Document Title

Tier 2 Summary of the Metabolism and Residues Data for Flupyradifurone (BYI 02960)

- Part 3 of 3 -

Data Requirements

Regulation (EC) No 1107/2009

Regulatory Directive 2003-01/Canada/PMRA
OPPTS guidelines/US/EPA

Annex IIA
Section 4, Point 6.4 to Point 6.11.2
Document M

According to OECD format guidance for industry data submissions on plant protection products and their active substances

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IIA 6.4 Livestock feeding studies

In chapter 6.3 of this dossier, residue trials are presented in which the residue behavior of BYI 02960 in two "EU safe use" crops (lettuce and hops) and in three rotational crop groups (root, leafy, and cereal crops) is described. However, as also mentioned there, additional crops will be presented in subsequent documents, including primary programs in vegetable, fruit, and cereal crops, etc., many of which will yield feed-relevant residues. The primary crops tested thus far in the EU include fruiting vegetables (tomatoes, peppers, cucumbers, melons), brassica vegetables (head, leafy, and flowering, as well as Brussels sprouts and kohlrabi), pome and stone fruit, grapes, strawberries and raspberries, peas, potatoes, and cereals, with additional import-tolerance relevant crops such as coffee, cocoa, blueberries, soybeans, and citrus fruit being tested in North and South America and in Africa. These trials will be submitted in batches, with the first large batch to be submitted later in 2012. Also, a large package of rotational crop tests in crops representing seven further groups has been conducted in the EU for 2012 submission.

Due to the nature of BYI 02960, measurable residues have been determined in virtually every crop tested. Many of these crops are relevant as feed items, either in the EU or in Australia or NAFTA. Thus, based on the results of metabolism studies which showed that animal matrices will also likely contain measurable residues, livestock feeding studies were conducted. Multi-region livestock diet calculations were conducted in order to conduct the studies in a manner appropriate to the entire scope of BYI 02960 use, allowing data to be generated in a fashion such that, for animal 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 study should be representative of the residue in the feedstuffs. In the case of the new BCS insecticide BYI 02960, by far the major part of the residue in plants is formed by parent compound BYI 02960 and its metabolite DFA, in varying ratios. Animal metabolism studies show that these two components are also the major contributors to the relevant residue in animals. To cover the needs of all involved countries and regions, several concepts for feeding studies might be applied. After discussion with the EU Rapporteur (Ctgb, NL), it was decided to feed parent BYI 02960 and derive separate transfer factors for the total residue of BYI 02960 + DFA, as well as separately for DFA alone.

While the nature of the calculations/evaluations for the total residue and for parent compound itself are relatively straightforward, using the study data to evaluate the metabolite DFA required careful consideration. As agreed with the Rapporteur Member State, separate transfer factors for DFA were estimated in both the poultry and cattle feeding studies on the basis of the available data after dosage of the active substance BYI 02960 to laying hens and cattle. In order to accomplish this, a theoretical dose of DFA must be estimated in each study. For the estimation of the theoretical dose, the amounts of DFA in all organs/tissues and particularly in the urine (ruminant) or excreta (poultry) must be considered. These absolute residues are representative of the minimum systemic exposure to DFA during the studies and therefore provide the basis for the calculation of a theoretical dose of DFA in the feed. This, in turn, allows the calculation of transfer factors and, thus, the contribution of DFA to MRLs in animal matrices.

In the following sections (KIIA 6.4.1 and 6.4.2), the basic study data will be presented first, followed by the specific calculations for the transfer factors for total residues and for DFA alone.

Calculation of dietary burden

The estimated dietary burden of total BYI 02960 residues in livestock commodities, based on EU crop residue data and the European dietary burden calculator, are presented for poultry and cattle below in tables 6.4-1 and 6.4-2, respectively.

Table 6.4-1: Anticipated dietary burden for BYI 02960 residues in poultry diet based on EU residue data and guideline

Feedstuff	Dry matter (DM) content (%)	Dry matter (DM) intake (%)[1]	Residue level fresh weight basis (mg/kg)[2]	Residue level dry weight basis (mg/kg)[3]	Dietary burden / dose in diet (mg/kg feed)	Dietary burden / dose per animal (mg a.s./kg b.w./day)
Wheat grain[4]	86	70	0.78	0.91	0.635	
Kale[4]	14	5	1.36	9.71	0.486	
Turnips	10	20	0.14	1.40	0.280	
Total:		*95*			**1.401**	**0.0885**

1: Percentage of feedstuff in the diet for poultry in EU
2: Highest residue value (BYI 02960 + DFA) from European field trials
3: Corrected residue = residue level ÷ % dry matter × 100
4: Residue trials in these crops will be submitted at a later date

Table 6.4-2: Anticipated dietary burden for BYI 02960 residues in cattle diet based on EU residue data and guideline

Feedstuff	Dry matter (DM) content (%)	Dry matter (DM) intake (%)[1]	Residue level fresh weight basis (mg/kg)[2]	Residue level dry weight basis (mg/kg)[3]	Dietary burden / dose in diet (mg/kg feed)	Dietary burden / dose per animal (mg a.s./kg b.w./day)
Kale[4]	14	35	1.36	9.714	3.40	0.146
Turnips	10	60	0.14	1.400	0.84	0.036
Wheat grain[4]	86	5	0.78	0.907	0.05	0.002
Total:		*100*			**4.29**	**0.184**

1: Percentage of feedstuff in the diet for cattle in EU
2: Highest residue value (BYI 02960 + DFA) from European field trials
3: Corrected residue = residue level ÷ % dry matter × 100
4: Residue trials in these crops will be submitted at a later date

As stated above, the feeding studies were designed to meet the necessary criteria in several regions, including NAFTA and Australia. The OECD calculator was also used but it was found that the current regional guidelines lead to more critical dietary burden values, thus these needed to be taken into consideration when designing the studies. The NAFTA base anticipated dietary burden for BYI 02960 residues in livestock feed was calculated using the Revisions of Feedstuffs in Table 1 of OPPTS Test Guideline 860.1000, the Guidance on Constructing Maximum Reasonably Balanced Diets (MRBD) that provide adequate nutrition and are consistent with modern feeding practices, and the anticipated tolerances based on field crop residue data generated from residue studies conducted in USA and Canada. The results are presented below in tables 6.4-3 and 6.4-4.

Table 6.4-3: NAFTA dietary burden based on NAFTA crop residue data and maximum reasonably balanced diet for poultry

Feedstuff	Type[1]	Residue level: Tolerance[2] (mg/kg)	Residue level: Corrected[3] (mg/kg)	% of diet[4]	Dietary burden / dose: in diet (mg a.s./kg feed)	Dietary burden / dose: per animal (mg a.s./kg b.w./day)
Alfalfa meal	PC	40.0	40.0	5	2.0	
Soybean seed	PC	2.0	2.0	20	0.4	
Rye grain	CC	4.0	4.0	35	1.4	
Wheat, milled by-products	CC	4.0	4.0	40	1.6	
Total:				*100*	**5.4**	**0.3411**

1: PC=Protein Concentrate, CC=Carbohydrate Concentrate
2: Proposed tolerance values (BYI 02960 + DFA)
3: Poultry diet residues are on as-fed basis (not adjusted to % dry matter)
4: Poultry livestock diet as listed in Table 1 of the EPA OPPTS 860.1000, based on 0.12 kg feed consumption and 1.9 kg body weight

Table 6.4-4: NAFTA dietary burden based on NAFTA crop residue data and maximum reasonably balanced diet for cattle

Feedstuff	Type[1]	Dry Matter: Dietary Intake (%)	Dry Matter: Content (%)	Residue levels: fresh weight basis (mg/kg)[2]	Residue levels: dry weight basis (mg/kg)[3]	Dietary burden / dose: in diet (mg/kg feed)	Dietary burden / dose: per animal (mg/kg bw/day)[4]
Soybean forage/silage	R	20	35	20.0	57.14	11.43	
Wheat, hay	R	25	88	40.0	45.46	11.36	
Corn, sweet, cannery waste	CC	10	30	3.96	13.20	1.32	
Rye, grain	CC	20	88	4.0	4.55	0.91	
Wheat, milled byproducts	CC	15	88	4.0	4.55	0.68	
Alfalfa, meal	PC	10	89	40.0	44.94	4.49	
Total			*100*			**30.20**	**1.01**

1: R= Roughage, PC=Protein Concentrate, CC=Carbohydrate Concentrate
2: Proposed tolerance values (BYI 02960 + DFA)
3: Corrected residue = residue level ÷ % dry matter × 100
4: Based on 20 kg feed consumption and 550 kg body weight

IIA 6.4.1 Poultry

Report:	**KIIA 6.4.1/01, [redacted], J.M., & [redacted], D.J.; 2012**
Title:	BYI 02960 – Magnitude of the residue in laying hens
Report No. & Document No.:	RARVP041 M-428933-01-1
Guidelines:	– OPPTS 860.1480 – Meat/milk/poultry/eggs – OECD Guideline 505 – APVMA Residue Guideline No. 23 – DACO 7.5 – Meat/milk/poultry/eggs – OPPTS 860.1340 – Residue Analytical Method
GLP:	yes (certified laboratory)

I. Materials and Methods

Test system, dosing

Eighty-four mature laying hens (*Gallus gallus domesticus*) were dosed orally, via capsule, for 29 consecutive days with BYI 02960 at dose rates of 0 mg/kg feed/day (control; 24 hens, 6 subgroups), 1.5 mg/kg feed/day (1X EU dose group; 12 hens, 3 subgroups), 6.5 mg/kg feed/day (4.3X EU dose group; 12 hens, 3 subgroups), 19.4 mg/kg feed/day (13X EU dose group; 12 hens, 3 subgroups), and 65.1 mg/kg feed/day (43X EU dose group; 24 hens, 6 subgroups). These levels were approximately 0.3X, 1.3X, 3.3X and 11X the anticipated maximum dietary burden of BYI 02960 residues in livestock feed based on NAFTA residue data and livestock diet.

Dose rates used in this study were calculated according to both EU (Appendix G, Livestock feeding studies, 7031/VI/95 rev4 [1996] and in Annex 4 of the OECD Guidance Document ENV/JM/MONO [2006]32, European Food Safety Authority [EFSA]) and NAFTA (Revisions of Feedstuffs in Table 1 of OPPTS Test Guideline 860.1000 and Guidance on Constructing Maximum Reasonably Balanced Diets [MRBD], Table 1 Feedstuffs [June 2008]) guidance.

The target and actual dose rates employed in the study are summarized below in table 6.4.1-1. The dose rates were adjusted weekly, based on the actual weekly feed consumption by the hens in each dose group during the previous week.

Table 6.4.1-1: Summary of target and actual BYI 02960 dose administration.

Dose groups		Number of hens	Dose levels in feed		Dose levels per animal
EU[1]	NAFTA[2,3]		target[4] (mg/kg feed)	actual[5] (mg/kg feed)	actual[6] (mg a.s./kg b.w./day)
control		24	0	0	0
1.0X dose	0.3X dose	12	1.4	1.5	0.10
4.3X dose	1.3X dose	12	6.0	6.5	0.45
13X dose	3.3X dose	12	18	19.4	1.31
43X dose	11.1X dose	24	60	65.1	4.54

Footnotes:
1: EU dose rate exaggerations are based on EU dietary burden of 1.4 mg a.s./kg feed (see table 6.4-1)
2: NAFTA dose rate exaggerations are based on NAFTA dietary burden of 5.4 mg a.s./kg feed (see table 6.4-3)
3: Report RARVP041 uses the NAFTA exaggerations, reported there as 0.3X, 1X, 3X, and 11X
4: Target dose was calculated based on NAFTA and EU dietary burdens (tables 6.4-1 and 6.4-3)
5: Actual dose based on average feed consumption data collected from the study and average amount (mg) test substance for each dose group over the entire dosing period
6: Actual dose based on average amount (mg) test substance and the average body weight for each dose over the entire dosing period

The hens were dosed orally once per day each morning after collection of eggs and feeding. The control animal received a placebo (empty capsule) concurrently with the treated animals.

Sampling

Eggs were collected twice daily (afternoon and morning prior to the day's dosing). The eggs collected in the afternoon from each sub-group were combined with the eggs collected the following morning from the same sub-group. The egg contents were combined (shells discarded) by sub-group into a labeled container, weighed, and thoroughly mixed by vigorous shaking. Composite egg samples collected on days 0, 2, 4, 7, 10, 14, 17, 21, 24, 28, 35, 42 and 49 were shipped to Bayer CropScience for analysis for the 43X dose group; for all other doses, only the egg samples from days 24 and 28 were analyzed.

On day 29 of the study, twelve hens from the control and 43X dose groups and all hens in the 1X, 4.3X dose, and the 13X dose groups were sacrificed by CO_2 asphyxiation within 24 hours of the administration of the final dose. Liver (entire), muscle (thigh and breast), and fat (abdominal and subcutaneous) were collected, homogenized in the presence of dry ice, and the samples were shipped to Bayer CropScience.

Twenty four hens (12 from the control group and 12 from the 43X group) entered into a 21-day depuration phase, as required for Australia, following the administration of the final dose. Egg and tissue samples were collected on study days 35, 42, and 49 for analysis.

To estimate the extent of exposure of laying hens to DFA following the oral administration of BYI 02960, excreta was also collected daily from all the subgroups of the 4.3X and from the A, B and C subgroups of the 43X group during the entire dosing period and composited by sub-group. The entire sample from each sub-group was mixed at the end of the dosing period, and a subsample was homogenized for analysis.

Analysis

BYI 02960 and its metabolites were analytically determined using analytical method RV-004-A11-04 (supplied as an appendix to the main study report; cf. KIIA 4.3/08 for details relating to the method), which was validated prior to and parallel to the residue analysis of the samples. The LOQ was 0.01 mg/kg for all analytes (parent compound, DFA, BYI 02960-acetyl-AMCP, and BYI 02960-OH), expressed in BYI 02960 equivalents.

II. Findings

Main study

The mean values of the concurrent recovery rates per compound, sample material, and spiking level were in the range of 72-116%, with relative standard deviations in the range of 1-16%. (In the few cases of mean recoveries outside of the desired range -- BYI 02960-OH in fat at 4.0 mg/kg, BYI 02960-acetyl-AMCP in muscle at the LOQ – the RSD values were low [2.1 and 11.6%, respectively] and thus the values were considered to be acceptable.) Details of recovery data are shown in table 6.4.1-5.

Feed consumption, body weights, and egg production were not adversely affected by treatment with BYI 02960. In fact, feed consumption increased significantly relative to increases in body weight during the dosing period. Subsequently, the dose levels (mg a.s./hen in a given dose group), which were calculated using the feed consumption data and the corresponding dose rates based on mg a.s./kg body weight, also increased during the 29-day dosing period, as shown in table 6.4.1-2.

In the groups representing the nominal worst-case EU and NAFTA dietary burden (EU 1X and 4.3X groups, respectively), the total residues of BYI 02960 – comprising parent compound, DFA, BYI 02960-acetyl-AMCP, and BYI 02960-OH – were measured at sacrifice in poultry tissues and were as follows: 0.0883 and 0.3038 mg/kg in muscle, 0.0330 and 0.1213 mg/kg in fat, and 0.1077 and 0.4335 mg/kg in liver, respectively. In eggs taken on days 24 and 28, total residues in the 1X group were 0.057 and 0.053 mg/kg, respectively; the parallel values in the 4.3X group were 0.166 and 0.183 mg/kg. These values, as shown in the study report ([redacted] & [redacted], 2012; KIIA 6.4.1/01), reflect the standard practice in the USA of using all residue values as shown, even if they are below the nominal LOQs.

The proposed residue definition for both enforcement and risk assessment will include only parent BYI 02960 plus DFA, which are by far the two major components of the residue. The following values were determined for the nominal worst-case EU and NAFTA dietary burden groups (EU 1X and 4.3X groups, respectively) at sacrifice for the combined residue of the two components (calculated in the "traditional" manner, i.e. if one component is <LOQ, it is calculated as being *at* the LOQ):

0.093 and 0.30 mg/kg in muscle, 0.039 and 0.13 mg/kg in fat, and 0.11 and 0.43 mg/kg in liver, respectively. In eggs taken on days 24 and 28, total residues in the 1X group were 0.061 and 0.057 mg/kg, respectively; the parallel values in the 4.3X group were 0.17 mg/kg at both days.

The residues found in the eggs, tissues, and excreta collected from the laying hens during dosing, at the end of the dosing period, and during the depuration phase are presented in tables 6.4.1-3 and 6.4.1-4.

With respect to eggs, the highest total BYI 02960 residues were found in the day-28 eggs from the 43X dose group. However, as stated previously, dose rates calculated with respect to mg a.s./kg bw increased during the dosing period (cf. table 6.4.1-2). The residue data from the 43X egg samples, when evaluated against the dose rate increases calculated as mg a.s./kg bw, suggest that BYI 02960 residues actually reached a plateau between day 4 and day 7 (for details, cf. table 6.4.1-6); increases in residue levels appear only to be due to increased dose rates. This estimation is in line with the results of the poultry metabolism studies, in which the plateau level in whole eggs was reached at day 6 (pyridinylmethyl label, cf. KIIA 6.2.2/01) or day 9 (furanone label, cf. KIIA 6.2.2/02).

In the depuration phase, total BYI 02960 residues in eggs, fat, liver, and muscle from the 43X dose group hens declined from 1.722, 1.230, 3.480, and 2.410 mg/kg, respectively, to <LOQ at 14 days after cessation of dose administration (=day 42 of the study). The residue data provided in this study are suitable for regulatory purposes. (Depuration data are also presented in tables 6.4.1-3 and 6.4.1-4.)

The levels of DFA residues found in the excreta are summarized in table 6.4.1-7. DFA residues represented 65% to 74% of the total residues of BYI 02960 in the excreta samples, suggesting significant exposure of the laying hens to DFA following the daily oral administration of BYI 02960 to laying hens over 29 days.

Transfer factors for total residues and for DFA alone

Additional calculations were conducted to describe the transfer of both total residues and of DFA alone into poultry tissues and eggs following exposure to BYI 02960 *and* DFA via the diet. As they were not part of the main study and are not included in the study report RARVP041 ([redacted] & [redacted], 2012; KIIA 6.4.1/01), they are not presented here, but rather later in this section.

III. Conclusions (main study)

A feeding study was conducted with BYI 02960 on poultry in order to elucidate the levels of relevant residues in poulty tissues and in eggs. The study was designed to cover the regulatory needs of various regions in the world in which BYI 02960 is to be registered, including the EU, NAFTA, and Australia.

BYI 02960 was administered orally (via capsule) to laying hens for 29 consecutive days at average dose rates of 1.5 mg/kg feed (1X EU dose), 6.5 mg/kg feed (4.3X, which approximated a 1X NAFTA dose), 19.4 mg/kg feed (13X), and 65.1 mg/kg feed (43X). Feed consumption, body weights, and egg production were not adversely affected by compound administration.

After the final dose, the animals were sacrificed and the key edible tissues were analyzed for the relevant residues of BYI 02960. While data were generated for four analytes in the study itself, only two – BYI 02960 and DFA – are proposed for the residue definitions (enforcement and risk assessment) for BYI 02960. The combined residues of BYI 02960 + DFA in poultry tissues at sacrifice in the EU 1X dosing group were 0.093 mg/kg in muscle, 0.039 mg/kg in fat, and 0.11 mg/kg in liver, expressed in parent compound equivalents. Prior to sacrifice, residues in eggs were measured at various intervals in the high-dose group, and on days 24 and 28 in the three lower dose groups. In the EU 1X dose group, residues (BYI 02960 + DFA) in eggs amounted to 0.061 and 0.057 mg/kg, respectively.

Residue analysis of the high-dose eggs showed that levels reached a plateau in eggs. Though residues were highest at day 28, residue data from the 43X egg samples, when evaluated against the dose rate increases calculated as mg a.s./kg bw, suggest that BYI 02960 residues actually reached a plateau between day 4 and day 7; increases in residue levels were only due to increased dose rates. This estimation is in line with the results of the poultry metabolism studies, in which the plateau level in whole eggs was reached at day 6 (pyridinylmethyl label) or day 9 (furanone label).

Depuration occurred quickly. Total BYI 02960 residues in eggs, fat, liver, and muscle from the 43X dose level hens declined from 1.722, 1.230, 3.480, and 2.410 mg/kg, respectively, to <LOQ at 14 days after cessation of dose administration (=day 42 of the study). The residue data provided in this study are suitable for regulatory purposes.

DFA residues represented 65% to 74% of the total BYI 02960 residues in the excreta samples, suggesting significant exposure of the laying hens to DFA residues following the administration of BYI 02960 for 29 days.

