram applications at a high dose rate under protected conditions on a melliferous crop at flowering, no residues of fluopyram and its metabolites were measured in honey.

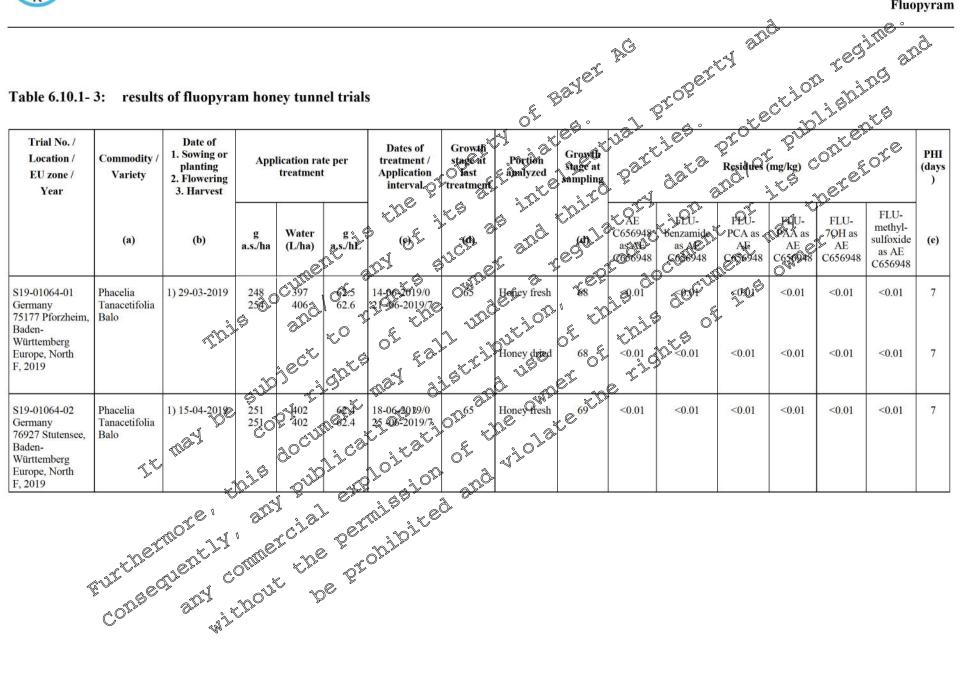
Sample material	FL (mg/kg)	Single values (%)	Mean value (%)	RSD*(%)							
Fluopyram (AE C65	6948)			× · · ·							
honey	0.01	405,98,402	Q 102	0 ⁷ 30 ⁷ 4							
	0.10	×¥11, 112, 108	A10 0	¥. ¥.9 Q							
		Overall recovery (n=6)	0 [×] 106, [×]	\$ \$ 5.1 5							
Fluopyram-benzamide (AEF148815) S & C A A A A											
	0.01	98,76 °C	Ĩ ĵ92 ĉ	\$ .6							
honey	0.10	Ý 🖉 97, 99, 98, O 🖉	2 98	0 × 1.0							
	~(?)	^o Overall recovery (n=6)	25 O	10.1							
Fluopyram-pyridyl-carboxille-acid (AE C65/188)											
honey	<u>_</u> €01 €	^۲ ^۲ 97, <i>9</i> , 95	\$95 \$	1.6							
	0.10	25 95 94, 26 ×	<u>د 96</u>	2.8							
		≪ Overall recovery (n=6)	0 ⁴ 96 2	2.1							
Fluopyram-pyridyl Scetic, acid (BCS AA19139) 2 2											
, S	0.01 ×	🔊 9 <b>4,</b> 91,77 Q	4 87 Q Q 90	10.4							
honey	0.10	& <b>97</b> , 98, <b>4</b> 5	A W	1.6							
le la		Overall recovery (n=6)	© @92	8.4							
Fluopyram 7-hydro	xy (BCŠ-AĄ 🕼	<u>065) 1 2 2 0 2 .</u>		-							
	0.01	103, 100, 102	<u>∽</u> 102	1.5							
honey	0.19	NO, 111, 0107	× 109	1.9							
		Overall recovery (n=6)	106	4.3							
Fluopyram-methylsulfoxide (AF1344122)											
Ő,	0.0 ⁰	2 37, 90 32 5 ⁵	93	3.9							
honey			96	3.3							
EL: fortification level RSD	or Si	Overall recovery (n=6)	95	3.8							
I . fortificate ab laval PSD	D Mativa Standard	Dorifition 1 N									

Table 6.10.1-2: recovery data for fluopyram and its metabolites in honey

FL: fortification level, RSD - Relative Standard Deviation Final determination as: fluopytain Residue's calculated as: fluopytain Final determination as: FLU-PAA Residue's calculated as: fluopytain Final determination as: FLU-therhylsulford FLU-therhyls

BAYER

Page 800 of 801 2021-02-26 Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram



Page 801 of 801 2021-02-26



Document MCA – Section 6: Residues in or on treated products, food and feed Fluopyram

												- -	<u>ð</u> .	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	in Color	
Trial No. / Location / EU zone / Year	Commodity / Variety	Date of 1. Sowing or planting 2. Flowering 3. Harvest	Application rate per treatment				Portion analyzed	Growth stage at sampling	BC 4	or ^{oper}	Residues (mg/kg)			,119 ,119 ,71	PHI (days )	
	(a)	(b)	g a.s./ha	Water (L/ha)	g a.s./hL	(c)	COP CE	Y Filias		2656948 as AB C656948	Denzamide as APS Croose48	FQU- OPCA as AE C656948	ELIÚ PÀA as AE C656948	FLUC 701 fas	FLU- methyl- suffoxide Oas AE C656948	(e)
S19-01064-03 France, south 47460 Monheurt, Lot-et-Garonne Europe, South F, 2019	Phacelia Tanacetifolia Stala	1) 22-02-2019 2	251 253	401 403	62.6 62.8	25 05 2019/0 01 06-2019/7 0		Hondy Tresh	egul o	-08124 -08124			NOT COMPLE	€0.01	<0.01	10
S19-01064-04 Spain 46820, Anna, Comunidad Valenciana Europe, South F, 2019	Phacelia Tanacetifolia Stala	1) Natural emergence from 2018 seeding	270 246) 9	C 432 389 D	0 62.5 * *	09 00-2019/0 2 04-2019/6 04-2019/6 6 5	60WL	Hofiey fresh	64-65 64-65 66-67	<0.01 <0.01 <0.01 <0.01		<0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	2 10 2 10
<ul> <li>(a) According to CODEX Classification / Guido</li> <li>(b) Only if relevant</li> <li>(c) Year must be indicated</li> <li>(d) Either growth stage description of BBCH Code</li> <li>(g) Field</li> <li>(h) Formulation type</li> <li>(h) Formulation type</li> <li>(i) Method validation</li> <li>(m) Storage (max)</li> <li>(m) Sto</li></ul>																
SI9-0106-04 Phacelia I nancetiolia Stala Tanacetiolia Stala																