Bayer CropScience

Document Title

Summary of the residues in or on treated products, food and feed
Diflufenican + Flurtamone SC 350 (100+250 g/L)

Data Requirements

EU Regulation 1107/2009 & EU Regulation 284/2013
Document MCP
Section 8: Residues in or on treated products, food and feed

According to the guidance document, SANCO/10181/2013, for preparing dossiers for the approval of a chemical active substance

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Version history

Date	Data points containing amendments or additions[1] and brief description	Document identifier and version number

[1] It is suggested that applicants adopt a similar approach to showing revisions and version history as outlined in SANCO/10180/2013 Chapter 4 How to revise an Assessment Report.

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CP 8 RESIDUES IN OR ON TREATED PRODUCTS, FOOD OR FEED

Stability of residues

Stability of residues during storage of samples

Since Annex I inclusion, a new study has been generated with a longer storage period for flurtamone, up to 18 months in wheat (grain and green material), sunflower seed and pea seed.

In addition, in some samples of supportive trials from two residue studies (M-459799-01-1 and M-459808-01-1) the requested temperature of -18°C was exceeded due to problems during the shipment of these samples. In order to address this deviation, a short term storage stability study was conducted. The storage conditions tested were such that the most unfavorable conditions which were determined for all shipments are covered. The findings from short-term storage stability study demonstrate that the temperature deviations during shipment did not result in a negative impact on the quality of the residue studies concerned. Residues of flurtamone proved to be stable under the experimental conditions tested.

These studies have been submitted within the Section 6 of the active substance for flurtamone (Cf. Document MCA, Section 6 – Residues in or on treated products, food and feed).

Stability of residues in samples extracts

The stability of the residues in the sample extracts was not checked specifically. However, control samples fortified with the test substance were always extracted and analysed concurrently with the untreated and treated samples of the studies. The satisfactory recovery rates obtained from the fortified samples demonstrate the stability of the residues in the sample extracts throughout the analytical procedure, from extraction until chromatographic determination.

Studies on metabolism in plants or livestock

Metabolism in plants

Table CP 8-1: Summary of available metabolism studies in plants

Group	Crop	Label position	Application details				Reference
			pre/post emergence	Rate (kg as/ha)	No	Growth stage BBCH	
Cereals	Barley	trifluomethyl-phenyl ring	pre post	0.065 0.650	1 1	- 21-31	M-204819-02-1
	Wheat	phenyl ring	pre post	0.375 0.375	1 1	- 21	M-206857-01-1
		trifluomethyl-phenyl ring	pre post	0.301 0.350	1 1	01-07 19-31	M-446949-01-1
Oilseed	Peanut	trifluomethyl-phenyl + phenyl ring	pre	1.12	1	-	M-276618-01-1
	Sunflower	trifluomethyl-phenyl ring	pre	0.460 0.920(2x)	1	-	M-165807-02-1
		phenyl ring	pre	0.374 0.753(2x)	1	01-08	M-397170-01-1

Metabolism in animals

The calculated dietary burdens do not exceed the trigger value of 0.004 mg/kg bw/day for cattle, sheep, swine and poultry. Therefore, livestock metabolism and feeding studies are not required.

However, metabolism studies were nevertheless conducted to satisfy formal requirements in the course of an anticipated registration of the active substance flurtamone.

All these studies have been submitted within the Section 6 of the active substance for flurtamone (Cf. Document MCA, Section 6c, Residues in or on treated products, food and feed).

A summary is presented below in Table CP 8-2.

Table CP 8-2: Summary of available metabolism studies in animals

Group	Animal	Label position	Dosing		Number of animals		Reference
			Duration (days)	Rate (mg/kg bw)	dosed	control	
Poultry	Laying hen	trifluomethyl-phenyl ring	7	7.8	10	5	M-162898-02-1
		phenyl ring	14	16.7	6	-	M-448149-02-1
Lactating ruminants	Goat	trifluomethyl-phenyl ring	7	11	2	1	M-162921-01-1
		phenyl ring	5	22.9	1	-	M-445646-01-1

Residue trials (supervised field trials)

Cereals

Flurtamone belongs to the group of pyridazinone compounds which are used as herbicides. It is used pre-emergence or post-emergence for the control of broad-leaved and grass weeds in cereals by blocking carotenoid biosynthesis via the inhibition of phytoene desaturase causing chlorophyll depletion.

The representative use supported on cereals within the Section 8 of the active substance for flurtamone is the use pattern of DFF+FLT SC 100+250AG product (Cf. Document MCA, Section 6 – Residues in or on treated products, food and feed).