Table 6.4.1-2: Dosing regime used in the poultry feeding study

Dose Group	Timing	Dose rate* (mg/kg feed)	Feed intake fresh (g/bird/d)	Feed intake dry (g/bird/d)	Administered dose (mg)	Average body weight** (kg)	Average BYI 02960 a.s. (mg/kg bw)
Control	4 Weeks		127.8		0	1.47	0
1X (US 0.3X)	Week 1	1.5	110.6	95.0	0.14	1.49	0.09
	Week 2	1.5	131.3	112.8	0.16	1.50	0.10
	Week 3	1.4	127.9	109.9	0.14	1.51	0.11
	Week 4	1.6	140.4	120.6	0.17	1.52	0.13
Overall Average		1.5	134.1	109.6	0.15	1.50	0.10
4.3X (US 1.3X)	Week 1	6.6	108.4	93.6	0.62	1.41	0.43
	Week 2	6.4	121.9	106.8	0.67	1.47	0.46
	Week 3	6.5	116.5	102.5	0.65	1.47	0.45
	Week 4	6.4	134.2	116.6	0.74	1.45	0.51
Overall Average		6.5	125.4	104.9	0.67	1.45	0.46
13X (US 3X)	Week 1	19.6	108.3	93.1	1.83	1.44	1.27
	Week 2	19.8	119.0	103.4	2.03	1.48	1.37
	Week 3	19.7	116.2	100.5	1.96	1.49	1.32
	Week 4	18.3	137.1	117.5	2.16	1.49	1.45
Overall Average		19.4	126.6	103.6	1.99	1.47	1.35
43X (US 11X)	Week 1	64.6	109.2	93.8	6.05	1.45	4.18
	Week 2	67.4	120.4	103.4	6.97	1.48	4.72
	Week 3	65.6	117.1	100.6	6.6	1.49	4.42
	Week 4	62.9	134.8	115.7	7.28	1.50	4.84
Overall Average		65.1	125.9	103.4	6.72	1.48	4.54

* dose rate in feed calculated on a dry weight basis

** these weights reflect those determined at the end of the given study week

Table 6.4.1-3: Levels of the relevant residues of BYI 02960 in eggs

group	sampling day	Residue levels of individual analytes (mg/kg)				Total residue levels (mg/kg)	
		BYI 02960 LOD = 0.004 LOQ = 0.01	**DFA** LOD = 0.003 LOQ = 0.01	**-AMCP*** LOD = 0.003 LOQ = 0.01	**-OH** LOD = 0.003 LOQ = 0.01	**sum of 4†**	**BYI 02960 + DFA‡**
1X	24	<LOD/LOQ	0.051	<LOD/LOQ	<LOD/LOQ	0.057	0.061
	28	<LOD/LOQ	0.047	<LOD/LOQ	<LOD/LOQ	0.053	0.057
4.3X	24	<LOD/LOQ	0.155	<LOD/LOQ	<LOD/LOQ	0.166	0.165
	28	<LOD/LOQ	0.163	<LOD/LOQ	<LOD/LOQ	0.183	0.173
13X	24	0.019	0.497	0.017	0.014	0.545	0.516
	28	0.023	0.508	0.015	0.018	0.565	0.532
43X⅄	0	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	<0.02
	2	0.048	0.334	0.019	0.024	0.424	0.382
	4	0.068	0.898	0.045	0.027	1.037	0.966
	7	0.054	1.022	0.042	0.026	1.143	1.076
	10	0.065	1.211	0.052	0.041	1.368	1.276
	14	0.063	0.972	0.038	0.038	1.110	1.035
	17	0.080	1.170	0.043	0.055	1.347	1.250
	21	0.071	1.202	0.043	0.050	1.366	1.273
	24	0.082	1.486	0.059	0.050	1.676	1.568
	28	0.173	1.414	0.051	0.084	1.722	1.587
	35**	<LOD/LOQ	0.130	<LOD/LOQ	<LOD/LOQ	0.140	0.140
	42**	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	0.013	<0.02
	49**	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	<0.02

All metabolite residues expressed in parent compound equivalents

* AMCP = BYI 02960-acetyl-AMCP
** depuration phase, no dosing (sampling days 35-49)
† this value, as shown in the study report, includes values below the LOQ calculated *at the apparent residue value*
‡ this value reflects the proposed residue definition, and as such calculates each component at or above the respective LOQ
⅄ day 0-28 values shown for the high-dose group reflect an average of *all* animals, including those designated for depuration

Table 6.4.1-4: Levels of the relevant residues of BYI 02960 in poultry tissues

group	sampling day	Residue levels of individual analytes (mg/kg)				Total residue levels (mg/kg)	
		BYI 02960	**DFA**	**-AMCP***	**-OH**	**sum of 4†**	**BYI 02960 + DFA‡**
	*POULTRY **FAT***						
1X	29	<LOD/LOQ	0.029	<LOD/LOQ	<LOD/LOQ	0.033	0.039
4.3X	29	<LOD/LOQ	0.117	<LOD/LOQ	<LOD/LOQ	0.121	0.127
13X	29	<LOD/LOQ	0.272	<LOD/LOQ	<LOD/LOQ	0.281	0.282
43X▲	29	0.192	1.006	0.021	0.010	1.230	1.198
	35**	<LOD/LOQ	0.041	<LOD/LOQ	<LOD/LOQ	0.056	0.051
	42**	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	0.009	<0.02
	49**	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	0.013	<0.02
	*POULTRY **LIVER***						
1X	29	<LOD/LOQ	0.104	<LOD/LOQ	<LOD/LOQ	0.108	0.114
4.3X	29	0.006/0.011	0.413	0.011	0.006/0.011	0.444	0.423
13X	29	>LOD/<LOQ	1.012	0.025	>LOD/<LOQ	1.043	1.022
43X▲	29	0.032	3.313	0.083	0.051	3.480	3.345
	35**	<LOD/LOQ	0.085	<LOD/LOQ	<LOD/LOQ	0.089	0.088
	42**	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	0.012	<0.02
	49**	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	0.006	<0.02
	*POULTRY **MUSCLE***						
1X	29	<LOD/LOQ	0.083	<LOD/LOQ	<LOD/LOQ	0.0883	0.086
4.3X	29	>LOD/<LOQ	0.290	0.010	>LOD/<LOQ	0.304	0.300
13X	29	>LOD/<LOQ	0.719	0.024	>LOD/<LOQ	0.750	0.729
43X▲	29	0.039	2.27	0.069	0.032	2.410	2.309
	35**	<LOD/LOQ	0.051	<LOD/LOQ	<LOD/LOQ	0.055	0.061
	42**	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	0.011	<0.02
	49**	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	<LOD/LOQ	0.007	<0.02

All metabolite residues expressed in parent compound equivalents

* AMCP = BYI 02960-acetyl-AMCP
** depuration phase, no dosing (sampling days 35-49)
† this value, as shown in the study report, includes values below the LOQ calculated *at the apparent residue value*
‡ this value reflects the proposed residue definition, and as such calculates each component at or above the respective LOQ
▲ values shown for the high-dose group reflect an average of *all* animals, including those designated for depuration

Table 6.4.1-5: Concurrent recovery data for the relevant residues of BYI 02960 in poultry matrices

Study No.	Matrix	a.s./metabolite	*n*	Spike level (mg/kg)	Recovery (%) Individual recoveries	Min	Max	Mean	RSD
RARVP041	eggs	BYI 02960	17	0.01	113,115,118,103, 109,94,98,87,84, 77, 93, 76, 115, 94, 84, 94, 84	76	118	96	14.2
			3	4.0	100, 81, 95	81	100	92	10.7
		DFA	17	0.01	100,112,109,78, 87,74,81,76,78, 68,77,70,83,73, 79, 76, 71	68	112	82	15.9
			3	4.0	75, 70, 71	70	75	72	3.7
		BYI 02960-acetyl-AMCP	16	0.01	84,97,89,120,92, 103,100,76,86, 100, 70, 89, 99, 104, 91, 90	70	120	93	12.7
			3	4.0	93, 81, 90	81	93	88	7.1
		BYI 02960-OH	17	0.01	102,109,101,89, 99, 90,96, 83, 90, 72, 95, 89, 113, 107, 73, 96, 99	72	113	94	12.0
			3	4.0	102, 89, 96	89	102	96	6.8
	fat	BYI 02960	12	0.01	87, 88, 77, 85, 95, 105, 96, 94, 88, 93, 75, 105	75	105	91	9.5
			3	4.0	110, 104, 106	104	110	107	2.6
		DFA	12	0.01	97, 91, 94, 97, 84, 80, 88, 96, 83, 85, 75, 74	74	97	87	9.4
			3	4.0	100, 96, 92	92	100	96	4.2
		BYI 02960-acetyl-AMCP	12	0.01	119,81,96,85, 99, 77, 100, 92, 95, 107, 95, 87	77	119	94	12.2
			3	4.0	109, 111, 108	108	111	109	1.4
		BYI 02960-OH	12	0.01	95, 106, 100, 87, 100, 88, 90, 93, 87, 86, 90, 102	86	106	94	7.2
			3	4.0	117, 113, 118	113	118	116	2.1
	liver	BYI 02960	12	0.01	93,104,121,114, 102, 114,90,94, 110, 95, 84, 92	84	121	101	11.4
			3	4.0	112, 102, 100	100	112	104	6.2
		DFA	12	0.01	75, 90, 83, 97, 89, 93, 81, 103, 84, 77, 78, 82	75	103	86	10.2
			3	4.0	91, 85, 82	82	91	86	5.2
		BYI 02960-acetyl-AMCP	12	0.01	108,112,116,117, 96, 116, 96, 114, 115, 89, 96, 94	89	117	106	10.1
			3	4.0	115, 100, 99	99	115	105	8.4
		BYI 02960-OH	12	0.01	84, 85, 120, 83, 74, 88, 89, 97, 101, 72, 91, 71	71	120	88	15.6
			3	4.0	108, 106, 107	106	108	107	0.7

All concentrations are expressed in parent compound equivalents.

Continued next page…

Table 6.4.1-5 (cont'd): Concurrent recovery data for the relevant residues of BYI 02960 in poultry matrices

Study No.	**Matrix**	**a.s./metabolite**	***n***	**Spike level (mg/kg)**	**Recovery (%)**				
					Individual recoveries	**Min**	**Max**	**Mean**	**RSD**
RARVP041	muscle	BYI 02960	12	0.01	117,106,115,119, 96, 119, 82, 81, 116, 94, 115, 98	81	119	105	13.5
			3	4.0	108, 112, 108	108	112	109	2.1
		DFA	12	0.01	91, 95, 101, 85, 82, 92, 88, 118, 98, 87, 86, 104	82	118	95	10.4
			3	4.0	86, 83, 80	80	86	83	3.6
		BYI 02960-acetyl-AMCP	12	0.01	114,116,117,135, 103,119,118,116, 110, 101, 92, 88	88	135	111	11.6
			3	4.0	108, 107, 101	101	108	105	3.5
		BYI 02960-OH	12	0.01	100,112,114,97, 105,93,120,119, 111, 107, 107, 81	81	120	106	10.6
			3	4.0	108, 112, 110	108	112	110	1.8
	excreta	BYI 02960	8	0.01	87, 110, 104, 91, 112, 109, 88, 111	87	112	102	10.8
			3	4.0	98, 96, 93	93	98	95	2.6
		DFA	8	0.01	118,110,103,114, 112, 121, 99, 92	92	121	109	9.1
			3	4.0	86, 86, 88	86	88	87	1.3
		BYI 02960-acetyl-AMCP	8	0.01	112,106, 98,101, 99, 108, 109, 109	98	112	105	5.0
			3	4.0	98, 91, 91	91	98	93	4.3
		BYI 02960-OH	8	0.01	102,104,100,110, 102,105,101,91	91	105	102	5.3
			3	4.0	97, 99, 91	91	99	95	4.4

All concentrations are expressed in parent compound equivalents.

Table 6.4.1-6: Weekly dose rates versus total residues of BYI 02960 residues in eggs from 43X dose group

Dose group	Dose week	Sampling interval	Dose administered (mg)	Average body weight (kg)	Dose rate (mg a.s./kg bw)	Total residues* of BYI 02960 (mg/kg)
43X	1	day Zero	6.05	1.45	4.17	<LOD
		day 2				0.424
		day 4				1.037
	2	day 7	6.97	1.48	4.71	1.143
		day 10				1.368
	3	day 14	6.60	1.49	4.43	1.110
		day 17				1.347
	4	day 21	7.28	1.50	4.85	1.366
		day 24				1.676
		day 28				1.722

* total residues here are the sum of BYI 02960, DFA, BYI 02960-acetyl-AMCP, and BYI 02960-OH, expressed as parent cpd.

Table 6.4.1-7: Proportion of DFA in the total residues of BYI 02960 in excreta

Matrix	Dose group	Composite sample*	Total BYI 02960 residue** (mg/kg)	DFA residues† (mg/kg)	Proportion of DFA in total residue (%)
excreta	4.3X	Subgroup A	1.628	1.097	67
		Subgroup B	1.587	1.077	68
		Subgroup C	1.824	1.247	68
	43X	Subgroup A	12.647	8.253	65
		Subgroup B	14.445	9.493	66
		Subgroup C	15.374	11.300	74

* Composite sample from entire 29-day dosing period per subgroup
** "total BYI 02960 residue" is the sum of BYI 02960, BYI 02960-OH, BYI 02960-acetyl-AMCP, and DFA residues, expressed in BYI 02960 equivalents
† expressed in BYI 02960 equivalents

► *Transfer factors calculated for DFA and the total residue*

As agreed with the EU Rapporteur (Ctgb, NL), separate transfer factors for DFA (difluoroacetic acid) were estimated from the poultry feeding study on the basis of the data available after dosage of the active substance BYI 02960 to laying hens. In order to accomplish this, a theoretical dose of DFA must be estimated. For this estimation, the amounts of DFA in all organs/tissues and particularly in excreta must be considered. The absolute amount of DFA formed in the animals, and which has thus been systemically available, can then be equated with a minimum dose theoretically fed to the animals.

The estimation of the dose of DFA theoretically fed to the animals was conducted on the basis of the data collected for the highest dose group (43X in EU, corresponding to 11X in NAFTA) ([redacted] & [redacted], 2012; KIIA 6.4.1/01), using the animals of the subgroups A to C (actual mean dose of BYI 02960 = 65.1 mg/kg feed).

For a better understanding, the data used in the different calculations are summarized separately at the end of this section in tables, as listed here:

- Table 6.4.1-12: Calculation of the mean body weight of the laying hens in the 43X dose group, subgroups A to C
- Table 6.4.1-13: Liver weights of laying hens in the 43X dose group, subgroups A to C
- Table 6.4.1-14: Estimation of the average weight of excreta collected from white leghorn hens in a 24-h period based on data from the metabolism studies
- Table 6.4.1-15: Calculation of the average weight of an egg
- Table 6.4.1-16: Individual egg production of laying hens in the 43X dose group, subgroups A to C
- Table 6.4.1-17: Calculation of the weighted residue level in eggs
- Table 6.4.1-18: Residue levels in animal matrices after dosing of BYI 02960 to laying hens
- Table 6.4.1-19: Total residues calculated for animal matrices after dosing of BYI 02960 to laying hens

Minimum dose of DFA theoretically fed to poultry:

The residue levels in excreta, eggs, tissues, and organs, as well as the weights of the animal matrices (total weight of 12 birds) used for the calculation of the minimum theoretical dose are summarized in the Table 6.4.1-8.

Table 6.4.1-8: Calculation of absolute DFA amounts in animal matrices on basis of the sample weights and the residues in the samples (43X dose group)

Animal matrix	Weight [kg]	DFA residue [mg a.s. equiv./kg]	Absolute DFA amounts [mg a.s. equiv.]
eggs*	16.695[1]	1.130[5]	18.863
liver*	0.487	3.313	1.614
muscle*	7.058[2]	2.27	16.023
fat*	2.118[3]	1.006	2.131
excreta	73.08[4]	9.682	707.577
total (12 birds)			**746.208**

* animals of subgroups A to C were used to calculate the average/weighted residues (*without* "depuration" animals)

[1] the total weight of the eggs was calculated based on the total number of eggs collected during the in-life phase of the study (day 1 to 29) and the average egg weight determined from the eggs used for analysis; see Table 6.4.1-15 and Table 6.4.1-16

[2] total muscle weight was calculated assuming a value of 30% of the mean body weight (1.47 kg) for this tissue

[3] total fat weight was calculated assuming a value of 12% of the mean body weight (1.47 kg) for this tissue

[4] the total weight of excreta was estimated based on the mean excreta weight (210 g/day/hen) determined from the 12 white leghorn hens used in the BYI 02960 poultry metabolism studies (mean body weight: 1.60 kg); see Table 6.4.1-14

[5] weighted DFA residue value of eggs collected at day 2, 4, 7, 10, 14, 17, 21, 24 and 28; see Table 6.4.1-17

According to the balance established, the minimum amount of DFA systemically available was 746.2 mg a.s. equiv. for twelve animals (animals of subgroups A, B & C), corresponding to **62.2 mg a.s. equiv. per animal**.

Calculation of transfer factors:

The total amount of BYI 02960 administered in the feeding study accounted for 193.5 mg per animal (4.54 mg/kg bw/day × 1.47 kg bw × 29 days). Thus the total amount of systemically available DFA represented 32.1% of the amount administered as BYI 02960 (62.2 mg/193.5 mg = 32.1%).

Expressing the dose of BYI 02960 in [mg/kg dry feed], the mean dose level in the 43Xdose group accounted for 65.1 mg a.s./kg dry feed. The theoretical dose of DFA can thus be calculated to be **20.9 mg a.s. equiv./kg dry feed** (65.1 mg a.s./kg feed × 32.1% = 20.9 mg a.s. equiv./kg dry feed).

On the basis of the DFA residues in eggs and organs/tissues and the theoretical dose of DFA, transfer factors have been calculated, according to the following equation:

$$TF = \frac{\text{residue level in edible commodity}}{\text{residue level in the diet}}$$

The following tables summarise the residue values determined in the animal matrices and the corresponding transfer factors derived from them.

DFA transfer:

Assuming that the theoretical dose of DFA is reflected by the same proportion (32.1% of the parent dose) for all dose levels, transfer factors for DFA can be estimated at all levels.

It has to be mentioned that, except for the highest dose level, no composite samples of eggs were collected which covered the whole administration phase. Thus for the 1X, 4.3X, and 13X dose levels, only egg samples from day 28 (the plateau level had been reached by that time) were considered when calculating the transfer.

Table 6.4.1-9: Transfer factors calculated for DFA

Animal matrix	DFA residue [mg a.s equiv./kg]	Transfer factor
Theoretical dose administered: 20.9 mg DFA/kg dry feed (expressed in parent equivalents)		
egg composite* (days 1 to 29)	1.130	0.054
muscle*	2.270	0.108
fat*	1.006	0.048
liver*	3.313	0.158
Theoretical dose administered: 6.2 mg DFA/kg dry feed (expressed in parent equivalents)		
egg (day 28)	0.508	0.082
muscle	0.719	0.115
fat	0.272	0.044
liver	1.012	0.163
Theoretical dose administered: 2.1 mg DFA/kg dry feed (expressed in parent equivalents)		
egg (day 28)	0.163	0.078
muscle	0.290	0.139
fat	0.117	0.056
liver	0.413	0.198
Theoretical dose administered: 0.5 mg DFA/kg dry feed (expressed in parent equivalents)		
egg (day 28)	0.047	0.097
muscle	0.083	0.172
fat	0.029	0.060
liver	0.104	0.216

* animals of subgroups A to C were used to calculate the average/weighted residues (*without* "depuration" animals)

Comparing the transfer factors estimated for the animal matrices at different dose levels, it is evident that the transfer of DFA into animal matrices is less pronounced at higher doses. The residue levels in the animal matrices do not increase linearly with the dose levels. The residues detected in eggs and organs/tissues are slightly higher at lower dose levels indicating even more pronounced excretion of DFA at higher dose levels.

Transfer of BYI 02960 residues:

The transfer of the relevant residues of BYI 02960 into edible matrices was also calculated on the basis of the dose administered to the animals in [mg/kg dry feed] and the total residues of BYI 02960 detected in the animal matrices in [mg/kg].

Since the total residue for data collection is different to the relevant residue for enforcement and risk assessment, separate transfer factors were calculated for all animal matrices in all dose groups tested. The total residue as defined for data collection comprises the compounds BYI 02960, BYI 02960-OH, BYI 02960-acetyl-AMCP, and DFA, wheras only parent compound BYI 02960 and DFA were proposed as relevant residue for enforcement and risk assessment (cf. KIIA 6.7.1).

The following tables refer to calculations on the basis of the total residue for data collection (BYI 02960, BYI 02960-OH, BYI 02960-acetyl-AMCP and DFA):

Table 6.4.1-10: Transfer factors calculated for the total residue as defined in the data collection method (parent compound BYI 02960, BYI 0296-acetyl-AMCP, BYI 02960-OH and DFA)

Animal matrix	Total residue [mg a.s equiv./kg]	Transfer factor
Average dose administered: 65.1 mg a.s./kg dry feed (43X)		
egg composite* (days 1 to 29)	1.308	0.020
muscle*	2.409	0.037
fat*	1.229	0.019
liver*	3.480	0.053
Average dose administered: 19.4 mg a.s./kg dry feed (13X)		
egg (day 28)	0.565	0.029
muscle	0.759	0.039
fat	0.302	0.016
liver	1.054	0.055
Average dose administered: 6.5 mg a.s./kg dry feed (4.3X)		
egg (day 28)	0.193	0.030
muscle	0.320	0.049
fat	0.147	0.023
liver	0.444	0.068
Average dose administered: 1.5 mg a.s./kg dry feed (1X)		
egg (day 28)	0.077	0.051
muscle	0.113	0.075
fat	0.059	0.039
liver	0.134	0.089

* animals of subgroups A to C were used to calculate the average/weighted residues (*without* "depuration" animals)

In the subsequent table, the transfer factors were elucidated for the combined residues of BYI 02960 + DFA (*without* the other analytes), as these two compounds have been proposed as the relevant residues of BYI 02960 in poulty matrices for enforcement and risk assessment (cf. KIIA 6.7.1).

Table 6.4.1-11: Transfer factors calculated for the compounds relevant for enforcement/risk assessment (parent compound BYI 02960 and DFA)

Animal matrix	Total residue [mg a.s equiv./kg]	Transfer factor
Average dose administered: 65.1 mg a.s./kg dry feed (43X)		
egg composite* (days 1 to 29)	1.212	0.019
muscle*	2.309	0.035
fat*	1.199	0.018
liver*	3.346	0.051
Average dose administered: 19.4 mg a.s./kg dry feed (13X)		
egg (day 28)	0.532	0.027
muscle	0.729	0.038
fat	0.282	0.015
liver	1.022	0.053
Average dose administered: 6.5 mg a.s./kg dry feed (4.3X)		
egg (day 28)	0.173	0.027
muscle	0.300	0.046
fat	0.127	0.020
liver	0.423	0.065
Average dose administered: 1.5 mg a.s./kg dry feed (1X)		
egg (day 28)	0.057	0.038
muscle	0.093	0.062
fat	0.039	0.026
liver	0.114	0.076

* animals of subgroups A to C were used to calculate the average/weighted residues (*without* "depuration" animals)

As was the case for the transfer factors calculated for DFA, the transfer factors for the total residue (either as defined for data collection or for enforcement/risk assessment) are not independent of the dose fed. Higher doses result in a lower transfer of the compounds into the animal matrices. This is in line with the findings that DFA represents the predominant component of the BYI 02960 residues in poultry matrices. Moreover, the "total residue" transfer factors calculated for the lower doses overestimate the transfer of the residues into the animal matrices since all/most components, except for DFA, are well below the LOD in all/most matrices. Although the compounds were not detectable, they were considered to be *at* the LOQ level of 0.01 mg/kg when calculating the total residues. Therefore it is more appropriate to use the transfer factors calculated for parent compound + DFA (relevant residues of BYI 02960 for risk assessment and enforcement) rather than using the transfer factors calculated for the total residue as defined for data collection.