Table CP 8-3: Use pattern (GAPs) for the spray application of flurtamone containing formulations on cereals in Europe (northern and southern regions)

Crop	Member state or country	F / G or I	Formulation Conc. of as	Pests or group of pests controlled	Growth stage	Number	Water (L/ha)	Application (g as/ha)	PHI
Spring cereals (Barley, wheat) Winter cereals (Barley, oat, rye, spelt, triticale, wheat)	Europe North / South	F	SC 250 g/L flurtamone + 100 g/L diflufenican	Broad leaved weeds & grass weeds	Pre-emergence (BBCH00-09) Or Post-emergence (BBCH 10-89)	1	200-400	125 g flurtamone + 50 g diflufenican	None - Covered by the normal vegetation period between last application and harvest

A total of 24 supplementary trials were performed on barley and wheat since Annex I inclusion to support this new use pattern. Within these 24 trials, 8 (4 northern + 4 southern EU trials) were performed with SC350 product at the cGAP. In addition, 16 additional trials (8 northern + 8 southern EU trials) performed with SC360 product support also the cGAP with a flurtamone application rate slightly lower (120 g a.s./ha vs 125 g a.s./ha). Despite the fact that the SC350 trials were realized with applications done at BBCH 25 while SC360 trials were performed with applications between BBCH 22 and BBCH 30, no residue were found in all sample material (<LOQ of 0.01 mg/kg):

- green material harvested at BBCH 51 corresponding to the forage stage,
- whole plant without roots at BBCH83 corresponding to the silage stage,
- grain at BBCH 89,
- straw at BBCH 89, with only one exception at 0.021 mg/kg in a European southern trial (11-2094-04 – barley). For that reason all these trials are reported altogether for a better overview.

Livestock Feeding Studies

All details about livestock feeding studies have been submitted within the Section 6 of the active substance for flurtamone (Cf. Document MCA, Section 6 – Residues in or on treated products, food and feed).

The cereal commodities likely to be fed to livestock consist of grain (which is fed to poultry, pigs and cattle) and straw (which is fed to cattle only). Use of flurtamone in cereals according to the recommended GAP is not likely to result in significant residues in any of these commodities, except in straw at 0.021 mg/kg.
Furthermore, livestock metabolism studies showed that flurtamone do not accumulate in eggs, milk or edible tissues. Using the OECD model, the calculated dietary burdens do not exceed the trigger value of 0.004 mg/kg bw/day for cattle, sheep, swine and poultry. Therefore, no livestock feeding studies to investigate the residue levels of flurtamone in food of animal origin are required.

Effects of processing

All details about the effect of processing have been submitted within the Section 6 of the active substance for flurtamone (Cf. Document MCA, Section 6 – Residues in or on treated products, food and feed).

In the supervised field residue trials, no residues of flurtamone above 0.01 mg/kg (Limit of Quantification) were found in grain. In addition, it is unlikely that potential for concentration in processed food is likely occur. Otherwise, a default processing factor of 8 for bran (used as animal feed) could be used. It has been shown in chapter CA 6.4 that the dietary burden is still under the trigger value of 0.004 mg/kg bw/d when this value is used in the dietary burden calculations.

Furthermore flurtamone is of low toxicity.

Therefore, no processing study is required to investigate the residues of flurtamone in processed cereal commodities.

Studies for Residues in Representative Succeeding Crops

All details about the nature and the magnitude of residues in representative succeeding crops have been submitted within the Section 6 of the active substance for flurtamone (Cf. Document MCA, Section 6 – Residues in or on treated products, food and feed).

Nature of residues

Metabolism in rotational crops was found to be very similar to primary crop metabolism. Metabolic products and discovered metabolic pathways are covered by the common plant metabolism. Therefore a specific residue definition for rotational crops is not deemed necessary.

Table CP 8-4: Summary of available metabolism studies in rotational crops

Group	Crop	Label position	Application details				Reference
			Replanting intervals	Nominal Rate (kg as/ha)	No	Applied to	
Leafy vegetables	Lettuce	trifluomethyl-phenyl ring	30 120 365	375	1	Bare soil	M-158591-01-1
Root crop	Radish				1		
Leafy vegetables	Lettuce	phenyl ring	30 120 365	250	1	Bare soil	M-222225-02-1
Root crop	Radish				1		
Cereals	Wheat	trifluomethyl-phenyl			1		
Cereals	Wheat	phenyl ring	30 156	125	1	Bare soil	M-440369-01-1

Magnitude of residues in rotational crops

Metabolism studies on rotational crops have shown that no residue of parent flurtamone at or above the limit of quantification (0.01 mg eq./kg) would be expected in food items of succeeding crops (lettuce representative of the leafy vegetables, radishes representative of root vegetables and wheat grain representative of cereals). Flurtamone was only found in feed items at low residue levels: 0.015 mg eq./kg in wheat straw ([trifluoromethylphenyl-UL-^{14}C]flurtamone study; 30d rotation with an application rate of 250 g as/ha on soil) and 0.036 mg eq./kg in wheat hay and 0.041 mg eq./kg in wheat straw ([phenyl-UL-^{14}C]Flurtamone study; 30d rotation with an application rate of 120 g as/ha on soil).