It is evident that parent compound BYI 02960 was metabolized rather quickly to DFA after feeding of BYI 02960 to poultry, and quite high amounts of DFA were systemically available. As expected, the highest DFA concentration – and therefore the highest transfer factor – was detected in the metabolizing organ liver, followed by muscle and eggs. However, the transfer of total BYI 02960 residues into all edible matrices is rather low at all dose levels tested.

Feeding of DFA only would thus result in approx. threefold higher transfer factors, as demonstrated above (cf. Table 6.4.1-9). The highest transfer was also determined for liver, followed by muscle and eggs. The lowest transfer factor was determined for fat.

Using these transfer factors derived for the combined residue of BYI 02960 + DFA as well as for DFA alone, estimations of the residue levels reasonably expected to be determined in poultry tissues and eggs after feeding of a mixture of BYI 02960 and DFA (as would realistically be anticipated in the feed crops) can be calculated.

<u>Supporting information:</u>

Estimation of the total weight of muscle and fat of hens and determination of the total liver weight (subgroups A to C)

Table 6.4.1-12: Calculation of the mean body weight of the laying hens in the 43X dose group; subgroups A to C

Group	Animal No.	Weight at Study Day [g]						Average Weight [g]
		-7	1	8	15	22	29	
11X-A	954	1467.3	1449.5	1481.5	1455.5	1473.1	1469.6	1466.1
11X-A	955	1624.6	1639.7	1603.2	1657.8	1669.7	1714.5	1651.6
11X-A	952	1422.2	1393.5	1449.2	1428.2	1428.9	1440.1	1427.0
11X-A	951	1516.5	1540.7	1556.4	1595.4	1613.3	1590.9	1568.9
11X-B	967	1393.3	1418.4	1388.5	1444.8	1469.8	1463.2	1429.7
11X-B	968	1325.7	1320.1	1371.3	1367.6	1377.3	1367.7	1355.0
11X-B	970	1477.3	1536.9	1481.3	1543.8	1560.7	1561.1	1526.9
11X-B	969	1346.5	1407.9	1404.9	1438.4	1463.0	1442.8	1417.3
11X-C	823	1438.6	1459.2	1324.7	1498.2	1501.2	1505.9	1454.6
11X-C	821	1521.1	1535.3	1555.7	1593.1	1618.4	1516.4	1556.7
11X-C	825	1389.7	1425.3	1391.3	1439.3	1456.5	1450.9	1425.5
11X-C	822	1338.2	1329.7	1367.7	1426.3	1362.9	1366.5	1365.2
Overall average weight								**1470.5**

Based on the average body weight of 1470.5 g, the average weights of muscle (40% of the total body weight) and fat (12% of the total body weight) were estimated to be 588.2 g and 325.8 g, respectively. Thus the total **muscle** weight amounts to **7058 g** for **twelve animals** and the total **fat** weight amounts to **2118 g** for **twelve animals.**

Table 6.4.1-13: Liver weights of laying hens in the 43X dose group; subgroups A to C

Dose Group-Subgroup	Animal No.	Liver weight [g]
11X-A	954	44.2
11X-A	955	59.1
11X-A	952	39.8
11X-A	951	35.0
11X-B	967	34.3
11X-B	968	36.3
11X-B	970	50.5
11X-B	969	33.4
11X-C	823	41.2
11X-C	821	40.2
11X-C	825	34.6
11X-C	822	38.6
Total liver weight of 12 hens		**487.2**

At necropsy the entire liver of each animal was collected, weighed, and pooled per subgroup. The total **liver** weight amounts to **487.2 g** for **twelve animals**.

Estimation of the total excreta weight of hens (subgroup A to C)

Table 6.4.1-14: Estimation of the average weight of excreta collected from white leghorn hens in a 24-h period based on data from the metabolism studies

Time after the 1st admin. [d]	Weight of excreta [g]					
Poultry metabolism study conducted with [furanone-4-^{14}C]BYI 02960 (see KIIA 6.2.2/02)						
	animal 956	animal 957	animal 958	animal 959	animal 960	animal 961
0	-----	-----	-----	-----	-----	-----
1	183.23	220.76	217.46	192.94	185.40	185.40
2	208.07	197.27	244.21	178.59	174.99	174.99
3	229.33	209.54	230.93	209.24	180.52	180.52
4	207.48	225.63	229.07	166.95	207.94	207.94
5	227.77	225.91	251.07	161.09	199.49	199.49
6	221.91	218.23	215.58	221.74	211.72	211.72
7	245.23	214.06	216.23	169.87	202.52	202.52
8	241.05	293.95	236.26	200.62	219.34	219.34
9	217.93	303.16	239.60	230.71	228.64	228.64
10	216.23	278.29	253.51	228.34	220.73	220.73
11	242.78	296.54	219.67	239.19	218.84	218.84
12	213.44	222.15	184.08	229.71	235.84	235.84
13	226.80	216.55	208.81	229.64	221.67	221.67
13.25	97.48	183.36	131.27	141.64	122.07	122.07
average weight day 1 to 13	221.63	240.16	226.65	204.51	208.28	208.28

Table continued on next page…

Time after the 1st admin. [d]	Weight of excreta [g]					
Poultry metabolism study conducted with [pyridinylmethyl-^{14}C]BYI 02960 (see KIIA 6.2.2/01)						
	animal 962	animal 963	animal 964	animal 965	animal 966	animal 967
0	-----	-----	-----	-----	-----	-----
1	221.63	208.24	180.33	122.69	227.60	211.21
2	219.64	227.64	151.96	119.05	193.77	204.10
3	213.68	217.76	126.35	186.00	208.25	178.51
4	236.13	193.85	135.26	160.08	198.49	203.95
5	231.74	215.88	167.17	166.01	213.74	186.55
6	250.23	198.97	173.20	188.65	244.92	186.90
7	368.86	194.35	208.94	175.82	263.03	201.91
8	178.52	178.89	191.19	169.49	174.85	165.08
9	222.68	212.98	176.45	221.20	230.97	225.28
10	227.84	191.95	163.88	187.79	225.24	176.40
11	250.38	195.19	193.51	170.27	246.21	187.62
12	210.87	177.87	159.08	175.46	183.33	190.20
13	258.11	174.14	154.96	153.46	230.41	197.32
13.25	72.36	72.67	63.92	59.71	101.60	70.15
average weight day 1 to 13	237.72	199.05	167.87	168.92	218.52	193.46
overall average						**207.92**

----- no excreta collected
Body weights were determined at the day before the first administration.

Based on the average weight of excreta collected in the poultry metabolism studies, the average excreta weight in the present study was estimated to be **210 g in a 24-h period**. Thus the total **excreta** weight was estimated to be **73080 g** for **twelve hens**.

Estimation of the total egg weight of hens (subgroups A to C)

Table 6.4.1-15: Calculation of the average weight of an egg

Dose Group-Subgroup	Number of birds	Day of treatment	Weight of eggs [g]	Number of eggs	Average weight of one egg [g]
11X-A	4	2	202.8	4	50.7
11X-B	4	2	149.8	3	49.9
11X-C	4	2	140.2	3	46.7
11X-A	4	4	200.1	4	50.0
11X-B	4	4	242.6	5	48.5
11X-C	4	4	235.1	5	47.0
11X-A	4	7	228.2	4	57.1
11X-B	4	7	287.0	6	47.8
11X-C	4	7	189.6	4	47.4
11X-A	4	10	154.6	3	51.5
11X-B	4	10	145.3	3	48.4
11X-C	4	10	186.0	4	46.5
11X-A	4	14	214.0	4	53.5
11X-B	4	14	203.7	4	50.9
11X-C	4	14	194.2	4	48.6
11X-A	4	17	215.2	4	53.8
11X-B	4	17	201.7	4	50.4
11X-C	4	17	151.9	3	50.6
11X-A	4	21	211.4	2	105.7
11X-B	4	21	251.7	5	50.3
11X-C	4	21	198.4	4	49.6
11X-A	4	24	209.9	4	52.5
11X-B	4	24	210.7	4	52.7
11X-C	4	24	200.3	4	50.1
11X-A	4	28	219.4	4	54.9
11X-B	4	28	211.7	4	52.9
11X-C	4	28	96.0	2	48.0
Total			**5351.5**	**104**	
Average weight of one egg					**52.5**

Table 6.4.1-16: Individual egg production of laying hens in the 43X dose group; subgroups A to C

Dose Group-Subgroup	Study day [week 1]							Total # of eggs per week
	1	**2**	**3**	**4**	**5**	**6**	**7**	
11X-A	3	4	4	4	3	4	4	26
11X-B	1	3	4	5	3	4	6	26
11X-C	1	3	4	5	4	4	4	25
	Study day [week 2]							
	8	**9**	**10**	**11**	**12**	**13**	**14**	
11X-A	4	4	3	4	4	4	4	27
11X-B	4	4	3	5	2	4	4	26
11X-C	3	4	4	4	4	5	4	28
	Study day [week 3]							
	15	**16**	**17**	**18**	**19**	**20**	**21**	
11X-A	3	4	4	8	0	4	2	25
11X-B	6	4	4	5	2	4	5	30
11X-C	4	4	3	6	2	4	4	27
	Study day [week 4]							
	22	**23**	**24**	**25**	**26**	**27**	**28**	
11X-A	4	4	4	3	5	4	4	28
11X-B	1	6	4	1	5	4	4	25
11X-C	2	5	4	3	5	4	2	25
Total number of eggs								**318**

Based on the average weight of an egg and the total number of the eggs laid during the study phase (day 1 to 28), the total **egg** weight in the present study was estimated to be **16695 g** for **twelve hens** (52.5 g × 318 = 16695 g).

Table 6.4.1-17: Calculation of the weighted residue level in eggs

Dose Group-Subgroup	Number of birds	Day of treatment	Weight of eggs [kg]	Total residue level [mg a.s. equiv./kg]	Absolute residue level [mg a.s. equiv.]
11X-A	4	2	0.2028	0.381	0.0773
11X-B	4	2	0.1498	0.345	0.0517
11X-C	4	2	0.1402	0.342	0.0479
11X-A	4	4	0.2001	0.808	0.1617
11X-B	4	4	0.2426	1.000	0.2426
11X-C	4	4	0.2351	0.952	0.2238
11X-A	4	7	0.2282	1.07	0.2442
11X-B	4	7	0.2870	1.10	0.3157
11X-C	4	7	0.1896	1.03	0.1953
11X-A	4	10	0.1546	1.35	0.2087
11X-B	4	10	0.1453	1.26	0.1831
11X-C	4	10	0.1860	1.27	0.2362
11X-A	4	14	0.2140	1.03	0.2204
11X-B	4	14	0.2037	1.12	0.2281
11X-C	4	14	0.1942	0.982	0.1907
11X-A	4	17	0.2152	1.02	0.2195
11X-B	4	17	0.2017	1.32	0.2662
11X-C	4	17	0.1519	1.09	0.1656
11X-A	4	21	0.2114	1.22	0.2579
11X-B	4	21	0.2517	1.2	0.3020
11X-C	4	21	0.1984	1.29	0.2559
11X-A	4	24	0.2099	1.43	0.2991
11X-B	4	24	0.2107	1.63	0.3434
11X-C	4	24	0.2003	1.50	0.2994
11X-A	4	28	0.2194	1.41	0.3094
11X-B	4	28	0.2117	1.68	0.3557
11X-C	4	28	0.0960	1.51	0.1450
Total			**5.3515**		**6.0466**
Weighted residue [mg a.s. equiv./kg]			**1.130**		

Residue levels detected in animal matrices

Table 6.4.1-18: Residue levels in animal matrices after dosing of BYI 02960 to laying hens

Dose level [mg/kg feed]	Residues [mg a.s. equiv./kg]				
	Animal matrix	**BYI 02960**	**DFA**	**BYI 02960-acetyl-AMCP**	**BYI 02960-OH**
1X (1.5 mg/kg dry feed)	eggs (day 28)	< 0.004 (LOD)	0.047	< 0.003 (LOD)	< 0.003 (LOD)
	fat	< 0.003 (LOD)	0.029	< 0.003 (LOD)	< 0.002 (LOD)
	liver	< 0.003 (LOD)	0.104	< 0.003 (LOD)	< 0.002 (LOD)
	muscle	< 0.004 (LOD)	0.083	< 0.003 (LOD)	< 0.003 (LOD)
4.3X (6.5 mg/kg dry feed)	eggs (day 28)	< 0.004 (LOD)	0.163	< 0.003 (LOD)	< 0.003 (LOD)
	fat	< 0.003 (LOD)	0.117	< 0.003 (LOD)	< 0.002 (LOD)
	liver	0.006	0.413	0.011	0.006
	muscle	< 0.004 (LOD)	0.290	0.010	< 0.003 (LOD)
13X (19.4 mg/kg dry feed)	eggs (day 28)	0.023	0.508	0.015	0.018
	fat	< 0.003 (LOD)	0.272	< 0.003 (LOD)	< 0.002 (LOD)
	liver	< 0.003 (LOD)	1.012	0.025	0.005
	muscle	0.004	0.719	0.024	0.005
43X (65.1 mg/kg dry feed)	egg composite	0.082[1]	1.130[1]	0.048[1]	0.048[1]
	fat	0.192	1.006	0.021	0.010
	liver	0.032	3.313	0.083	0.052
	muscle	0.039	2.270	0.068	0.032

[1] weighted residue values, according to Table 6.4.1-16

Table 6.4.1-19: Total residues calculated for animal matrices after dosing of BYI 02960 to laying hens

Dose level [mg/kg feed]	Residues [mg a.s. equiv./kg]		
	Animal matrix	**total residue for data collection[1]**	**total residue for enforcement / risk assessment[2]**
1X (1.5 mg/kg dry feed)	eggs	0.077	0.057
	fat	0.059	0.039
	liver	0.134	0.114
	muscle	0.113	0.093
4.3X (6.5 mg/kg dry feed)	eggs	0.193	0.173
	fat	0.147	0.127
	liver	0.444	0.423
	muscle	0.320	0.300
13X (19.4 mg/kg dry feed)	eggs	0.565	0.532
	fat	0.302	0.282
	liver	1.054	1.022
	muscle	0.759	0.729
43X (65.1 mg/kg dry feed)	eggs	1.308	1.212
	fat	1.229	1.199
	liver	3.480	3.346
	muscle	2.409	2.309

[1] total residue for data collection: BYI 02960, DFA, BYI 02960-acetyl-AMCP and BYI 02960-hydroxy
[2] total residue for enforcement / risk assessment: BYI 02960 and DFA

Remark: All values <LOQ of 0.01 mg/kg were considered as being *at* 0.01 mg/kg to calculate the total residue

IIA 6.4.2 Lactating ruminants (goat or cow)

Report:	**KIIA 6.4.2/01, [redacted], S.M., & [redacted], A.M.; 2012**
Title:	BYI 02960 – Magnitude of the residue in dairy cows
Report No. & Document No.:	RARVP050 M-428416-02-1
Guidelines:	– OPPTS 860.1480 – Meat/milk/poultry/eggs – OECD Guideline 505 – APVMA Residue Guideline No. 23 – DACO 7.5 – Meat/milk/poultry/eggs
GLP:	yes (certified laboratory)

I. Materials and Methods

<u>Test system, dosing</u>

Twenty Holstein dairy cows (*Bos Taurus*, approximately 2.5 to 3.5 years of age) purchased from a local dairy were transferred to [redacted] fourteen days prior to the initiation of the study (study day -14). Following randomization, the animals were labeled by study number, pen number, dose group (when assigned) and animal identification. The animals were allowed *ad libitum* access to water and feed throughout the study.

Dose rates used in this study were calculated according to both EU (Appendix G, Livestock feeding studies, 70.1/VI/95 rev4 [1996] and in Annex 4 of the OECD Guidance Document ENV/JM/MONO [2006]32, European Food Safety Authority [EFSA]) and NAFTA (Revisions of Feedstuffs in Table 1 of OPPTS Test Guideline 860.1000 and Guidance on Constructing Maximum Reasonably Balanced Diets [MRBD], Table 1 Feedstuffs [June 2008]) guidance.

Individual cows were weighed within 24 hours of initial dosing and the dose rate (mg BYI 02960/kg body weight) was calculated, based on this weight, and administered daily each study day. The target and actual dose rates employed in the study are summarized below in table 6.4.2-1.

Table 6.4.2-1: Summary of target and actual BYI 02960 dose administration.

Dose groups		Number of cows	Dose levels		
			in feed		per animal
EU[1]	NAFTA[2]		target[3] (mg/kg feed)	actual[4] (mg/kg feed)	actual[5] (mg a.s./kg b.w./day)
control		2	0	0	0
1.3X dose	0.2X dose	4	5.5	4.8	0.184
6.3X dose	0.9X dose	3	27	23	0.898
13X dose	1.8X dose	3	55	50	1.838
34X dose	4.9X dose	7	147	135	4.90

Footnotes:
1: EU dose rate exaggerations are based on EU dietary burden of 4.3 mg a.s./kg feed (see table 6.4-2)
2: NAFTA dose rate exaggerations are based on NAFTA dietary burden of 30.2 mg a.s./kg feed (see table 6.4-4). These are the values shown in the report RARVP050.
3: Target dose was calculated based on NAFTA and EU dietary burdens (tables 6.4-2 and 6.4-4) and est. 20 kg/d food consumption
4: Actual dose based on average feed consumption data collected from the study and amount (mg) test substance for each dose group over the entire dosing period
5: Actual dose based on average amount (mg) test substance and the average body weight for each dose over the entire dosing period

Cows were randomly assigned to the five dose groups: control, EU 1.3X, 6.3X (=0.9X for the NAFTA calculation), 13X, and 34X.. Two cows were assigned as controls, four cows were assigned to the 1.3X treatment group (one of which was designated as a urine-collection cow), three cows were each were assigned to the 6.3X and to the 13X treatment groups, and seven cows were assigned to the 34X group (three of which were designated as depuration cows and one as a urine collection cow.) The animals were dosed orally once per day each morning after milking and feeding. The control animal received a placebo (empty capsule) concurrently with the treated animals.

Sampling

Milk was collected twice daily (afternoon and morning), and the milk was weighed after each milking. On study days 0, 2, 4, 7, 10, 14, 17, 19, 25, 28, 29, 30, 31, 35, 38, and 42, a subsample of the evening milk was retained (refrigerated) and then composited with the morning milk proportional to the amount collected at each milking. Samples from all of these sampling events were analyzed for the 34X group; only day-28 samples were analyzed from the other dose groups. Additional 25-day milk was collected for processing into whey (skim milk) and cream (milk fat) from the one control cow and three of the 34X dose group cows.

On study day 29, all animals except the four depuration cows were humanely sacrificed at least three hours following the last dose. The depuration cows (34X) were sacrificed on study days 32, 36, and 43 (a control cow was also sacrificed on day 43).

Representative samples of liver (each lobe), kidney (center and ends), fat (approximately equal composite of omental, renal, and subcutaneous), and muscle (composite of loin, round, and flank) were collected. The tissue samples were homogenized in the presence of dry ice and the homogenized samples were placed in a freezer prior to shipping.

To estimate the levels of exposure of dairy cows to DFA residues following administration of BYI 02960, urine was collected from two cows (one each from 1.3X and 34X dose groups). Starting on study day 1, prior to morning dosing, the 24-hour collected sample from each cow was weighed and a 50-g aliquot was subsampled. (Unfortunately, these samples were not always composited in a manner proportional to the amounts collected. However, since a 24-hour period was always covered, the "inaccuracy" will be negligible.) These subsamples were pooled by week, resulting in one sample per week for four weeks. The samples were frozen prior to shipping.

All samples were shipped frozen to Bayer CropScience for analysis.

Analysis

BYI 02960 and its metabolites were analytically determined using analytical method RV-004-A11-04 (supplied as an appendix to the main study report; cf. KIIA 4.3/08 for details relating to the method), which was validated prior to and parallel to the residue analysis of the samples. The LOQ was 0.01 mg/kg for all analytes (parent compound, BYI 02960-acetyl-AMCP, and BYI 02960-OH) except DFA, for which it was 0.02 mg/kg (0.05 mg/kg in whey). All values are expressed in BYI 02960 equivalents.

II. Findings

Main study

The mean values of the concurrent recovery rates per compound, sample material, and spiking level were generally in the range of 70-110%, with very few (and minor) exceptions. As the relative standard deviations were always low – in the range of 0-13% – all concurrent recoveries were considered to be acceptable. Details of recovery data are shown in table 6.4.2-4.

Feed consumption and milk production were not adversely affected by treatment with BYI 02960. Although some animals gained weight while others lost weight, average body weights decreased slightly in all groups, including the control, but somewhat more in the highest dose group. Thus it appears that 34X dosing may have had an effect on body weight. One cow in the 34X group suffered health complications (chronic mastitis, metritis) for which she was treated, but which could not be resolved during the study period. Her condition affected both her feed consumption and body weight, although no effect was evident with respect to milk production.

In the groups representing the nominal worst-case EU and NAFTA dietary burden (EU 1.3X and 6.3X groups, respectively), the total residues of BYI 02960 – comprising parent compound, DFA, BYI 02960-acetyl-AMCP, and BYI 02960-OH – were measured at sacrifice in bovine tissues and were as follows: 0.057 and 0.307 mg/kg in muscle, 0.061 and 0.151 mg/kg in fat, 0.159 and 0.824 mg/kg in liver, and 0.193 and 0.893 mg/kg in kidney, respectively. In milk taken on day 28, total residues in the 1.3X and 6.3X groups were 0.063 and 0.125 mg/kg, respectively. These values, as shown in the study report ([redacted] & [redacted], 2012; KIIA 6.4.2/01), reflect the standard practice in the USA of using all residue values as shown, even if they are below the nominal LOQs.

As the proposed residue definition for both enforcement and risk assessment will include only parent BYI 02960 + DFA, which are by far the two major components of the residue, the critical values for this study may not reflect the total of all components as listed above. In the nominal worst-case EU and NAFTA dietary burden groups (EU 1.3X and 6.3X groups, respectively), the combined residues of the two components (calculated in the "traditional" manner, i.e. if one component is <LOQ, it is calculated as being *at* the LOQ) were as follows: 0.063 and 0.304 mg/kg in muscle, 0.041 and 0.147 mg/kg in fat, 0.165 and 0.812 mg/kg in liver, and 0.180 and 0.867 mg/kg in kidney, respectively. In milk taken on day 28, total residues in the 1.3X and 6.3X groups were 0.043 and 0.129 mg/kg, respectively.

In addition to the general testing, day-25 milk samples from the 34X dose group were separated into cream and whey, in order to determine if the residues preferentially collect in more aqueous or fatty compartments. The processing/transfer factors (PF) for the total residue (four components) indicated a very slight preference for more aqueous conditions, with a PF of 1.15 to whey and 0.79 to cream. These factors were also representative for the 2 analytes of primary concern, BYI 02960 parent compound and DFA.

The residues found in the milk, tissues, and excreta collected from the dairy cows during dosing, at the end of the dosing period, and during the depuration phase are presented in tables 6.4.2-2 and 6.4.2-3.

With respect to milk, the highest total BYI 02960 residues were found in the day-17 sample from the 34X dose group. Thus, BYI 02960 residues reached a plateau between at that time and remained at that approximate level for the remainder of the dosing period. The highest total residues in milk at any time in the study in this group were 0.979 mg/kg (total of 4 components); when evaluating only the two analytes of import, BYI 02960 and DFA, the level was 0.974 mg/kg. This was only slightly higher than 0.886 and 0.806 mg/kg, the values determined in the 34X group on days 28 and 29, respectively.

In the depuration phase, total BYI 02960 residues in milk, fat, liver, kidney, and muscle from the 34X dose group cows declined from 0.81, 1.40, 1.59, 5.39, and 1.91 mg/kg, respectively, to <LOQ at 6-7 days after cessation of dose administration (= day 35-36 of the study). The residue data provided in this study are suitable for regulatory purposes. (Depuration data are also presented in tables 6.4.2-2 and 6.4.2-3.)

The levels of DFA residues found in urine are summarized in table 6.4.2-5. DFA residues represented 6% to 8% of the total residues of BYI 02960 in the urine samples, suggesting low but significant exposure of the dairy cattle to DFA following the daily oral administration of BYI 02960 over 29 days.

Transfer factors for total residues and for DFA alone

Additional calculations were conducted to describe the transfer of both total residues and of DFA alone into bovine tissues and milk following exposure to BYI 02960 *and* DFA via the diet. As they were not part of the main study and are not included in the study report RARVP050 ([redacted] & [redacted], 2012; KIIA 6.4.2/01), they are not presented here, but rather later in this section.

III. Conclusions (main study)

A feeding study was conducted with BYI 02960 on dairy cattle in order to elucidate the levels of relevant residues in bovine tissues and in milk. The study was designed to cover the regulatory needs of various regions in the world in which BYI 02960 is to be registered, including the EU, NAFTA, and Australia.

BYI 02960 was administered orally (via capsule) to dairy cows for 29 consecutive days at average *actual* dose rates of 4.8 mg/kg feed (1.3X EU dose), 23 mg/kg feed (6.3X, which approximated a 0.9X NAFTA dose), 50 mg/kg feed (13X), and 135 mg/kg feed (34X). Feed consumption, body weights, and milk production were not adversely affected by compound administration.

After the final dose, the animals were sacrificed and the key edible tissues were analyzed for the relevant residues of BYI 02960. While data were generated for four analytes in the study itself, only two – BYI 02960 and DFA – are proposed for the residue definitions (enforcement and risk assessment) for BYI 02960. The combined residues of BYI 02960 + DFA in bovine tissues at sacrifice in the EU 1.3X dosing group were 0.063 mg/kg in muscle, 0.041 mg/kg in fat, 0.18 mg/kg in kidney, and 0.17 mg/kg in liver, expressed in parent compound equivalents. Prior to sacrifice, residues in milk were measured at various intervals in the high-dose group, and on day 28 in the three lower dose groups. In the EU 1.3X dose group, the residues (BYI 02960 + DFA) amounted to 0.043 mg/kg.

Residue levels reached a plateau in milk. Highest residue were determined at day 17 in the 34X milk samples, remaining at similar levels for the remainder of the study.

Depuration occurred quickly. Total BYI 02960 residues in milk, fat, liver, kidney, and muscle from the 34X dose level cows declined from 0.81, 1.40, 1.59, 5.39, and 1.91 mg/kg, respectively, to <LOQ at 6-7 days after cessation of dose administration (=day 35-36 of the study). The residue data provided in this study are suitable for regulatory purposes.

DFA residues represented 6% to 8% of the total BYI 02960 residues in the urine samples, suggesting low but significant exposure of the dairy cows to DFA residues following the administration of BYI 02960 for 29 days.

Table 6.4.2-2: Levels of the relevant residues of BYI 02960 in milk

group	sampling day	Residue levels of individual analytes (mg/kg)				Total residue levels (mg/kg)	
		BYI 02960	DFA	-AMCP*	-OH	sum of 4**	BYI 02960 + DFA
1.3X⅄	28	0.023	<0.02	<0.01	<0.01	0.028	0.043
6.3X	28	0.108	0.021	<0.01	<0.01	0.125	0.129
13X	28	0.267	0.041	<0.01	<0.01	0.310	0.308
34X⅄	2	0.759	0.081	<0.01	<0.01	0.831	0.840
	4	0.869	0.105	<0.01	<0.01	0.978	0.973
	7	0.688	0.138	<0.01	<0.01	0.830	0.826
	10	0.763	0.137	<0.01	<0.01	0.906	0.900
	14	0.783	0.151	<0.01	<0.01	0.940	0.935
	17	0.831	0.143	<0.01	<0.01	0.979	0.974
	19	0.825	0.130	<0.01	<0.01	0.960	0.955
	25	0.651	0.115	<0.01	<0.01	0.770	0.765
	25†	0.553	0.050	<0.01	<0.01	0.607	0.603
	25‡	0.758	0.123	<0.01	<0.01	0.887	0.881
	28	0.748	0.138	<0.01	<0.01	0.892	0.886
	29***	0.667	0.140	<0.01	<0.01	0.811	0.806
	30***	0.059	0.078	<0.01	<0.01	0.138	0.137
	31***	<0.01	0.043	<0.01	<0.01	0.050	0.053
	35***	<0.01	<0.02	<0.01	<0.01	<0.05	<0.03

* AMCP = BYI 02960-acetyl-AMCP
** this value, as shown in the study report, includes values below the LOQ calculated *at the apparent residue value*
*** depuration phase, no dosing (sampling days 35-49)
† values for cream
‡ values for whey
⅄ day-28 values for the 1.3X and 34X groups include samples from all animals (including "urine" and "depuration" animals)

Table 6.4.2-3: Levels of the relevant residues of BYI 02960 in bovine tissues

group	sampling day	Residue levels of individual analytes (mg/kg)				Total residue levels (mg/kg)	
		BYI 02960	DFA	-AMCP*	-OH	sum of 4‡	BYI 02960 + DFA
	Bovine ***fat***						
1.3X†	29	0.021	<0.02	<0.01	<0.01	0.032	0.041
6.3X	29	0.109	0.038	<0.01	<0.01	0.151	0.147
13X	29	0.285	0.099	<0.01	<0.01	0.388	0.384
34X†	29	0.977	0.392	<0.01	0.020	1.390	1.369
	32**	<0.01	0.100	<0.01	<0.01	0.111	0.110
	36**	<0.01	<0.02	<0.01	<0.01	0.019	<0.03
	43**	<0.01	<0.02	<0.01	<0.01	<LOD	<0.03
	Bovine ***kidney***						
1.3X†	29	0.159	0.017	<0.01	0.019	0.193	0.176
6.3X	29	0.786	0.081	<0.01	0.026	0.893	0.867
13X	29	1.789	0.203	<0.01	0.045	2.037	1.992
34X†	29	4.720	0.558	<0.01	0.103	5.380	5.279
	32**	0.045	0.141	<0.01	<0.01	0.187	0.186
	36**	<0.02	<0.01	<0.01	<0.01	0.010	<0.03
	43**	<0.02	<0.01	<0.01	<0.01	<LOD	<0.03
	Bovine ***liver***						
1.3X†	29	0.145	<0.02	<0.01	0.011	0.159	0.165
6.3X	29	0.755	0.057	<0.01	0.011	0.824	0.812
13X	29	1.680	0.132	<0.01	0.020	1.842	1.812
34X†	29	3.451	0.390	<0.01	0.035	3.890	3.841
	32**	0.033	0.106	<0.01	<0.01	0.140	0.139
	36**	<0.02	<0.01	<0.01	<0.01	0.012	<0.03
	43**	<0.02	<0.01	<0.01	<0.01	<LOD	<0.03
	Bovine ***muscle***						
1.3X†	29	0.043	<0.02	<0.01	<0.01	0.057	0.063
6.3X	29	0.250	0.054	<0.01	<0.01	0.307	0.304
13X	29	0.597	0.136	<0.01	<0.01	0.739	0.733
34X†	29	1.505	0.385	<0.01	0.014	1.901	1.890
	32**	0.017	0.095	<0.01	<0.01	0.114	0.112
	36**	<0.02	<0.01	<0.01	<0.01	0.018	<0.03
	43**	<0.02	<0.01	<0.01	<0.01	<LOD	<0.03

* AMCP = BYI 02960-acetyl-AMCP
** depuration phase, no dosing (sampling days 35-49)
† day-29 values for the 1.3X and 34X groups include samples from all animals (including "urine" and "depuration" animals)
‡ this value, as shown in the study report, includes values below the LOQ calculated *at the apparent residue value*

Table 6.4.2-4: Concurrent recovery data for the relevant residues of BYI 02960 in bovine matrices

Study No.	Matrix	a.s./metabolite	n	Spike Level (mg/kg)	Recovery (%) [a] Individual recoveries	Min	Max	Mean	RSD
RARVP050	milk	BYI 02960	7	0.010	109,109,108, 110,108,107,102	102	110	108	2
			1	0.0250	107	107	107		
			5	0.050	10,102,97,105, 105	97	105	102	3
			3	0.10	103, 109 ,104	103	109	105	3
			1	0.250	103	103	103		
			3	2.0	10, 102, 103	10	103	102	2
		difluoroacetic acid	7	0.020	85,88,80,88,92, 76, 84	76	88	85	6
			7	0.050	81,77,78,89,91, 93, 93	77	93	86	8
			3	0.20	91, 92 ,94	91	94	92	2
			3	0.40	85, 85 ,93	85	93	88	5
		BYI 02960-acetyl-AMCP	7	0.010	103,105,104,104, 109 ,106, 101	101	109	105	2
			1	0.0250	112	112	112		
			5	0.050	103, 102 ,103, 109, 107	102	109	105	3
			3	0.10	108, 112 ,107	107	112	109	2
			1	0.250	103	103	103		
			3	2.0	98, 99 ,99	98	99	99	1
		BYI 02960-OH	7	0.010	115,110,111,105, 113 ,110, 108	105	115	110	3
			1	0.0250	106	106	106		
			5	0.050	101, 104 ,10, 106, 106	10	106	103	3
			3	0.10	110, 108 ,105	105	110	108	2
			1	0.250	105	105	105		
			3	2.0	101, 105 ,101	101	105	102	2
	cream	BYI 02960	7	0.010	109,112,107,118, 105 ,110, 106	105	118	110	4
			3	0.10	109, 107 ,113	107	113	110	3
			3	1.0	111, 109 ,111	109	111	110	1
		difluoroacetic acid	7	0.020	103, 95 ,89, 93, 85 ,103, 96	85	103	95	7
			3	0.20	101, 102 ,106	101	106	103	3
		BYI 02960-acetyl-AMCP	7	0.010	106, 108 ,102, 113, 93 ,98, 93	93	113	102	8
			3	0.10	111, 111 ,114	111	114	112	2
			3	1.0	114, 109 ,115	109	115	113	3
		BYI 02960-OH	7	0.010	116,115,113,124, 107 ,109, 111	107	124	114	5
			3	0.10	110, 111 ,113	110	113	111	1
			3	1.0	114, 111 ,114	111	114	113	2

All concentrations are expressed in parent compound equivalents.

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Table 6.4.2-4 (cont'd): Concurrent recovery data for the relevant residues of BYI 02960 in bovine matrices

Study No.	**Matrix**	**a.s./metabolite**	**n**	**Spike Level (mg/kg)**	**Recovery (%) [a]** Individual recoveries	Min	Max	Mean	RSD
RARVP050	whey	BYI 02960	7	0.010	98, 99 ,10, 98, 105 ,101, 104	98	105	101	3
			7	0.0250	104,106,102,102, 101 ,102, 106	101	106	103	2
			3	0.10	101, 102 ,102	101	102	102	1
			3	0.250	105, 103 ,104	103	105	104	1
			3	1.0	102, 10 ,104	10	104	102	2
		difluoroacetic acid	7	0.050	96,94,95,95, 87,96,89	87	96	93	4
			3	0.50	102, 94 ,99	94	102	98	4
		BYI 02960-acetyl-AMCP	7	0.010	99,10,102,103, 104 ,103, 106	99	106	102	2
			3	0.10	102, 102 ,103	102	103	102	1
		BYI 02960-OH	7	0.010	104,104,104,104, 102 ,10, 103	10	104	103	1
			7	0.0250	107,112,104,109, 107 ,108, 107	104	112	108	2
			3	0.10	101, 10 ,102	10	102	101	1
			3	0.250	106, 112 ,107	106	112	108	3
	fat	BYI 02960	7	0.010	104,101,105,96, 107 ,106, 103	96	107	103	4
			2	0.050	93, 10	93	10	97	
			3	0.10	97, 10 ,101	97	101	99	2
			3	1.50	92, 95 ,99	92	99	95	4
		difluoroacetic acid	7	0.020	81, 96 ,88, 95, 92,86, 87	81	96	89	6
			2	0.050	89, 93	89	93	91	
			3	0.60	88, 89 ,90	88	90	89	1
		BYI 02960-acetyl-AMCP	7	0.010	94, 97 ,10, 98, 99 ,97, 96	94	10	97	2
			2	0.050	97, 98	97	98	98	
			3	0.10	96, 98 ,101	96	101	98	3
			3	1.50	101, 102 ,106	101	106	103	3
		BYI 02960-OH	7	0.010	106,107,109,101, 108 ,107, 105	101	109	106	2
			2	0.050	98, 105	98	105	102	
			3	0.10	97, 101 ,106	97	106	101	4
			3	1.50	94, 97 ,98	94	98	96	2

All concentrations are expressed in parent compound equivalents.

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Table 6.4.2-4 (cont'd): Concurrent recovery data for the relevant residues of BYI 02960 in bovine matrices

Study No.	Matrix	a.s./metabolite	n	Spike Level (mg/kg)	Recovery (%) [a] Individual recoveries	Min	Max	Mean	RSD
RARVP050	kidney	BYI 02960	7	0.010	98,99,95,91,94, 98, 95	91	99	96	3
			3	0.050	93, 87 ,98	87	98	93	6
			3	0.10	96, 96 ,94	94	96	95	1
			3	6.0	90, 92 ,97	90	97	93	4
		difluoroacetic acid	7	0.020	74,73,74,79,66, 69, 66	66	79	72	7
			2	0.050	69, 72	69	72	71	
			3	0.80	84, 79 ,84	79	84	82	4
		BYI 02960-acetyl-AMCP	7	0.010	102, 103 ,105, 99, 99 ,99, 96	96	105	10	3
			3	0.050	10, 94 ,90	90	10	95	5
			3	0.10	98, 99 ,97	97	99	98	1
			3	6.0	91, 93 ,95	91	95	93	2
		BYI 02960-OH	7	0.010	101, 90 ,99, 94, 90 ,105, 98	90	105	97	6
			3	0.050	97, 93 ,95	93	97	95	2
			3	0.10	98, 98 ,98	98	98	98	0
			3	6.0	95, 94 ,10	94	10	96	3
	liver	BYI 02960	7	0.010	98, 90 ,89, 93, 91,85, 84	84	98	90	5
			3	0.050	96, 98 ,96	96	98	97	1
			3	0.10	87, 88 ,91	87	91	89	2
			3	4.0	90, 93 ,91	90	93	91	2
		difluoroacetic acid	7	0.020	87, 75 ,97, 68, 73,73, 82	68	97	79	13
			2	0.050	64, 72	64	72	68	
			3	0.60	79, 80 ,89	79	89	83	7
		BYI 02960-acetyl-AMCP	7	0.010	99, 85 ,104, 93, 98 ,86, 80	80	104	92	9
			3	0.050	103, 109 ,95	95	109	102	7
			3	0.10	93, 92 ,98	92	98	94	3
			3	4.0	93, 94 ,94	93	94	94	1
		BYI 02960-OH	7	0.010	93, 88 ,88, 90, 95,90, 87	87	95	90	3
			3	0.050	98, 10 ,93	93	10	97	4
			3	0.10	91, 91 ,92	91	92	91	1
			3	4.0	97, 98 ,95	95	98	97	2

All concentrations are expressed in parent compound equivalents.

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Table 6.4.2-4 (cont'd): Concurrent recovery data for the relevant residues of BYI 02960 in bovine matrices

Study No.	**Matrix**	**a.s./metabolite**	**n**	**Spike Level (mg/kg)**	**Recovery (%) [a]** Individual recoveries	Min	Max	Mean	RSD
RARVP050	muscle	BYI 02960	7	0.010	92, 97 ,92, 10, 96 ,98, 10	92	10	96	3
			2	0.050	95, 99	95	99	97	
			3	0.10	93, 98, 93	93	98	95	3
			3	2.0	92, 90 ,89	89	92	90	2
		difluoroacetic acid	7	0.020	66, 71 ,76, 76, 77,78, 73	66	78	74	6
			3	0.050	71, 78 ,70	70	78	73	6
			3	0.50	67, 65 ,73	65	73	68	6
		BYI 02960-acetyl-AMCP	7	0.010	89, 101 ,92, 98, 98 ,101, 99	89	101	97	5
			2	0.050	95, 103	95	103	99	
			3	0.10	93, 103 ,91	91	103	96	7
			3	2.0	96, 96 ,95	95	96	96	1
		BYI 02960-OH	7	0.010	93, 10 ,106, 95, 101 ,101, 99	93	106	99	4
			2	0.050	117, 96	96	117	107	
			3	0.10	96, 101 ,94	94	101	97	4
			3	2.0	92, 92 ,92	92	92	92	0
	urine	BYI 02960	7	0.010	102,104,103,103, 104 ,103, 101	101	104	103	1
			3	0.10	102, 102 ,102	102	102	102	0
			3	40.0	109, 103 ,104	103	109	105	3
		difluoroacetic acid	7	0.020	78, 85 ,67, 73, 79,70, 76	67	85	75	8
			3	0.20	92, 91 ,92	91	92	92	1
			3	5.0	106, 102 ,101	101	106	103	3
		BYI 02960-acetyl-AMCP	7	0.010	112,119,106,109, 113 ,111, 110	106	119	111	4
			3	0.10	108, 109 ,107	107	109	108	1
			3	40.0	109, 105 ,107	105	109	107	2
		BYI 02960-OH	7	0.010	109,116,110,108, 113 ,113, 112	108	116	112	2
			3	0.10	107, 105 ,105	105	107	106	1
			3	40.0	110, 106 ,105	105	110	107	2

All concentrations are expressed in parent compound equivalents.

Table 6.4.2-5: Proportion of DFA in the total residues of BYI 02960 in urine

Matrix	Dose group	Sampling week	Urine collected (kg)*	Total BYI 02960 residue** (mg/kg)	DFA residues† (mg/kg)	Proportion of DFA in total residue (%)
urine	1.3X	week 1	146	1.85	0.112	6
		week 2	122	2.18	0.185	8
		week 3	125	2.24	0.184	8
		week 4	142	1.81	0.142	8
	34X	week 1	226	29.1	1.92	7
		week 2	218	30.8	2.33	8
		week 3	159	46.0	3.71	8
		week 4	152	40.9	3.23	8

* Daily average (determined for each of the four study weeks) was multiplied by 7 days to determine the weekly urine output. Both the 1.3X and 34X animals experienced some hose blockages; the urine lost during these events was estimated by the in-life phase facility but is not included

** "total BYI 02960 residue" is the sum of BYI 02960, BYI 02960-OH, BYI 02960-acetyl-AMCP, and DFA residues, expressed in BYI 02960 equivalents

† expressed in BYI 02960 equivalents

► *Transfer factors calculated for DFA and the total residue*

As agreed with the EU Rapporteur (Ctgb, NL), separate transfer factors for DFA were estimated from the cattle feeding study on the basis of the data available after dosage of the active substance BYI 02960 to lactating cows. In order to accomplish this, a theoretical dose of DFA must be estimated. For this estimation, the amounts of difluoroacetic in all organs/tissues and particularly in urine must be considered. In the rat ADME study, the major amount of the total radioactivity, i.e. > 80% of the dose administered, was excreted via the urine. DFA is a polar compound with a low molecular weight, so it can be assumed that is excreted mainly via the urine. Thus the role of excretion via faeces will be minimal, and this matrix was not considered in the dairy cow balance. The absolute amount of DFA formed in the cows and which was thus systemically available can then be equated with a minimum dose theoretically fed to the animals.