Only one metabolite has been seen above the LOQ. This metabolite is the TFA metabolite (trifluoroacetate), a known soil metabolite of flurtamone which has been considered as a non-relevant metabolite. Indeed, the assessment of the properties and characteristics of the metabolite TFA has been made with a particular emphasis on the DG Sanco Guidance Document on the Assessment of the Relevance of Metabolites in Groundwater within the Document N4 .

It is therefore considered that relevant residues are not expected to exceed 0.01 mg/kg in rotational crops following realistic practice and provided that flurtamone is applied according to the reported GAPs. Consequently, field rotational crop studies are not required.

Proposed Residue Definition and Maximum Residue Levels

All details about the residue definitions and MRLs have been submitted within the Section 6 of the active substance for flurtamone (Cf. Document MCA, Section 6 – Residues in or on treated products, food and feed).

Proposed residue definition

According to Article 12 of Regulation (EC) No 396/2005, the European Food Safety Authority (EFSA) has reviewed the Maximum Residue Levels (MRLs) currently established at European level for the pesticide active substance flurtamone. A reasoned opinion on the review of the existing

maximum residue levels (MRLs) for flurtamone was published in EFSA Journal 2012; 10(12):3009.

Table CP 8-5: Current residue definitions

Matrices	Residue definition		Reference
Food of plant origin	Risk assessment and Monitoring	flurtamone	EFSA Journal 2012; 10(12):3009
Food of animal origin	Risk assessment and Monitoring	None, as no residue anticipated	

Considering all metabolism studies in plants and animals, including the new reported within the Section 6 of the active substance for flurtamone (Cf. Document MCA, Section 6 – Residues in or on treated products, food and feed), residues of flurtamone other than TFA and parent compound are not expected above 0.01 mg/kg. Therefore, the relevant residue for enforcement and risk assessment in plants is proposed to be maintained with the parent compound only. For monitoring of misuse in commodities of animal origin the same definition of residue is proposed despite the fact that dietary burden calculations have demonstrated that livestock feeding studies and consequently residue definition in animal commodities are not needed.

Table CP 8-6: Proposed residue definitions

Matrices	Residue definition	
Food of plant origin	Risk assessment and Monitoring	flurtamone
Food of animal origin	Risk assessment and Monitoring	flurtamone

Proposed maximum residue levels (MRLs)

Table CP 8-7: Current MRLs established by EFSA and proposed MRLs

Commodity (code no.)	Existing MRLs (mg/kg) Reg. (EC) No 149/2008	MRL (mg/kg) EFSA Journal 2012; 10(12):3009	Proposed MRLs (mg/kg)
CEREALS (0500000)			
Barley grain (0500010)	0.02*	0.01*	0.01*
Oats grain (0500050)	0.02*	0.01*	0.01*
Rye grain (0500070)	0.02*	0.01*	0.01*
Wheat grain (0500090)	0.02*	0.01*	0.01*
PRODUCT S OF ANIMAL ORIGIN-TERRESTRIAL ANIMALS (1000000)			
Tissue (1010000)	-	-	0.01*
Milk (1020000)	-	-	0.01*
Bird eggs (1030000)	-	-	0.01*

* indicates that the MRL is set at the limit of analytical quantification

Proposed Pre-Harvest Intervals, Re-Entry or Withholding Periods

It is not necessary to define a pre-harvest interval. Instead, the pre-harvest interval is given by the growing period between the growth stage at treatment and harvest.

The product is not intended for use in areas where livestock animals may be grazed. Therefore no re-entry period needs to be proposed.

The product is applied early post-emergence on very young plants. Thus, dermal exposure to persons entering a treated field is negligible. No use in buildings is intended. Therefore no re-entry period needs to be proposed for man.

Handling of treated cereals is generally not required before harvest, which is always done mechanically. Therefore there is no need to define a waiting period between application and handling of treated products.

The use of flurtamone in cereals is not likely to result in significant uptake of residues by succeeding crops. Thus, it is not necessary to set a waiting period between last application and sowing or planting succeeding crops.

Estimation of Exposure Through Diet and Other Means

All details about the estimation of exposure through diet and other means have been submitted within the Section 6 of the active substance for flurtamone (Cf. Document MCA, Section 6 – Residues in or on treated products, food and feed).

TMDI calculations

In order to evaluate the potential chronic exposure to flurtamone residues through the diet, the Theoretical Maximum Dietary Intakes (TMDI) were estimated using the EFSA PRIMo model (revision 2). For the evaluation of the chronic exposure the model uses 5 WHO diets relevant to the EU and 22 national diets from 13 different EU Member States.

The highest TMDI calculated for flurtamone represented about 3% of the ADI, which denotes considerable margins of safety.