The estimation of the dose of DFA theoretically fed to the animals was conducted on the basis of the data collected for the 34X dose group (4.9X dose group in NAFTA), using the animals 5152, 5155, 5158, and animal 5153 for collection of urine (actual mean dose of BYI 02960 = 135 mg/kg feed), and additionally on the basis of the data collected for the 1.3X dose group using animals 5150, 5159, 5163, and animal 5151 for collection of urine (actual mean dose of BYI 02960 = 4.8 mg/kg feed).

For a better understanding, the data used in the different calculations are summarized separately at the end of this section in tables, as listed here:

- Table 6.4.2-10: Calculation of the mean body weight of cattle in the 34X and 1.3X dose group
- Table 6.4.2-11: Estimation of the kidney weight as percent of the body weight
- Table 6.4.2-12: Estimation of the liver weight as percent of the body weight
- Table 6.4.2-13: Weight of organs and tissues of the lactating cows in the 34X and 1.3X dose group

Minimum dose theoretically fed to lactating cows:

The residue levels in urine, milk, tissues and organs and the weights of the animal matrices (average weight for one animal) used for the calculation of the minimum theoretical dose are summarized in Table 6.4.2-6 (34X and 1.3X dose).

Table 6.4.2-6: Calculation of absolute DFA amounts in cattle matrices on the basis of the sample weights and the residues in the samples

Animal matrix	Weight [kg]	DFA residue* [mg a.s. equiv./kg]	Absolute DFA amounts [mg a.s. equiv.]
Actual dose administered: 135 mg/kg dry feed (34X)			
milk composite (day 1-28)	874	0.118[5]	103.13
muscle	162[1]	0.381	61.72
fat	64.9[2]	0.335	21.74
liver	8.1[3]	0.380	3.078
kidneys	1.4[4]	0.512	0.717
urine	754	2.70[5]	2035.8
total (one animal)			**2226.2**
Actual dose administered: 4.8 mg/kg dry feed (1.3X)			
milk (day 28)	845	0.004	3.50
muscle	165[1]	0.013	2.09
fat	65.9[2]	0.011	0.75
liver	8.2[3]	0.012	0.10
kidneys	1.4[4]	0.018	0.02
urine	535	0.153[5]	82.10
total (one animal)			**88.56**

* milk and organs/tissues:
average/weighted residues were calculated for the "residue animals" using samples from animals 5152, 5155, and 5158 for the 34X dose group and from animals 5150, 5159, and 5158 for the 1.3X dose group
urine:
residues were calculated from samples of the "urine collection" animals " 5153 (34X) and 5151 (1.3X)
[1] total muscle weight was calculated assuming a value of 30%of the mean body weight for this tissue
[2] total fat weight was calculated assuming a value of 12%of the mean body weight for this tissue
[3] total liver weight was calculated assuming a value of 1.5% of the mean body weight for this tissue
[4] total kidney weight was calculated assuming a value of 0.25% of the mean body weight for this tissue
[5] weighted DFA residue value, see Table 6.4.2-18 (urine 34X), Table 6.4.2-19 (urine 1.3X) and Table 6.4.2-21 (milk 34X)

According to the balance established, the minimum amount of DFA systemically available was **2226.2 mg a.s. equiv. per animal** in the 34X dose experiment and **88.6 mg a.s. equiv. per animal** in the 1.3X dose experiment.

Calculation of transfer factors:

34X dose:
The total amount of BYI 02960 administered in the 34X dose experiment of the feeding study accounted for 76876 mg per animal (4.9 mg/kg bw/day × 541 kg bw × 29 days). Thus the total amount of DFA being systemically available represented 2.9% of the amount administered as BYI 02960.

Expressing the dose of BYI 02960 in [mg/kg dry feed], the mean dose level in the 34X dose group accounted for 135 mg a.s./kg dry feed. The theoretical dose of DFA can thus be calculated as being **3.9 mg a.s. equiv./kg dry feed** (135 mg a.s./kg feed × 2.9% = 3.9 mg a.s. equiv./kg dry feed).

1.3X dose:
The total amount of BYI 02960 administered in the 1.3X dose experiment of the feeding study accounted for 2929.5 mg per animal (0.184 mg/kg bw/day × 549 kg bw × 29 days). Thus the total amount of DFA being systemically available represented 3.0% of the amount administered as BYI 02960. This proportion fits very well with the percentage calculated for the 34X dose (2.9% of the BYI 02960 dose administered).

Expressing the dose of BYI 02960 in [mg/kg dry feed], the mean dose level in the 1.3X dose group accounted for 4.8 mg a.s./kg dry feed. The theoretical dose of DFA can thus be calculated as being **0.14 mg a.s. equiv./kg dry feed** (4.8 mg a.s./kg feed × 3.0% = 0.14 mg a.s. equiv./kg dry feed).

On the basis of the DFA residues in milk and organs/tissues and the theoretical dose of DFA, transfer factors have been calculated, according to the following equation:

$$TF = \frac{\text{residue level in edible commodity}}{\text{residue level in the diet}}$$

The following tables summarise the residue values determined in the animal matrices and the corresponding transfer factors derived from them.

DFA transfer:

Assuming that the theoretical dose of DFA is reflected by the same proportion for all dose levels (as shown for the 34X and the 1.3X dose), transfer factors for DFA were estimated at all levels. In contrast to the 34X dose experiment (where weighted residues in milk have been calculated), residues in milk were estimated in all other dose groups on the basis of the 28-day sample, i.e. at a point in time at which the plateau had clearly been reached.

Table 6.4.2-7: Transfer factors calculated for DFA

Animal matrix	DFA residue* [mg a.s equiv./kg]	Transfer factor
Theoretical DFA dose administered: 3.9 mg/kg dry feed; expressed in parent equivalents (34X)		
milk composite (days 1 to 28)	0.118	0.030
muscle	0.381	0.097
fat	0.335	0.086
liver	0.380	0.097
kidney	0.512	0.131
Theoretical DFA dose administered: 1.45 mg/kg dry feed; expressed in parent equivalents (13X)		
milk (day 28)	0.041	0.028
muscle	0.136	0.094
fat	0.099	0.068
liver	0.132	0.091
kidney	0.203	0.140
Theoretical dose administered: 0.67 mg/kg dry feed; expressed in parent equivalents (6.3X)		
milk (day 28)	0.016	0.024
muscle	0.054	0.081
fat	0.038	0.057
liver	0.057	0.085
kidney	0.081	0.121
Theoretical dose administered: 0.14 mg/kg dry feed; expressed in parent equivalents (1.3X)		
milk (day 28)	0.004	0.028
muscle	0.013	0.088
fat	0.011	0.079
liver	0.012	0.086
kidney	0.018	0.125

* average/weighted residues were calculated using samples from animals 5152, 5155, 5158 ("residue" animals) for the 34X dose group and from animals 5150, 5159 and 5158 for the 1.3X dose group, in agreement with calculation of residues in the samples of all other dose groups which consisted of "residue" animals, only. Samples of the "urine collection" (34X and 1.3X) and "depuration" animals (34X) were not included.

Comparing the transfer factors estimated for the animal matrices at different dose levels, it is obvious that the transfer factors correspond very well. The transfer factors for all matrices were in a very narrow range, e.g. the transfer factor for milk ranged from 0.024 to 0.030 and the one for muscle from 0.081 to 0.097. The residue levels in the animal matrices increase linearly with increasing dose levels.

Transfer of BYI 02960 residues:

The transfer of BYI 02960 residues into edible matrices was also calculated on the basis of the dose administered to the animals in [mg/kg dry feed] and the total residue of BYI 02960 detected in the animal matrices in [mg/kg].

Since the total residue for data collection is different from the relevant residue for enforcement and risk assessment, separate transfer factors were calculated for all animal matrices in all dose groups tested. The total residue as defined for data collection comprises the compounds BYI 02960, BYI 02960-OH, BYI 02960-acetyl-AMCP, and DFA, wheras only parent compound BYI 02960 + DFA were proposed as relevant residue for enforcement and risk assessment (cf. KIIA 6.7.1).

The following tables refer to calculations on the basis of the total residue for data collection (BYI 02960, BYI 02960-OH, BYI 02960-acetyl-AMCP and DFA):

Table 6.4.2-8: Transfer factors calculated for the total residue consisting of parent compound BYI 02960, BYI 0296-acetyl-AMCP, BYI 02960-OH and DFA

Animal matrix	**Total residue* [mg a.s equiv./kg]**	**Transfer factor**
Average dose administered: 135 mg/kg dry feed (34X)		
milk composite (days 1 to 28)	0.942 (0.928)	0.007 (0.007)
muscle	1.784 (1.776)	0.013 (0.013)
fat	1.206 (1.197)	0.009 (0.009)
liver	3.903 (3.896)	0.029 (0.029)
kidney	5.027 (5.018)	0.037 (0.037)
Average dose administered: 50 mg/kg dry feed (13X)		
milk (day 28)	0.328 (0.310)	0.007 (0.006)
muscle	0.753 (0.740)	0.015 (0.015)
fat	0.404 (0.388)	0.008 (0.008)
liver	1.841 (1.834)	0.037 (0.037)
kidney	2.046 (2.037)	0.041 (0.041)

Table continued on next page…

Table 6.4.2-8 (cont'd): Transfer factors calculated for the total residue consisting of parent compound BYI 02960, BYI 0296-acetyl-AMCP, BYI 02960-OH and DFA

Animal matrix	Total residue* [mg a.s equiv./kg]	Transfer factor
Average dose administered: 23 mg/kg dry feed (6.3X)		
milk (day 28)	0.148 (0.126)	0.006 (0.005)
muscle	0.324 (0.308)	0.014 (0.013)
fat	0.167 (0.151)	0.007 (0.007)
liver	0.833 (0.825)	0.036 (0.036)
kidney	0.903 (0.894)	0.039 (0.039)
Average dose administered: 4.8 mg/kg dry feed (1.3X)		
milk (day 28)	0.065 (0.030)	0.013 (0.006)
muscle	0.085 (0.060)	0.018 (0.013)
fat	0.062 (0.035)	0.013 (0.007)
liver	0.195 (0.180)	0.041 (0.037)
kidney	0.209 (0.198)	0.043 (0.041)

* average/weighted residues were calculated using samples from animals 5152, 5155, 5158 ("residue" animals) for the 34X dose group and from animals 5150, 5159 and 5158 for the 1.3X dose group, in agreement with calculation of the residues in the samples of all other dose groups which consisted of "residue" animals, only. Samples of the "urine collection" (34X and 1.3X) and "depuration" animals (34X) were not included.

Remark re. two values shown for total residue and transfer factors:
In a first step, all values below the LOQ of 0.01 mg/kg (BYI 02960, BYI 02960-acetyl-AMCP and BYI 02960-OH) or below the LOQ of 0.02 mg/kg (DFA) were considered as being *at* 0.01 or 0.02 mg/kg, respectively, to calculate the total residue.
Values in parentheses: In a second step, all values above the LOD but below the LOQ were considered "as reported"; values below the LOD were calculated as being *at* the LOD (values in brackets); see Table 6.4.2-23

In the subsequent table, the transfer factors were elucidated for the combined residues of BYI 02960 + DFA (*without* the other analytes), as these two compounds have been proposed as the relevant residues of BYI 02960 in poulty matrices for enforcement and risk assessment (cf. KIIA 6.7.1).

Table 6.4.2-9: Transfer factors calculated for the total residue consisting of parent compound BYI 02960 + DFA

Animal matrix	Total residue [mg a.s equiv./kg]	Transfer factor
Average dose administered: 135 mg/kg dry feed (34X)		
milk composite (days 1 to 28)	0.922 (0.922)	0.007
muscle	1.760 (1.760)	0.013
fat	1.182 (1.182)	0.009
liver	3.851 (3.851)	0.029
kidney	4.919 (4.919)	0.036
Average dose administered: 50 mg/kg dry feed (13X)		
milk (day 28)	0.308 (0.308)	0.006
muscle	0.733 (0.733)	0.015
fat	0.384 (0.384)	0.008
liver	1.811 (1.811)	0.036
kidney	1.992 (1.992)	0.040
Average dose administered: 23 mg/kg dry feed (6.3X)		
milk (day28)	0.128 (0.124)	0.006 (0.005)
muscle	0.304 (0.304)	0.013
fat	0.147 (0.147)	0.006
liver	0.812 (0.812)	0.035
kidney	0.867 (0.867)	0.038
Average dose administered: 4.8 mg/kg dry feed (1.3X)		
milk (day 28)	0.045 (0.028)	0.009 (0.006)
muscle	0.065 (0.057)	0.013 (0.012)
fat	0.042 (0.033)	0.009 (0.007)
liver	0.174 (0.166)	0.036 (0.035)
kidney	0.179 (0.178)	0.037 (0.037)

* average/weighted residues were calculated using samples from animals 5152, 5155, 5158 ("residue" animals) for the 34X dose group and from animals 5150, 5159 and 5158 for the 1.3X dose group, in agreement with calculation of the residues in the samples of all other dose groups which consisted of "residue" animals, only. Samples of the "urine collection" (34X and 1.3X) and "depuration" animals (34X) were not included.

Remark re. two values shown for total residue and transfer factors:
In a first step, all values below the LOQ of 0.01 mg/kg (BYI 02960) or below the LOQ of 0.02 mg/kg (DFA) were considered as being *at* 0.01 or 0.02 mg/kg, respectively, to calculate the total residue.
Values in parentheses: In a second step, all values above the LOD but below the LOQ were considered "as reported"; values below the LOD were calculated as being *at* the LOD (values in brackets); see Table 6.4.2-23

The predominant component of the residues in milk, edible tissues, and organs was parent compound BYI 02960, followed by DFA. The metabolite BYI 02960-acetyl-AMCP was below the LOD in all dose groups, and BYI 02960-OH was detected in the high dose groups only. When calculating the total residue, all constituents of the residue definition are considered. Compounds detected below the LOQ were estimated to be at the LOQ level. Thus the total residue overestimates the proportion of BYI 02960-acetyl-AMCP and BYI 02960-OH, especially at the 1X dose where neither of the two metabolites were detected. Therefore, calculation of transfer factors should be restricted to parent compound + DFA, the constituents of the residue definition for enforcement and risk assessment.

In milk, DFA concentrations were lower than those for parent by a factor of approx. 6 to 7, as soon as the plateau was reached in milk. DFA concentrations in muscle and fat were lower by a factor of approx. 2 to 4, and by a factor of approx. 9 in the metabolizing organs liver and kidney. Clearly, parent compound BYI 02960 was metabolized quite slowly to DFA after feeding BYI 02960 to lactating cows. As soon as DFA was formed, it was distributed equally within the body. Transfer into milk was rather low.

Feeding of DFA only would result in approx. three to tenfold higher transfer factors, as demonstrated above (cf. Table 6.4.2-7). The highest transfer was also detected into the metabolizing organs liver and kidney, followed by muscle and fat. The lowest transfer factor was determined for milk.

Using these transfer factors derived for the combined residue of BYI 02960 + DFA as well as for DFA alone, estimations of the residue levels reasonably expected to be determined in ruminant tissues and milk after feeding of a mixture of BYI 02960 and DFA (as would realistically be anticipated in the feed crops) can be calculated.

Supporting information:

Estimation of the total weight of muscle, fat, liver and kidney of cattle

Only subsamples of muscle, fat, liver and kidney were collected at necropsy from all animals of all dose groups tested. Therefore the total weight of the tissues and organs was estimated based on the average body weight of the animals of the 4.9X dose group determined on the day before administration (cows designated for depuration and urine collection were not considered).

Table 6.4.2-9: Calculation of the mean body weight of cattle in the 34X and 1.3X dose group

Dose Group	Animal No.	Body weight at study start [kg]
34X	5152	553
34X	5155	591
34X	5158	479
Average body weight		**541**
1.3X	5150	595
1.3X	5159	556
1.3X	5163	496
Average body weight		**549**

Based on the average body weight, the average weights of

- muscle (30% of the total body weight for total muscle),
- fat (12% of the total body weight for dissectable fat),
- liver (1.5% of the total body weight), and
- kidneys (0.25% of the total body weight)

were estimated.

Since no literature values were available for kidney, an average kidney weight was estimated based on the values from a recently conducted cattle feeding study ([redacted].; Mefenpyr-diethyl: Feeding study with dairy cows, Bayer CropScience internal report, 2012-01-11). The liver weights determined in that study confirmed the percentage cited in literature. The literature value was used for the estimation of the average liver weight as a worst-case assumption.

Table 6.4.2-10: Estimation of the kidney weight as a pecentage of the body weight (data collected in a feeding study recently performed[1])

Body weight [kg]	Weight of kidneys [g]			Percent of body weight [%]
	left	right	sum	
589	611.0	654.4	1265.4	0.21
460	601.8	587.2	1189.0	0.26
538	816.7	807.1	1623.8	0.30
572	592.7	591.3	1184.0	0.21
545	637.8	592.8	1230.6	0.23
504	658.6	645.9	1304.5	0.26
516	743.3	646.1	1389.4	0.27
481	673.4	633.9	1307.3	0.27
541	874.1	827.1	1701.2	0.31
531	588.5	609.9	1198.4	0.23
546	623.4	659.1	1282.5	0.23
505	544.6	579.9	1124.5	0.22
516	725.3	683.3	1408.6	0.27
572	669.3	722.9	1392.2	0.24
524	603.5	603.3	1206.8	0.23
540	697.8	659.3	1357.1	0.25
623	682.9	752.2	1435.1	0.23
511	619.6	610.2	1229.8	0.24
534 (average)	**664.7**	**659.2**	**1323.9**	**0.25 (average)**

[1] [redacted] Mefenpyr-diethyl: Feeding study with dairy cows, Bayer CropScience Report No. MR-11/040, 2012-01-11

Table 6.4.2-11: Estimation of the liver weight in proportion to the body weight (data collected in a feeding study recently performed[2])

body weight [kg]	weight of liver [g]	percent of body weight [%]
589	8571.3	1.46
460	7812.7	1.70
538	8113.3	1.51
572	8232.8	1.44
545	8183.3	1.50
504	8251.0	1.64
516	9533.1	1.85
481	7619.6	1.58
541	8438.9	1.56
531	7955.5	1.50
546	8497.9	1.56
505	8849.1	1.75
516	7280.7	1.41
572	8828.3	1.54
524	8400.3	1.60
540	8946.5	1.66
623	8679.3	1.39
511	8434.4	1.65
534 (average)	**8686.7 (average)**	**1.57 (average)**

Table 6.4.2-12: Weight of organs and tissues of the lactating cows in the 34X and 1.3X dose group

Animal matrix	percentage of body weight [%]	average weight [kg] 34X dose	average weight [kg] 1.3X dose
muscle	30	162.3	164.7
fat	12	64.9	65.9
liver	1.5	8.1	8.2
kidney	0.25	1.4	1.4

At necropsy, only subsamples of muscle, fat, liver and kidneys were collected. The subsamples were weighed and and pooled per subgroup for analysis. The total weight of the tissues and organs was estimated on the basis of the average body weight of the cows of the 34X and 1.3X dose groups and accounted for **162.3 kg / 164.7kg** for **muscle, 64.9 kg / 65.9 kg** for **fat, 8.1 kg / 8.2 kg** for **liver** and **1.4 kg / 1.4 kg** for **kidney** per animal.

2 [redacted] Mefenpyr-diethyl: Feeding study with dairy cows, Bayer CropScience Report No. MR-11/040, 2012-01-11

Table 6.4.2-13: Residue levels of DFA in organs and tissues of the lactating cows (34X dose group)

Animal number	DFA residues [mg a.s. equiv./kg]			
	muscle	fat	liver	kidney
5152	0.302	0.204	0.284	0.379
5155	0.368	0.427	0.348	0.528
5158	0.473	0.375	0.507	0.630
Average	**0.381**	**0.335**	**0.380**	**0.512**

Table 6.4.2-14: Residue levels of DFA in organs and tissues of the lactating cows (1.3X dose group)

Animal number	DFA residues [mg a.s. equiv./kg]			
	muscle	fat	liver	kidney
5150	0.013	0.012	0.014	0.022
5159	0.011	0.009	0.011	0.016
5163	0.014	0.013	0.012	0.016
Average	**0.013**	**0.011**	**0.012**	**0.018**

Total urine weight and calculation of weighted residues in urine

Table 6.4.2-15: Individual urine production of lactating cows (34X dose group)

Animal number	Study day [week 1]							Total weight of urine per week [g]
	1	**2**	**3**	**4**	**5**	**6**	**7**	
5153	16009	22937	24561	13937	20937	66603	60778	**225762**
	Study day [week 2]							
	8	**9**	**10**	**11**	**12**	**13**	**14**	
5153	63517	31041	27111	25937	20545	18232	31136	**217519**
	Study day [week 3]							
	15	**16**	**17**	**18**	**19**	**20**	**21**	
5153	24732	27801	20771	24801	23722	19152	17531	**158510**
	Study day [week 4]							
	22	**23**	**24**	**25**	**26**	**27**	**28**	
5153	21804	25560	25552	21831	19835	22739	14731	**152052**
Total weight of urine collected (animal 5153)								**753843**

On study day 1, animal 5153 lost approx. 5-6 liters of urine due to hose blockage
On study day 2, animal 5153 had mucus and blood plugging the urine hose leading to urine loss
On study day 13, animal 5153 lost approx. 2-3 liters of urine due to hose blockage
On study day 15, animal 5153 lost approx. 4-6 liters of urine due to urine device displacement
On study day 19, animal 5153 lost approx. 1 liter of urine
On study day 21, animal 5153 lost approx. 4.5 liters of urine
On study day 26, animal 5153 lost approx. 2-4 liters of urine
On study day 27, animal 5153 lost approx. 2 liters of urine

Animal 5153 had several incidences of anorexia / depression / lethargy and mastitis during the study. Further, upon necropsy she was found to have signs of metritis. Since she was under increased stress, which may have complicated her condition, urine collection was rather difficult and several liters of urine were lost. Nevertheless, no correction of the total urine amount was performed and thus a slightly lower systemic exposure to DFA has been calculated, which will lead to slightly overestimated transfer factors (worst-case consideration).

The total **urine** weight was approx. **754 kg** for animal 5153.

Table 6.4.2-16: Individual urine production of lactating cows (1.3X dose group)

Animal number	**Study day** [week 1]							**Total weight of urine per week [g]**
	1	**2**	**3**	**4**	**5**	**6**	**7**	
5151	20541	20972	21856	23705	19941	20939	18040	**145994**
	Study day [week 2]							
	8	**9**	**10**	**11**	**12**	**13**	**14**	
5151	19546	18018	12887	18810	16694	15727	20130	**121812**
	Study day [week 3]							
	15	**16**	**17**	**18**	**19**	**20**	**21**	
5151	16416	20920	17998	16082	16097	18724	19037	**125274**
	Study day [week 4]							
	22	**23**	**24**	**25**	**26**	**27**	**28**	
5151	22491	21558	20714	20168	20101	19607	17426	**142065**
Total weight of urine collected (animal 5151)								**535145**

On study day 3, animal 5151 lost approx. 1 liter of urine during dosing.

The total **urine** weight was approx. **535 kg** for animal 5151.

Table 6.4.2-17: Calculation of the weighted DFA concentration in urine of lactating cows (34X dose group)

Animal number	**Week of treatment**	**Weight of urine composite [kg]**	**DFA residue level [mg a.s. equiv./kg]**	**Absolute DFA level [mg a.s. equiv.]**
5153	1	225.8	1.92	433.5
5153	2	217.5	2.33	506.8
5153	3	158.5	3.71	588.0
5153	4	152.1	3.33	506.5
5153		753.8	**2.70**	2034.8

Table 6.4.2-18: Calculation of the weighted DFA concentration in urine of lactating cows (1.3X dose group)

Animal number	**Week of treatment**	**Weight of urine composite [kg]**	**DFA residue level [mg a.s. equiv./kg]**	**Absolute residue level [mg a.s. equiv.]**
5151	1	146.0	0.112	16.4
5151	2	121.8	0.185	22.5
5151	3	125.3	0.184	23.1
5151	4	142.1	0.142	20.2
5151		535.1	**0.153**	82.1

Total milk weight and calculation of weighted residue level in milk

Table 6.4.2-19: Individual milk production of lactating cows (34X dose group)

Animal number	**Study day** [week 1]							**Total weight of milk per week [g]**
	1	**2**	**3**	**4**	**5**	**6**	**7**	
5152	33263	30378	32333	32682	31758	32653	30268	223335
5155	35194	36404	36579	37549	38042	37595	36085	257448
5158	27781	27787	27430	26392	25779	26845	28959	190973
	Study day [week 2]							
	8	**9**	**10**	**11**	**12**	**13**	**14**	
5152	31961	30587	31401	29270	30247	30769	31062	215297
5155	35842	35224	37570	35058	35863	36608	35857	252022
5158	27146	27705	27157	26013	27081	26309	27037	188448
	Study day [week 3]							
	15	**16**	**17**	**18**	**19**	**20**	**21**	
5152	30574	30346	30299	29744	31796	29495	29777	212031
5155	36220	34145	33875	33813	34465	35924	34468	242910
5158	26401	26905	27605	28679	27533	28822	27160	193105
	Study day [week 4]							
	22	**23**	**24**	**25**	**26**	**27**	**28**	
5152	30289	31028	31594	30925	30623	29482	31424	215365
5155	32803	34031	35980	31826	34131	36530	36333	241634
5158	25566	24924	27203	27729	26123	28550	28369	188464
Total weight of milk collected								**2621032**

The total weight of the milk collected during the study phase (days 1 to 28) was 2621.0 kg for three animals, corresponding to approx. **874 kg per cow**.

Table 6.4.2-20: Calculation of the weighted DFA concentration in milk (34X dose group)

Animal number	Day of treatment	Weight ofmilk sample [kg]	DFA residue level [mg a.s. equiv./kg]	Absolute DFA level [mg a.s. equiv.]
5152	2	30.378	0.080	2.430
5152	4	32.682	0.114	3.726
5152	7	30.268	0.105	3.178
5152	10	31.401	0.112	3.517
5152	14	31.062	0.126	3.914
5152	17	30.299	0.121	3.666
5152	19	31.796	0.112	3.561
5152	25	30.925	0.093	2.867
5152	28	31.424	0.099	3.124
5152		280.235	**0.107**	29.982
5155	2	36.404	0.087	3.182
5155	4	37.549	0.108	4.055
5155	7	36.085	0.106	3.825
5155	10	37.570	0.107	4.020
5155	14	35.857	0.129	4.626
5155	17	33.875	0.119	4.031
5155	19	34.465	0.109	3.757
5155	25	31.826	0.092	2.922
5155	28	36.333	0.094	3.419
5155		319.964	**0.106**	33.836
5158	2	27.787	0.092	2.556
5158	4	26.392	0.128	3.378
5158	7	28.959	0.135	3.909
5158	10	27.157	0.159	4.318
5158	14	27.037	0.166	4.488
5158	17	27.605	0.156	4.306
5158	19	27.533	0.149	4.102
5158	25	27.729	0.141	3.910
5158	28	28.369	0.136	3.858
5158		248.568	**0.140**	34.827
Average weighted residue level			**0.118**	

Residue levels detected in animal matrices

Table 6.4.2-21: Residue levels in animal matrices after dosing of BYI 02960 to lactating cows

Dose level [mg/kg feed]	Residues [mg a.s. equiv./kg]				
	Animal matrix	**BYI 02960**	**DFA**	**BYI 02960-acetyl-AMCP**	**BYI 02960-OH**
1.3X (4.8 mg/kg dry feed)	milk	0.025	0.004[1]	<0.0008 (LOD)	<0.0008 (LOD)
	muscle	0.045	0.013[1]	<0.0015 (LOD)	<0.0014 (LOD)
	fat	0.022	0.011[1]	<0.0007 (LOD)	<0.0008 (LOD)
	liver	0.154	0.012[1]	<0.0027 (LOD)	<0.0009 (LOD)
	kidney	0.159	0.018[1]	<0.0010 (LOD)	<0.0017 (LOD)
6.3X (23 mg/kg dry feed)	milk	0.108	0.016[1]	<0.0008 (LOD)	<0.0008 (LOD)
	muscle	0.250	0.054	<0.0015 (LOD)	0.0021[2]
	fat	0.109	0.038	<0.0007 (LOD)	0.0037[2]
	liver	0.755	0.057	<0.0027 (LOD)	0.011
	kidney	0.786	0.081	<0.0010 (LOD)	0.026
13X (50 mg/kg dry feed)	milk	0.267	0.041	<0.0008 (LOD)	0.001[2]
	muscle	0.597	0.136	<0.0015 (LOD)	0.005[2]
	fat	0.285	0.099	<0.0007 (LOD)	0.003[2]
	liver	1.680	0.132	<0.0027 (LOD)	0.020
	kidney	1.789	0.203	<0.0010 (LOD)	0.045
34X (135 mg/kg dry feed)	milk	0.804[3]	0.118[3]	<0.0008 (LOD)	0.006[3]
	muscle	1.379	0.381	<0.0015 (LOD)	0.014
	fat	0.846	0.335	<0.0007 (LOD)	0.015
	liver	3.472	0.380	<0.0027 (LOD)	0.042
	kidney	4.407	0.512	<0.0010 (LOD)	0.098

1 > LOD, but < LOQ (0.02 mg/kg)
2 > LOD, but < LOQ (0.01 mg/kg)
3 weighted residue value

Table 6.4.2-22: Total residues calculated for animal matrices after dosing of BYI 02960 to lactating cows

Dose level [mg/kg feed]	Residues [mg a.s. equiv./kg]		
	Animal matrix	**total residue for data collection[1]**	**total residue for enforcement / risk assessment[2]**
1.3X (4.8 mg/kg dry feed)	milk	0.065 (0.030[3])	0.045 (0.028[3])
	muscle	0.085 (0.060[3])	0.065 (0.057[3])
	fat	0.062 (0.035[3])	0.042 (0.033[3])
	liver	0.195 (0.180[3])	0.174 (0.166[3])
	kidney	0.209 (0.198[3])	0.179 (0.178[3])
6.3X (23 mg/kg dry feed)	milk	0.148 (0.126[3])	0.128 (0.124[3])
	muscle	0.324 (0.308[3])	0.304 (0.304[3])
	fat	0.167 (0.151[3])	0.147 (0.147[3])
	liver	0.833 (0.825[3])	0.812 (0.812[3])
	kidney	0.903 (0.894[3])	0.867 (0.867[3])
13X (50 mg/kg dry feed)	milk	0.328 (0.310[3])	0.308 (0.308[3])
	muscle	0.753 (0.740[3])	0.733 (0.733[3])
	fat	0.404 (0.388[3])	0.384 (0.384[3])
	liver	1.841 (1.834[3])	1.811 (1.811[3])
	kidney	2.046 (2.037[3])	1.992 (1.992[3])
34X (135 mg/kg dry feed)	milk	0.942 (0.928[3])	0.922 (0.922[3])
	muscle	1.784 (1.776[3])	1.760 (1.760[3])
	fat	1.206 (1.197[3])	1.182 (1.182[3])
	liver	3.903 (3.896[3])	3.851 (3.851[3])
	kidney	5.027 (5.018[3])	4.919 (4.919[3])

1 total residue for data collection: BYI 02960, DFA, BYI 02960-acetyl-AMCP and BYI 02960-hydroxy

2 total residue for enforcement / risk assessment: BYI 02960 + DFA

3 values above the LOD were considered as measured, for values below the LOD the LOD was taken for calculation

Remark re. two values shown for total residue and transfer factors:

In a first step, all values below the LOQ of 0.01 mg/kg (BYI 02960, BYI 02960-acetyl-AMCP and BYI 02960-OH) or below the LOQ of 0.02 mg/kg (DFA) were considered as being *at* 0.01 or 0.02 mg/kg, respectively, to calculate the total residue.

Values in parentheses: In a second step, all values above the LOD but below the LOQ were considered "as reported", values below the LOD were calculated as being *at* the LOD (values in brackets); see Table 6.4.2-22

IIA 6.4.3 Pigs

No feeding study in pigs is required because metabolic pathways in the rat, in ruminants and in poultry are similar (cf IIA 6.2.4).

IIA 6.4.4 Fish

No feeding study in fish is required due to the low potential for accumulation in fish as indicated by the log P_{OW} of 1.2 in the range of pH 4 – 9 (cf IIA 6.2.5).

IIA 6.5 Effects of industrial processing and/or household preparation on residues

Numerous processing studies have been conducted to support the use of BYI 02960 in various crops. Representative processing studies were conducted with field samples collected from supervised residue trials conducted in Europe, USA, Canada or Brazil.

IIA 6.5.1 The nature of residue

A high temperature hydrolysis was conducted with BYI 02960 to evaluate if breakdown or reaction products arise from the parent compound in the raw agricultural commodities during processing.

No additional high-temperature hydrolyses were conducted for the metabolites DFA or DFEAF, even though DFA and DFEAF are – besides the parent compound – the proposed constituents of the residue definition for risk assessment in plant commodities. DFA is also – apart from parent – the predominant residue in animal matrices and together with parent the proposed constituent of the residue definition for risk assessment in animal matrices. However, due to the chemical structure of the metabolites, no further degradation of the compounds is expected when applying hydrolysis conditions representative of processing.

DFA is a small molecule and the only reasonable degradation reaction is decarboxylation. This thermal decomposition reaction occurs generally in the vapour phase and therefore at temperatures >130°C (temperature above the temperature needed for sterilization). This assumption is supported by the fact that two acids with very similar chemical structures – TFA (= trifluoroacetic acid) and HOAc (= acetic acid) – are stable under the conditions to be tested in processing studies. By interpolation of the properties of TFA and HOAc, it is concluded that DFA is also stable under the conditions relevant for processing, and therefore no additional hydrolysis study is deemed necessary.

The chemical structure of the metabolite DFEAF is a substructure of the parent compound. All functional groups, chemical moieties, and constituents of DFEAF are also present in the chemical structure of the parent compound. Therefore the chemical stability of DFEAF is covered by the study conducted with the parent compound. As parent compound was proved to be stable under the processing conditions (cf. KIIA 6.5.1/01), it is concluded that this is also true for DFEAF. Moreover, residue levels of DFEAF were <0.01 mg/kg in virtually all edible samples collected in field trials, and therefore almost no consumer exposure is expected. Thus, no addiotional hydrolysis study is deemed necessary for the metabolite DFEAF.

Report:	**KIIA 6.5.1/01, [redacted]; 2011**
Title:	Nature of the residues of [pyridinylmethyl-^{14}C]BYI02960 in processed commodities - high temperature hydrolysis
Report No. & Document No.:	MEF-10/856, dated February 9, 2011 M-402311-01-2
Guidelines:	– EU Council Directive 91/414/EEC amended by Commission Directive 96/68/EC Section 6.5, Subsection 6.5.1 – OECD Guideline for the Testing of Chemicals No. 507, Nature of the Pesticide Residues in Processed Commodities - High Temperature Hydrolysis, adopted 2007-10-16
GLP:	yes (certified laboratory)

Executive Summary

The behaviour of BYI 02960 was studied in buffered drinking water under conditions of processing. The radiolabelled test compound [pyridinylmethyl-^{14}C]BYI02960 was used for the hydrolysis investigations.

One concentration (approx. 1.0 mg/L) of the analyte was prepared in sterilized buffered drinking water and incubated under three representative sets of hydrolysis conditions:

Pasteurisation:	90°C at pH 4 for 20 min
Baking, brewing, boiling:	100°C at pH 5 for 60 min
Sterilisation:	120°C at pH 6 for 20 min

At test termination, the material balances in all tests were in the range of 97.3 to 104.9% of the applied radioactivity, indicating that no radioactivity and no volatile degradation products dissipated from the test system.

HPLC profiling of samples before and after processing proved that the test compound BYI 02960 was stable under the test conditions. The test compound amounted to 100.0% in all test solutions before and after hydrolysis. No hydrolysis products were detected above an estimated LOD of 0.5%.

I. Materials and Methods

A. Materials

Table 6.5.1-1 Test material

	Position of radiolabel	Radiochemical purity (%)	Specific Activity (MBq/mg)
BYI 02960	[pyridinylmethyl-^{14}C]	> 99% by HPLC > 99% by TLC	4.37

B. Study Design

Experimental conditions: One sample of the test solution was prepared for each of the three tests. An appropriate amount of the aqueous stock solution was diluted with buffer solution to give a theoretical concentration of approx. 1 mg/L in the test solution. The pH value of all samples was measured and three aliquots of each test solution were subjected to LS-measurement to determine the actual radioactivity in the test solution before starting the treatment. A further aliquot from each sample was taken for chromatographic analysis of the zero-time purity.

The test compound was incubated in buffered drinking water at the following three representative sets of conditions to investigate the effects of hydrolysis as appropriate for the relevant processing operations:

pH	Temperature [°C]	Test period [min]	Process
4 ± 0.1	90 ± 5	20 ± 1	pasteurisation
5 ± 0.1	100 ± 5	60 ± 1	baking, brewing and boiling
6 ± 0.1	120 ± 5	20 ± 1	sterilisation

The tests at 90°C and 100°C were carried out by using a dry block heater. The test at 120°C was performed in an autoclave. For the experiments at 90°C and 100°C, the actual temperature was recorded in a control vial filled with blank buffer solution. For the autoclave experiment at 120°C, the programmed figures were used as temperature data.

After the application procedure, the test vessels were closed with a septum and a crimp top and were subjected to the intended incubation conditions. Samples for hydrolysis were weighed before and after hydrolysis to correct for possible losses by evaporation of water.

Sampling: After termination of each test and cooling to room temperature, the pH value was measured. Three aliquots were again taken from each test solution for the determination of the radioactivity content by Liquid Scintillation Counting (LSC).

C. Analytical Procedure

Processing: The radioactivity content of each test solution was determined by LSC before starting and after termination the hydrolysis. Aliquots of all samples were analysed by HPLC for detection of possible hydrolysis products. All analyses were performed within approx. one day after sampling.

Quantitation: Parent compound was quantified by LSC.

Identification and characterisation: The identity of the test compound was confirmed by LC-MS/MS. In the test solutions, parent compound was identified by HPLC comparison.

II. Results and Discussion

pH, temperatures and test periods: The pH values of the test solutions were adjusted to pH 4, pH 5, and pH 6 (each ± 0.1) and remained as required. The temperatures were in the ranges of 90 ± 5°C, 100 ± 5°C and 120 ± 5°C during the test periods.

Material balance: The applied radioactivity was defined as the amount of radioactivity measured in the samples taken at the beginning of the incubation period. Based on the results of LSC measurements immediately after test termination, a radioactivity balance was established for each experiment.

All material balances were in the range between 97.3 to 104.9%. The material balances demonstrate that no radioactivity dissipated from the test systems.

Test compound and hydrolysis products in test samples: The radiochemical purity of the test compound was checked in the stock solution by HPLC and amounted to 100%. Aliquots of all tests solutions were analysed by HPLC before and after hydrolysis. All analyses were performed within approx. one day after sampling. No hydrolysis products were detected in any sample. The LOD was estimated as being approx. 0.5% of the total radioactivity.

III. Conclusions

The test compound BYI 02960 was stable under all conditions of high temperature hydrolysis for simulation of food processing. The following conditions were tested:

- pH 4 / 90°C (20 min) - pasteurisation
- pH 5 / 100°C (60 min) - baking, brewing, and boiling
- pH 6 / 120°C (20 min) - sterilisation

No hydrolysis products of BYI 02960 were detected above an estimated LOD of 0.5%.

IIA 6.5.2 Distribution of the residue in peel/pulp

The distribution of residues of BYI 02960 between peel and pulp is relevant for crops like citrus fruits and watermelon and has been reported in the context of the residue studies in paragraph IIA 6.3.2.1 and IIA 6.3.1.8, respectively. Generally, the residue levels in the edible portion of the commodity (pulp) were lower than those in the whole fruit.

For crops like apple, tomato and potato the distribution of the residues between peel and pulp/tuber was reported in the context of the processing studies in the respective paragraphs (IIA 6.5.4.4, IIA 6.5.4.8 or IIA 6.5.4.16).

IIA 6.5.3 Residue levels - balance studies on set of representative processes

As the newest OECD guidelines no longer specifically require balance studies, the processing trials on lettuce, hops, orange, apple, peach, grape, sugar beet, tomato, cucumber, barley, wheat, corn, coffee, cotton, peanut, potato, and soybean are presented below under point 6.5.4.

IIA 6.5.4 Residue levels-follow-up studies: concentration or dilution factors

General remarks:

Metabolite naming:

In this summary section (KIIA 6.5.4), the name DFEAF will be used for the metabolite BYI 02960-difluoroethyl-amino-furanone, which is relevant to the tested residue definition:

Name	*Metab. No.*	*Standard "dossier name"*
DFEAF	M34	BYI 02960-difluoroethyl-amino-furanone

References:

In the first edition of this dossier, two reports were presented here, for lettuce and hops, directly under point KIIA 6.5.4. These have now been moved to KIIA 6.5.4.1 and 6.5.4.2, respectively.

IIA 6.5.4.1 Lettuce

Report:	**KIIA 6.5.4.1/01, [redacted] & [redacted]; 2012**
Former Annex pt.	KIIA 6.5.4/01
Title:	Determination of the residues of BYI 02960 in/on lettuce and head lettuce and the processed fractions (head, inner parts; leaf, outer; leaf, inner; leaf, inner, washed and washings) after spraying of BYI 02960 SL 200 in the field in the Netherlands, Belgium and Germany
Report No. & Document No.:	10-3223, dated March 7, 2012 M-426982-01-1
Guidelines:	– EU Council Directive 91/414/EEC amended by Commission Directive 96/68/EC – EU Guidance Working Document 7035/VI/95 rev. 5 – OECD Guideline for the Testing of Chemicals No. 508, Magnitude of the Pesticide Residues in Processed Commodities – EPA Ref: OPPTS 860.1500, Crop Field Trials
GLP:	yes (certified laboratory)

I. Materials and Methods

Due to the presence of measurable residues of BYI 02960 on harvested lettuce determined in samples from field residue trials performed according to the intended commercial use conditions (see point IIA 6.3.1.1) as well as to the nature of lettuce use (preparation and consumption patterns) and the highly variable residue levels commonly seen in this crop, investigations on the effects of basic processing have been conducted. Four trials were conducted in the northern European residue region, in Germany (2), the Netherlands, and Belgium, in order to determine the total residues of BYI 02960 in unprocessed lettuce heads and then in washed and unwashed commodities including external and internal leaves ([redacted] & [redacted], 2012; KIIA 6.5.4.1/01).

The field trials were conducted as part of study 10-2223 (cf. KIIA 6.3.1.1/01 for details). Two of the trials were conducted on open-headed lettuces, two on closed-head varieties. BYI 02960 SL 200 was sprayed twice at an application rate of approx. 0.125 kg a.s./ha and a water volume of 300-500 L/ha. The final application was conducted at a pre-harvest interval of 3 days.

After processing (described below), residue analysis was performed according to method 01304 as used in the RAC trials themselves (for more information, cf. points IIA 6.3.1.1 and IIA 4.3). The limits of quantitation were 0.01 mg/kg (BYI 02960 and DFEAF) and 0.02 mg/kg (DFA), expressed in parent compound equivalents, yielding a calculated total-residue LOQ of 0.04 mg/kg, in all matrices. Prior and parallel to the residue analysis, the method was validated by recovery experiments.

Leaf removal, washing, etc.:
Lettuce "processing" was designed to simulate typical household kitchen practices in the use and preparation of lettuce for salads.

The complete outer layer of leaves were removed from the heads, yielding outer leaves and inner head parts. From the inner head parts, leaves were separated from the stalk (inner leaves), then washed in standing water (washed inner leaves and washing water). The process is illustrated in flow diagram 6.5.4.1-1.

II. Findings

The validation of the sample material lettuce head was done in study 10-2213 (cf. KIIA 6.3.1.1/03 for details), the validation of sample material washings was conducted within the present study. Limited validation sets and concurrent recoveries of BYI 02960 and its metabolites DFA and DFEAF were obtained from samples of lettuce matrices (head; head, inner parts; leaf, outer and washings). The recoveries for the sample material head, inner parts are also representative for the sample materials leaf, inner and leaf, inner, washed. Therefore, no additional recoveries were performed for these two sample materials.

In head samples, concurrent recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg and 0.10 mg/kg, as well as at 0.50 mg/kg, 1.0 mg/kg, and 5.0 mg/kg (expressed in BYI 02960 equivalents); in the washing water, spiking levels were 0.01 mg/kg and 0.50 mg/kg. Mean recoveries for all matrices were 90-107%, with RSDs in the larger validations sets (n > 2) of 2.2-10.7%; n=2-15.

For DFA, concurrent recovery samples for lettuce head were spiked at levels of 0.02, 0.05, and 0.50 mg/kg, as well as at 0.20, 1.0, and 5.0 mg/kg (expressed in BYI 02960 equivalents); fortification levels in the washing water were 0.02 and 0.50 mg/kg. Mean recoveries in all matrices were 90-98%, with RSDs in the larger validations sets (n > 2) of 3.2-10.2%; n=2-12.

Although very similar to lettuce head and thus technically covered by head-sample validation, additional individual concurrent recoveries were also run with samples of inner head parts and of outer leaves. Recovery values were very similar to those seen for head.

A tabular summary of the recovery values is presented below in table 6.5.4.1-3.

The total residues of BYI 02960 (parent compound plus DFA and DFEAF) in the harvested heads at day 3 ranged from 0.40-1.0 mg/kg, as summarized previously (cf. KIIA 6.3.1.1/01). These values were used for the calculation of "processing" factors.

● <u>Outer leaves and inner head parts</u>:
The outer leaves were analyzed separately after their removal; the residue levels were from 0.71-1.8 mg/kg. In the remaining inner head parts, residue levels were considerably lower, at 0.30-0.74 mg/kg.

Based on these values, it is evident that a large proportion of the residues result from surface deposits. The measured residue levels lead to mean "processing" factors of 1.8 for outer leaves and 0.73 for the inner head parts.

● <u>Inner leaves and washed inner leaves</u>:
After separation from the stalks, inner leaves samples prior and subsequent to washing. Residue values ranged from 0.08-0.83 mg/kg and 0.29-0.52 mg/kg in the unwashed and washed inner leaves, respectively. In the intermediate product washing water, they were very low, ranging from <0.04-0.05 mg/kg.

These findings indicate that the remainder of the residues are absorbed to a large extent. Washing does not affect them; indeed, the residues are virtually the same in both washed and unwashed leaves (and also essentially as in the inner head parts above). Based on these values, mean "processing" factors of 0.76 and 0.67 can be calculated from lettuce head to unwashed and washed inner leaves, respectively.

The transfer factors for the total residues of BYI 02960 are summarized below in table 6.5.4.1-1. All trial data are summarised further below in table 6.5.4.1-2a & b and in greater detail in the Tier 1 summary forms.

Table 6.5.4.1-1: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in lettuce RACs and processed products following application of BYI 02960 SL 200

Trial number	lettuce head*	outer leaves	inner head parts	inner leaves	washed inner leaves	washing water
10-3223-01	0.61	1.3 *(2.1)*	0.49 *(0.80)*	0.48 *(0.79)*	0.51 *(0.84)*	<0.04 *(<0.07)*
10-3223-02	0.40	0.71 *(1.8)*	0.30 *(0.75)*	0.46 *(1.2)*	0.29 *(0.73)*	0.05 *(0.13)*
10-3223-04	1.0	1.8 *(1.8)*	0.74 *(0.74)*	0.08 *(0.08)*	0.50 *(0.50)*	0.05 *(0.05)*
10-3223-05	0.87	1.4 *(1.6)*	0.55 *(0.63)*	0.83 *(0.95)*	0.52 *(0.60)*	0.05 *(0.06)*
Mean transfer factors:		*1.8*	*0.73*	*0.76*	*0.67*	*0.07*

* residue levels for "head" samples taken from study 10-2223 (cf. KIIA 6.3.1/01)

"<" the residue in the processed fraction was below LOQ and was set to LOQ for calculating processing factors.

III. Conclusions

In order to determine "processing" factors for total residues of BYI 02960 from lettuce heads to parts thereof, processing studies have been conducted. The mean value of total residue "processing" factors for the outer leaves was 1.8, and 0.73 to the inner head parts. Further washing is of little consequence, with mean "processing" factors for unwashed or washed inner leaves of 0.76 and 0.67, respectively. Typical household preparation steps, e.g. for salad preparation, will result in lower total residues of BYI 02960 than in the RAC itself, as the main portion of the residues is in/on the outer leaves.

Diagram 6.5.4.1-1: Household "processing" of lettuce heads

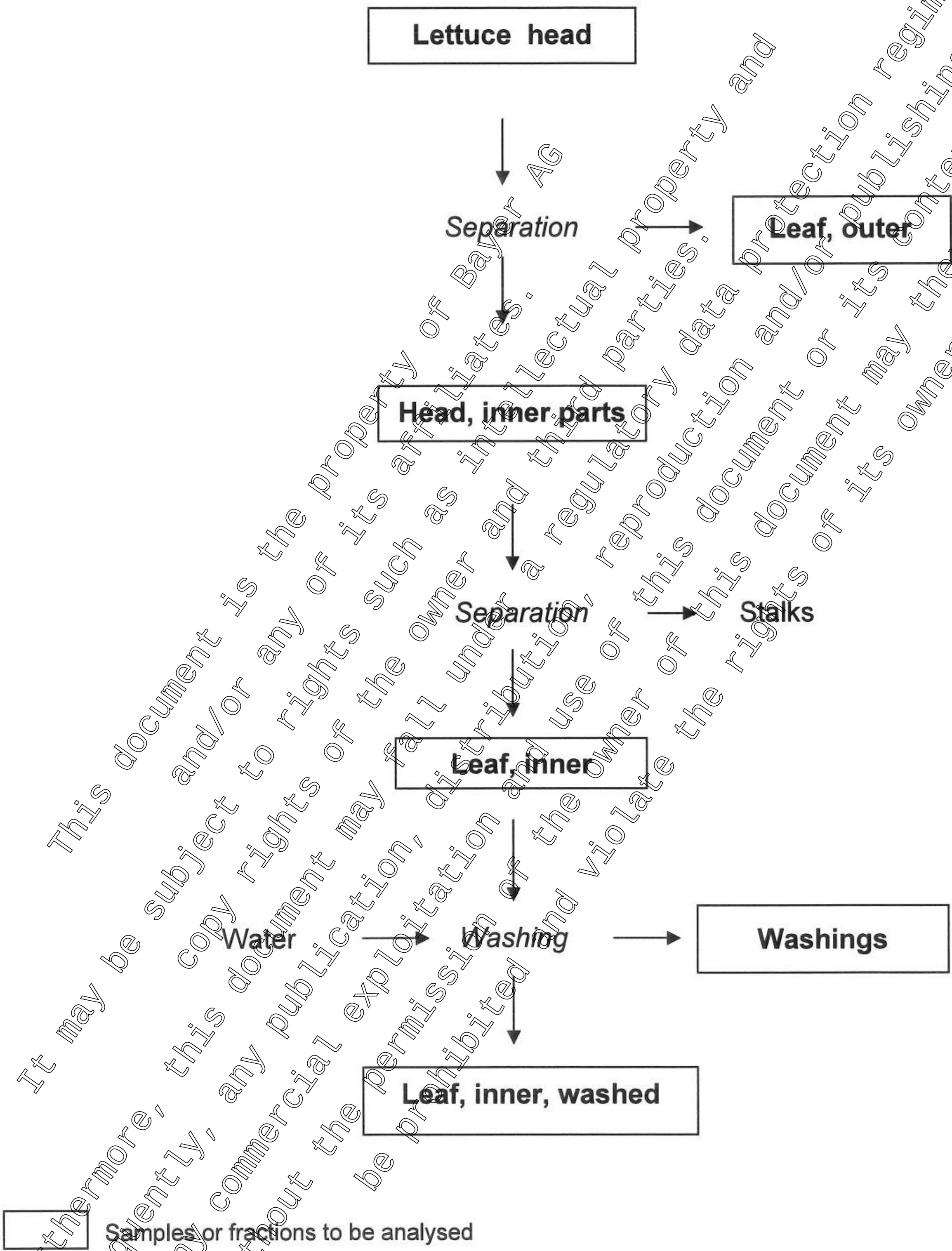


Table 6.5.4.1-2a: Application scenario in residue processing trials conducted in/on **lettuce** after spraying with BYI 02960 SL 200 in European fields*

Study No. **(Trial No.) Country Location Region Year**	**Crop Variety**	**FL**	**Application**			**GS**	**PHI (days)**
			No.	**kg/ha (a.s.)**	**kg/hl (a.s.)**		
10-3223 (10-3223-01) Netherlands [redacted] EU-N 2010	lettuce, head Gisela, Butterhead variety	200 SL	2	0.125	0.0417	48	3
10-3223 (10-3223-02) Belgium [redacted] EU-N 2010	lettuce, head Lucan, Butterhead variety	200 SL	2	0.125	0.0250	48	3
10-3223 (10-3223-04) Germany [redacted] EU-N 2010	lettuce Cavernet Lollo rosso, Loose leaf variety	200 SL	2	0.125	0.0417	48	3
10-3223 (10-3223-05) Germany [redacted] EU-N 2010	lettuce Chloe Lollo rosso, Loose leaf variety	200 SL	2	0.125	0.0313	48	3

FL=formulation GS=growth stage (BBCH-code) at last treatment
EU-N=northern European residue region

* The field part of these trials was conducted in study 10-2223

Table 6.5.4.1-2b: Results of residue processing trials conducted in/on **lettuce** after spraying with BYI 02960 SL 200 in European fields

Study No. **(Trial No.) Country** **GLP**	**Portion analyzed**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
			BYI 02960	**DFA**	**BYI 02960-DFEAF**	**total residue of BYI 02960 calc.**
10-3223 (10-3223-01) Netherlands GLP: yes	head	3	0.58	<0.02	<0.01	0.61
	head, inner parts	3	0.46	0.02	<0.01	0.49
	leaf, outer	3	1.3	0.02	0.02	1.3
	leaf, inner	3	0.45	0.02	<0.01	0.48
	leaf, inner, washed	3	0.48	<0.02	<0.01	0.51
	washings	3	<0.01	<0.02	<0.01	<0.04
10-3223 (10-3223-02) Belgium GLP: yes	head	3	0.37	<0.02	<0.01	0.40
	head, inner parts	3	0.27	<0.02	<0.01	0.30
	leaf, outer	3	0.68	<0.02	0.01	0.71
	leaf, inner	3	0.43	<0.02	<0.01	0.46
	leaf, inner, washed	3	0.26	<0.02	<0.01	0.29
	washings	3	0.02	<0.02	<0.01	0.05
10-3223 (10-3223-04) Germany GLP: yes	head	3	1.0	<0.02	0.01	1.0
	head, inner parts	3	0.71	<0.02	<0.01	0.74
	leaf, outer	3	1.8	0.02	0.01	1.8
	leaf, inner	3	0.05	<0.02	<0.01	0.08
	leaf, inner, washed	3	0.47	<0.02	<0.01	0.50
	washings	3	0.02	<0.02	<0.01	0.05
10-3223 (10-3223-05) Germany GLP: yes	head	3	0.83	<0.02	0.01	0.87
	head, inner parts	3	0.52	<0.02	<0.01	0.55
	leaf, outer	3	1.3	0.02	0.01	1.4
	leaf, inner	3	0.80	<0.02	0.01	0.83
	leaf, inner, washed	3	0.49	<0.02	<0.01	0.52
	washings	3	0.02	<0.02	<0.01	0.05

DALT=days after last treatment

Table 6.5.4.1-3: Recovery data for BYI 02960 in **lettuce** and **lettuce matrices**

Study No. **Trial No. GLP Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortification level (mg/kg)**	**Recovery (%) Individual recoveries**	**Min**	**Max**	**Mean**	**RSD**
10-3223 10-3223-01, 10-3223-02, 10-3223-04 and 10-3223-05 GLP: yes 2010	lettuce, head	head	BYI 02960	15	0.01	79; 87; 102; 106; 107; 109; 110; 116; 92; 97; 107; 108; 114; 116; 117	79	117	104	10.7
				5	0.10	88; 90;90; 92; 93	88	93	91	2.2
				2	0.50	103; 106	103	106	105	
				2	1.0	92; 94	92	94	93	
				2	5.0	90; 98	90	98	94	
				26	overall		79	117	100	10.5
			DFA	12	0.02	90; 93; 94; 95; 97; 112; 112; 116; 86; 89; 93; 95	86	116	98	10.2
				3	0.05	90; 94; 98	90	98	94	4.3
				2	0.20	92; 94	92	94	93	
				5	0.50	93; 101; 90; 91; 92	90	101	93	4.7
				2	1.0	90; 92	90	92	91	
				2	5.0	90; 89	89	90	90	
				26	overall		86	116	95	7.9
			BYI 02960-DFEAF	15	0.01	87; 93; 95; 100; 100;104; 105; 107; 83; 83; 86; 88; 90; 92; 96	83	107	94	8.4
				5	0.10	85; 98; 97; 97; 99	85	99	95	6.1
				2	0.50	97; 109	97	109	103	
				2	1.0	86; 101	86	101	94	
				2	5.0	97; 96	96	97	97	
				26	overall		83	109	95	7.7
		head, inner parts	BYI 02960	1	0.01	114	114	114		
				1	overall		114	114		
			DFA	1	0.02	93	93	93		
				1	overall		93	93		
			BYI 02960-DFEAF	1	0.01	93	93	93		
				1	overall		93	93		

Remark re. *head, inner parts*: also covers *leaf, inner parts* and *leaf, inner washed*

Continued on next page…

Table 6.5.4.1-3 (cont'd): Recovery data for BYI 02960 in **lettuce** and **lettuce matrices**

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortifi-cation level** (mg/kg)	**Recovery (%)**				
						Individual recoveries	**Min**	**Max**	**Mean**	**RSD**
10-3223 10-3223-01, 10-3223-02, 10-3223-04 and 10-3223-05 GLP: yes 2010 (cont.)	lettuce, head	leaf, outer	BYI 02960	1	0.01	115	115	115		
				1	10	94	94	94		
				2	overall		94	115	105	
			DFA	1	0.02	94	94	94		
				1	10	90	90	90		
				2	overall		90	94	92	
			BYI 02960-DFEAF	1	0.01	90	90	90		
				1	10	95	95	95		
				2	overall		90	95	93	
		washings	BYI 02960	5	0.01	99; 102; 106; 109; 117	99	117	107	6.5
				3	0.50	95; 97; 111	95	111	101	8.6
				8	overall		95	117	105	7.3
			DFA	5	0.02	95; 96; 97; 97; 103	95	103	98	3.2
				3	0.50	91; 94; 97	91	97	94	3.2
				8	overall		91	103	96	3.5
			BYI 02960-DFEAF	5	0.01	95; 99; 100; 100; 107	95	107	100	4.3
				3	0.50	86; 88; 96	86	96	90	5.9
				8	overall		86	107	96	7.1

IIA 6.5.4.2 Hops

Report:	**KIIA 6.5.4.2/01, [redacted] & [redacted]; 2012**
Former Annex pt.:	KIIA 6.5.4/02
Title:	Determination of the residues of BYI 02960 in/on hop (cone, green and cone, kiln-dried) and the processed fractions (hops draff, brewer's yeast and beer) after spraying of BYI 02960 SL 200 in the field in Germany
Report No. & Document No.:	10-3407, dated February 13, 2012 M-425311-01-1
Guidelines:	– EU Council Directive 91/414/EEC amended by Commission Directive 96/68/EC – EU Guidance Working Document 7035/VI/95 rev. 5 – OECD Guideline for the Testing of Chemicals No. 508, Magnitude of the Pesticide Residues in Processed Commodities
GLP:	yes (certified laboratory)

I. Materials and Methods

In view of the presence of measurable residues of BYI 02960 on harvested hop cones determined in samples from field residue trials performed according to the intended commercial use conditions (see point IIA 6.3.2), investigations on the effects of processing have been conducted. Two trials were conducted in Germany in order to determine the total residues of BYI 02960 in green and dried hop cones and then, after processing, in beer as well as the additional processing intermediates hops draff and brewer's yeast ([redacted] & [redacted], 2012; KIIA 6.5.4.2/01).

The field trials were conducted at approx. 2½ times the normal application rate for hops, in an attempt to ensure that quantifiable residues will be present in the RAC samples. BYI 02960 SL 200 was sprayed once at an application rate of approx. 360 g a.s./ha and a water volume of 3000 L/ha. The application was conducted at a pre-harvest interval of 21 days.

After processing (described below), residue analysis was performed according to method 01304 (for more information, cf. KIIA 4.3). The limits of quantitation were 0.1 mg/kg (BYI 02960 and DFEAF) and 0.2 mg/kg (DFA), expressed in parent compound equivalents, yielding a calculated total-residue LOQ of 0.4 mg/kg, in all matrices except beer, in which the LOQs were 10 times lower (0.01 and 0.02 mg/kg; total residue: 0.04 mg/kg). Prior and parallel to the residue analysis, the method was validated by recovery experiments.

<u>Preparation of beer:</u>
Beer processing simulated industrial brewing practices. Prior to the addition of hops to the wort, ground malted barley and water were mixed in a mash tun ("mashing"), then the wort was separated from the insoluble malt components ("lautering").

Green hop cones were dried in hop driers, according to standard industrial procedures, then ground and pelletted. Hop pellets were added to the wort, which was then boiled. Subsequently, the flocs were separated via a whirlpool in which the sludge (hops draff) deposited at the bottom of the cone-shaped vessel. After addition of yeast, the mixture was allowed to ferment in bottom-fermentation containers ("primary fermentation", temp. 9°C). As soon as the extract content of the young beer was sufficient, storing began. Before maturation, however, the young beer was cooled.

During the main fermentation, the yeast deposits on the bottom of the tank; this material is sampled (brewer's yeast). The beer is stored under pressure at approx. 2°C for 3-4 weeks. All further sludge-like materials settle to the bottom. The matured liquid is filtered and then the final product, beer, is sampled. The process is illustrated in flow diagram 6.5.4-2.

II. Findings

The validation of the sample material cone, green and cone-kiln-dried was done in the conduct of study 10-2225 (cf. KIIA 6.3.1.2/01 for details) and the present study (10-3407). The validation of hops draff, brewer's yeast and beer was done within the present study 10-3407. Concurrent recoveries were obtained from samples of cone, green; cone kiln-dried, hops draff, brewer's yeast, and beer.

In all matrices except for beer, recovery samples for parent compound and DFEAF were spiked at levels of 0.10 mg/kg and 1.0 mg/kg, as well as 5.0 mg/kg for hop cones (expressed in BYI 02960 equivalents); in beer, spiking levels were 0.01 and 0.10 mg/kg. Mean recoveries in the larger validations sets (n > 2) for all matrices were 81-111%, with RSDs of 1.4-13.9%; n = 3-6. Even in the case of values over 110%, these values were considered to be acceptable because they were only marginally higher and the RSD values were very low; also, in the cases of the exceptions, the overall means of all recovery analyses for the given matrices with each individual analyte were 107-108%, with overall RSDs of 4.2-7.1%.

For DFA, concurrent recovery samples for all matrices except beer were spiked at levels of 0.20 mg/kg and 1.0 mg/kg, as well as 5.0 mg/kg for hop cones (expressed in BYI 02960 equivalents); fortification levels in beer were 0.02 and 0.20 mg/kg. Mean recoveries in the larger validations sets (n > 2) in all matrices were 83-109%, with RSDs of 2.6-14.1%; n = 3-6. All values were within acceptable ranges.

A tabular summary of the recovery values is presented below in table 6.5.4.2-3.

● Beer:
The total residues of BYI 02960 (parent compound plus DFA and DFEAF) in the harvested green cones at day 21 were 0.73 and 1.5 mg/kg. After drying, the values were 3.0 and 5.0 mg/kg. As the dried cone is generally considered to be the "RAC" in the case of hops, all processing factors are based on the residues in the dried commodity.

Residue values in beer were 0.04 and 0.05 mg/kg. Based on these values, a mean transfer factor of 0.01 to beer can be calculated from dried hop cones (0.04 from green cones). Residue levels in all sampled intermediate products (hops draff and brewer's yeast) were below the LOQ of 0.4 mg/kg.

The transfer factors for the total residues of BYI 02960 are summarized below in table 6.5.4.2-3. All trial data are summarised further below in table 6.5.4.2-2a&b and in greater detail in the Tier 1 summary forms.

Table 6.5.4.2-1: Summary of total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in hop RACs and processed products following application of BYI 02960 SL 200

Trial number	green cone	dried cone (RAC)	hops draff	brewer's yeast	beer
10-3407-01	0.73	3.0	<0.4 *(<0.13)*	<0.4 *(<0.13)*	0.04 *(0.01)*
10-3407-02	1.5	5.0	<0.4 *(<0.08)*	<0.4 *(<0.08)*	0.05 *(0.01)*
Mean transfer factors:			*<0.1*	*<0.1*	*0.01*

"<" the residue in the processed fraction was below LOQ and was set to LOQ for calculating processing factors.

III. Conclusions

In order to determine transfer factors for total residues of BYI 02960 from hops (dried cones) to beer, processing studies have been conducted.

The mean value of total residue transfer factors for beer was 0.01. In the intermediates, the average processing factor was <0.1. Thus, for the total residues of BYI 02960, processing to beer will not result in any concentration of the residues.

Diagram 6.5.4.2-1: Processing of hop cones to beer

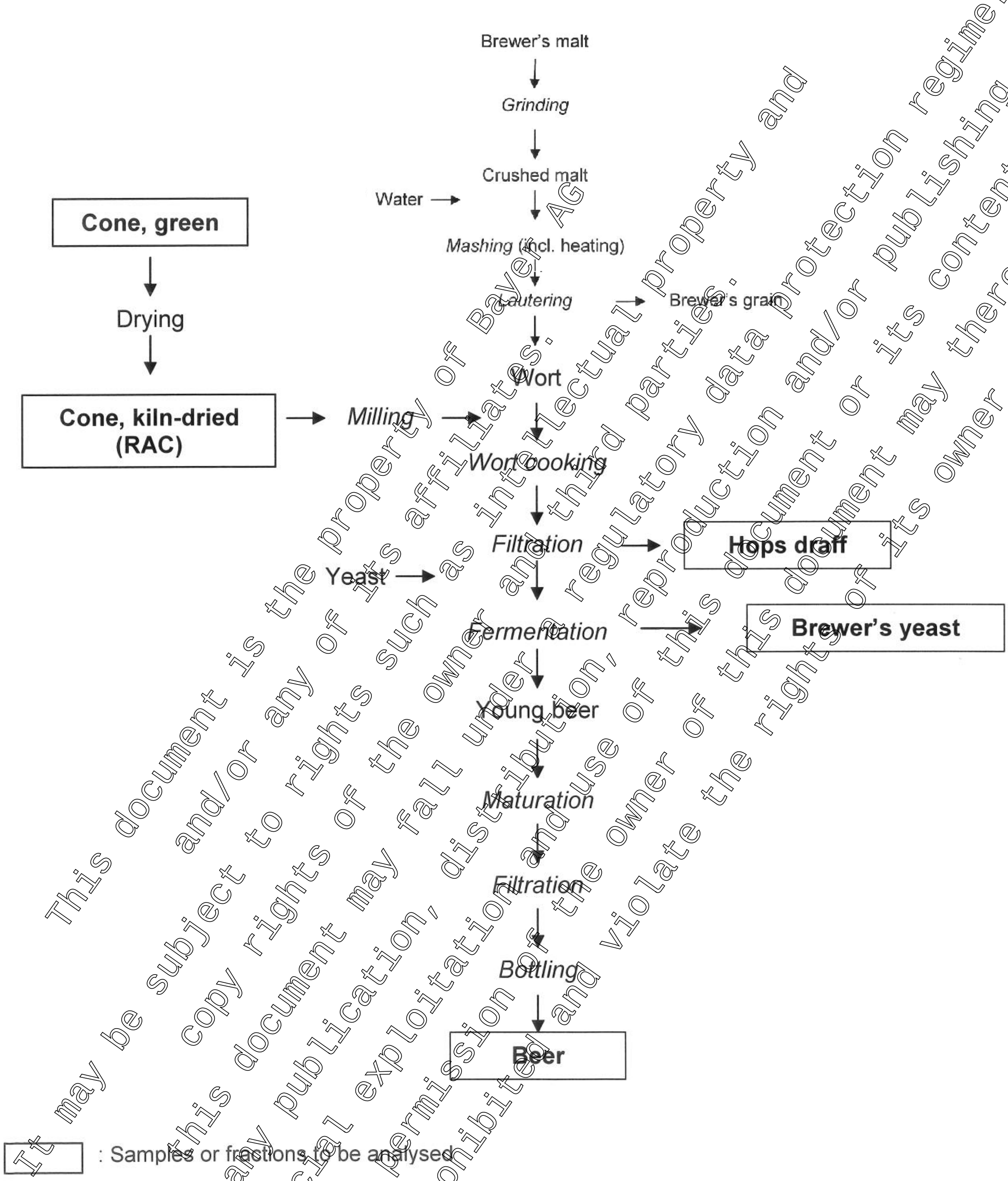


Table 6.5.4.2-2a: Application scenario in residue processing trials conducted in/on **hops** after spraying with BYI 02960 SL 200 in European fields

Study No. **(Trial No.) Country Location Region Year**	**Crop Variety**	**FL**	**Application**			**GS**	**PHI (days)**
			No.	**kg/ha (a.s.)**	**kg/hl**		
10-3407 (10-3407-01) Germany [redacted] EU-N 2010	hop Nugget	200 SL	1	0.36	0.012	71	21
10-3407 (10-3407-02) Germany [redacted] EU-N 2010	hop Nordischer Brauer	200 SL	1	0.36	0.012	75	21

FL=formulation GS=growth stage (BBCH-code) at last treatment
EU-N=northern European residue region

Table 6.5.4.2-2b: Results of residue processing trials conducted in/on **hops** after spraying with BYI 02960 SL 200 in European fields

Study No. **(Trial No.) Country GLP**	**Portion analyzed**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
			BYI 02960	**DFA**	**BYI 02960-DFEAF**	**total residue of BYI 02960 calc.**
10-3407 (10-3407-01) Germany GLP: yes	cone, green	21	0.43	<0.2	<0.1	0.73
	cone, kiln-dried	21	2.2	0.72	<0.1	3.0
	hops draff	21	<0.1	<0.2	<0.1	<0.4
	brewer's yeast	21	<0.1	<0.2	<0.1	<0.4
	beer	21	0.01	<0.02	<0.01	0.04
10-3407 (10-3407-02) Germany GLP: yes	cone, green	21	1.1	0.37	<0.1	1.5
	cone, kiln-dried	21	4.2	0.76	<0.1	5.0
	hops draff	21	<0.1	<0.2	<0.1	<0.4
	brewer's yeast	21	<0.1	<0.2	<0.1	<0.4
	beer	21	0.02	<0.02	<0.01	0.05

DALT=days after last treatment

Table 6.5.4.2-3: Recovery data for BYI 02960 in **hops** and **processed hop matrices**

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortifi-cation level** (mg/kg)	**Recovery (%)** **Individual recoveries**	**Min**	**Max**	**Mean**	**RSD**
10-3407 (10-3407-01) and (10-3407-02) GLP: yes 2010	hop	cone, green	BYI 02960	6	0.10	89; 89; 91; 94; 95; 107	89	107	94	7.2
				5	1.0	85; 86; 87; 92; 98	85	98	90	6.0
				1	5.0	87	87	87		
				12	overall		85	107	92	6.8
			DFA	6	0.20	91; 92; 95; 99; 100; 115	91	115	99	8.9
				5	1.0	76; 79; 83; 84; 94	76	94	83	8.2
				1	5.0	86	86	86		
				12	overall		76	115	91	11.7
			BYI 02960-DFEAF	6	0.10	68; 73; 79; 85; 95; 96	68	96	83	13.9
				5	1.0	76; 77; 78; 84; 91	76	91	81	7.8
				1	5.0	80	80	80		
				12	overall		68	96	82	10.6
		cone, kiln-dried	BYI 02960	6	0.10	102; 103; 103; 104; 105; 106	102	106	104	1.4
				5	1.0	107; 108; 111; 114; 115	107	115	111	3.2
				1	5.0	112	112	112		
				12	overall		102	115	108	4.2
			DFA	6	0.20	82; 96; 97; 103; 103; 106	82	106	98	8.9
				5	1.0	101; 105; 106; 107; 110	101	110	106	3.1
				1	5.0	98	98	98		
				12	overall		82	110	101	7.3
			BYI 02960-DFEAF	6	0.10	89; 100; 106; 107; 107; 108	89	108	103	7.2
				5	1.0	108; 109; 110; 112; 114	108	114	111	2.2
				1	5.0	112	112	112		
				12	overall		89	114	107	6.2

Continued on next page…

Table 6.5.4.2-3 (cont'd): Recovery data for BYI 02960 in **hops** and **processed hop matrices**

Study No. Trial No. GLP Year	Crop	Portion analyzed	a.s./ metabolite	n	Fortification level (mg/kg)	Recovery (%) Individual recoveries	Min	Max	Mean	RSD
10-3407 (10-3407-01) and (10-3407-02) GLP: yes 2010	hop	hops draff	BYI 02960	5	0.10	84; 94; 96; 105; 108	84	108	97	9.8
				3	1.0	101; 102; 105	101	105	103	2.0
				8	overall		84	108	99	7.8
			DFA	5	0.20	98; 99; 108; 109; 111	98	111	105	5.8
				3	1.0	97; 101; 102	97	102	100	2.6
				8	overall		97	111	103	5.3
			BYI 02960-DFEAF	5	0.10	103; 105; 105; 105; 109	103	109	105	2.1
				3	1.0	100; 104; 107	100	107	104	3.4
				8	overall		100	109	105	2.5
		brewer's yeast	BYI 02960	5	0.10	98; 109; 111; 111; 113	98	113	108	5.5
				3	1.0	77;99;102	77	102	93	14.7
				8	overall		77	113	103	11.5
			DFA	5	0.20	99; 107; 109; 115; 116	99	116	109	6.3
				3	1.0	76; 90; 101	76	101	89	14.1
				8	overall		76	116	102	13.2
			BYI 02960-DFEAF	5	0.10	97; 107; 107; 110; 111	97	111	106	5.2
				3	1.0	85; 99; 109	85	109	98	12.3
				8	overall		85	111	103	8.6
		beer	BYI 02960	5	0.01	95; 100; 110; 114; 115	95	115	107	8.3
				3	0.10	105; 112; 116	105	116	111	5.0
				8	overall		95	116	108	7.1
			DFA	5	0.02	93; 100; 110; 110; 113	93	113	105	8.0
				3	0.20	108; 108; 110	108	110	109	1.1
				8	overall		93	113	107	6.2
			BYI 02960-DFEAF	5	0.01	92; 94; 102; 111; 115	92	115	103	9.9
				3	0.10	102; 107; 112	102	112	107	4.7
				8	overall		92	115	104	8.0

IIA 6.5.4.3 Orange

➢ **EU processing study**

Report:	**KIIA 6.5.4.3/01, [redacted], [redacted], [redacted], & [redacted]; 2012**
Title:	Determination of the residues of BYI 02960 in/on orange (fruit and pulp) and the processed fractions (fruit, stored; whole fruit, washed; washings; raw juice; pomace, wet; pomace, dried; juice; marmalade; pulp; peel; peel washed; peel without oil; oil) after spraying of BYI 02960 SL 200 in the field in Spain
Report No. & Document No.:	10-3405, dated October 1, 2012 M-439410-01-2
Guidelines:	– EU Council Directive 91/414/EEC – EC Guidance working document 7029/VI/95 rev.5 – EU Guidance Working Document 7035/VI/95 rev. 5 – OECD Guideline for the Testing of Chemicals No. 508, Magnitude of the Pesticide Residues in Processed Commodities – EPA Ref. OPPTS 860.1520.SUPP
GLP:	yes (certified laboratory)

I. Materials and Methods

Due to the presence of measurable residues of BYI 02960 on harvested oranges determined in samples from field residue trials performed according to the intended commercial use conditions as well as to the nature of orange use (preparation and consumption patterns) investigations on the effects of industrial processing have been conducted. Two trials were conducted in the southern European residue region, both in Spain, in order to determine the total residues of BYI 02960 in unprocessed oranges and then in the primary processed commodities juice, marmalade, and oil, as well as in intermediate fractions ([redacted], [redacted], [redacted] & [redacted], 2012; KIIA 6.5.4.3/01).

In field trials, BYI 02960 SL 200 was sprayed once at an application rate of approx. 125-144 g a.s./(ha×m) and a water volume of 333-385 L/ha on trees with a maximum foliage height of 3 m. The application was conducted at a pre-harvest interval of 29 days. Although the trial was originally scheduled as a 3× overdose, the actualy application scenario does not reflect this since, by mistake, no adjustment of the application rate was made for the crown height of the trees. As residues were detected in relevant raw commodities, this deviation did not affect the quality of the study.

Orange fruits to be processed were sampled 29 days after the last treatment (DALT 29) at BBCH growth stage 89.

After processing (described below), residue analysis was performed according to method 01304 (for more information, cf. point IIA 4.3). The limits of quantitation were 0.01 mg/kg (BYI 02960 and DFEAF) and 0.02 mg/kg (DFA), expressed in parent compound equivalents, yielding a calculated total-residue LOQ of 0.04 mg/kg, in all matrices. Prior and parallel to the residue analysis, the method was validated by recovery experiments.

Processing procedures:
Orange "processing" was designed to simulate industrial procedures oranges into juice, marmalade and orange oil.

Before start of processing, specimens of stored fruit were taken in all of the three processes (6 days for marmalade production; 7-8 days for juice production, and 6-13 days for oil production). In all of the three processing procedures, orange fruit was washed manually in tap water for three minutes. The ratio water to fruit was approximately 1:1 (the water covered the fruits). After washing, the specimens of *whole fruit, washed* and *washings* were taken.

Some orange fruits were separated into peel and pulp without washing for the preparation of the specimen peel (unwashed).

Juice preparation*:*
Washed orange fruits of each trial were cut in halves and squeezed with a citrus fruit squeezer. The citrus fruit squeezer separated the fruit into raw juice, remaining pulp (without peel) and orange peel by a rotating cone and an integrated sieve.

The raw juice was pasteurized for 2 min at 80-92°C. Specimens of *raw juice* were taken before pasteurisation and specimens of *juice* after pasteurisation.

The remaining orange peel was cut into small pieces to produce (together with the remaining pulp) wet pomace. Specimens of *wet pomace* were taken. The wet pomace was dried in drying cupboards at 63-65°C until the moisture content was ≤10%. Subsequently, *dried pomace* was sampled.

Marmalade production:
Washed orange fruit was peeled by hand using a knife. Peel and peeled oranges were cut into smaller pieces. Sugar, glucose syrup, and citric acid were added to the mixture of approx. 85% peeled fruit (pulp) and 15% peel. Afterwards, the mixture was heated until boiling and cooked for a further 3 min. After addition of a 5% pectin solution, the intermediate was cooked further until a dry matter content of 60-62% was reached. The pH ranged between 2.5 and 2.6. After cooling down, the final product specimens of *marmalade* were taken.

Oil production:
Washed orange fruit was separated into peel and pulp. Specimens of *washed peel* and *pulp* were taken. Subsequently, the separated peel was used for the oil production in a steam distillation plant.

The peel was put in a special vessel with an inside stirrer. A direct steam jet was transferred through the bulk goods. This process resulted in a steam mixture which was cooled down, condensed in a cooler, and sampled in a collecting vessel. After self-separation of the oil-containing phase and the water-containing phase, the water was removed. The oil-containing phase was concentrated in a centrifuge. *Orange oil* and *peel without oil* were sampled. The processes are illustrated in flow diagrams 6.5.4.3-1–6.5.4.3-3.

II. Findings

The validation of the sample materials orange juice, marmalade, peel, and oil was conducted within this study. A set of validation recoveries for the sample material orange fruit was performed in the original validations of method 01304 as well as in study 10-2215 (to be submitted later; available on request).

Concurrent recoveries were obtained from samples of orange matrices (orange fruit, juice, marmalade, oil, peel, wet pomace, and washings). The recoveries for the sample material *fruit* are also representative for *whole fruit, washed*; *pulp*; and *stored fruit*; The sample material *juice* is also representative for *raw juice* and *washings*. The sample material *peel* is also representative for *peel, washed*; *peel without oil*; *pomace, wet*; and *pomace, dry*.

In all mentioned matrices, concurrent recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg, as well as at 0.50 mg/kg (expressed in BYI 02960 equivalents), with the exception of wet pomace and washings, which were only spiked at a level of 0.01 mg/kg. Orange fruit was additionally spiked at a level of 0.50 mg/kg, and peel additionally at a level of 1.0 mg/kg. Mean recoveries for all matrices were 81-111%, with RSDs in the larger validations sets (n > 2) of 0.9-11.8%; n=1-6.

For DFA, concurrent recovery samples for orange matrices (orange fruit, juice, marmalade, oil, peel, wet pomace, and washings) were spiked at levels of 0.02 mg/kg as well as at 0.50 mg/kg (expressed in BYI 02960 equivalents), with the exception of wet pomace and washings, which were only spiked at a level of 0.02 mg/kg. Orange fruit was additionally spiked at a level of 0.20 mg/kg and peel additionally at a level of 1.0 mg/kg. Mean recoveries for all matrices were 72-103%, with RSDs in the larger validations sets (n > 2) of 1.1-4.0%; n=1-6.

A tabular summary of the recovery values is presented below in table 6.5.4.3-5.

The total residues of BYI 02960 (parent compound plus DFA and DFEAF) in the harvested oranges fruit at day 29 ranged from 0.15-0.26 mg/kg. These values were used for the calculation of "processing" factors.

● <u>Juice production</u>:

<u>Stored fruit</u>: The levels of the total residue of BYI 02960 in stored were from 0.07-0.22 mg/kg. The measured residue levels led to a mean "processing" factor of 0.65 (range: 0.5-0.8, n=2), showing a reduction of the residue level of the total residue of BYI 02960 during storage (7-8 days).

<u>Washed whole fruit</u>: The levels of the total residue of BYI 02960 in washed whole fruit were from 0.21-0.22mg/kg. The measured residue levels led to a mean "processing" factor of 1.15 (range: 0.8-1.5, n=2), showing no effect of washing on the residue level of the total residue of BYI 02960 in/on orange fruit.

Washings: In washings, the levels of the total residue of BYI 02960 were <0.04 mg/kg in both processed specimens. The measured residue levels led to a mean "processing" factor of <0.25 (range: <0.2-<0.3, n=2), showing no effect of washing on the residue level of the total residue of BYI 02960 of orange fruit.

Wet pomace: In wet pomace, the levels of the total residue of BYI 02960 were 0.19-0.35 mg/kg. The measured residue levels led to a mean "processing" factor of 1.3 (range: 1.3, n=2), showing an accumulation of the total residues of BYI 02960 in wet pomace during juice production.

Dried pomace: In dried pomace, the levels of the total residue of BYI 02960 were 0.73-1.0 mg/kg. The measured residue levels led to a mean "processing" factor of 4.35 (range: 3.8-4.9, n=2), showing an increase in levels of the total residue of BYI 02960 during the process of drying.

Raw juice: In raw juice, the levels of the total residue of BYI 02960 were <0.04 mg/kg in both processed specimens. The measured residue levels led to a mean "processing" factor of <0.25 (range: <0.2-<0.3, n=2), showing a reduction of the residue level of the total residue of BYI 02960 as a result of the removal of wet pomace.

Juice: In juice, the levels of the total residue of BYI 02960 were <0.04 mg/kg in both processed specimens. The measured residue levels led to a mean "processing" factor of <0.25 (range: <0.2-<0.3, n=2), showing a reduction of the residue level of the total residue of BYI 02960 as a result of the removal of wet pomace. As the residues in raw juice were <0.04 mg/kg, it was not visible if pasteurisation additionally effects the reduction of total residues of BYI 02960.

● Marmalade production:

Stored fruit: In stored fruit taken in before the processing of marmalade, the levels of the total residue of BYI 02960 were 0.14-0.16 mg/kg. The measured residue levels led to a mean "processing" factor of 0.75 (range: 0.6-0.9, n=2), showing a reduction of the residue level of the total residue of BYI 02960 during storage (6 days).

Marmalade: In marmalade, the levels of the total residue of BYI 02960 were 0.04-0.05 mg/kg. The measured residue levels led to a mean "processing" factor of 0.25 (range: 0.2-0.3, n=2), showing a clear reduction of the residue level of the total residue of BYI 02960 during marmalade production.

● Oil production:

Stored fruit: The levels of the total residue of BYI 02960 in stored fruit taken before orange oil production were from 0.11-0.16 mg/kg. The measured residue levels led to a mean "processing" factor of 0.65 (range: 0.6-0.7, n=2), showing a reduction of the residue level of the total residue of BYI 02960 during storage (6-13 days).

Pulp: The levels of the total residue of BYI 02960 in orange pulp were from <0.04-0.06 mg/kg. The measured residue levels led to a mean "processing" factor of <0.25 (range: 0.2-<0.3, n=2).

Peel: The levels of the total residue of BYI 02960 in orange peel were from 0.24-0.52 mg/kg. The measured residue levels led to a mean "processing" factor of 1.8 (range: 1.6-2.0, n=2).

The residue results of the total residue of BYI 02960 for orange pulp and peel clearly show that the main residues are located in/on the orange peel.

Washed peel: The levels of the total residue of BYI 02960 in washed peel were from 0.31-0.67 mg/kg. The measured residue levels led to a mean "processing" factor of 2.35 (range: 2.1-2.6, n=2). The residue results of the total residue of BYI 02960 for washed peel show that washing does not reduce the residues in/on orange peel, but might indicate an increase in residues, possibly due to elimination of water-soluble fractions of the peel.

Peel without oil: The levels of the total residue of BYI 02960 in peel without oil were from 0.57-0.72 mg/kg. The measured residue levels lead to a mean "processing" factor of 3.3 (range: 2.8-3.8, n=2). The residue results of the total residue of BYI 02960 for peel without oil show that oil removal does not lead to a reduction of the residues in/on orange peel, but leads to a concentration of residues in peel without oil.

Both transfer factors for washed peel as well as peel without oil indicate an increase in total residues of BYI 02960. The findings show that residues are not extractable by water or steam extraction.

Oil: The levels of the total residue of BYI 02960 in oil were <0.04 mg/kg in both samples. The measured residue levels lead to a mean "processing" factor of <0.25 (range: <0.2-<0.3, n=2). These findings indicate that, in oil produced by steam extraction, there are no relevant residues present of the total residue of BYI 02960.

The transfer factors for the total residues of BYI 02960 are summarized below in table 6.5.4.3-1 to 6.5.4.3-3. All trial data are summarised further below in table 6.5.4.3-4a & b and in greater detail in the Tier 1 summary forms.

Table 6.5.4.3-1: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in orange RACs and processed products (**processing into juice of oranges**) following application of BYI 02960 SL 200

Trial number	orange	stored fruit	washed fruit	washings	wet pomace	dried pomace	raw juice	juice
10-3405-01	0.26	0.22 *(0.8)*	0.21 *(0.8)*	<0.04 *(<0.2)*	0.35 *(1.3)*	1.0 *(3.8)*	<0.04 *(<0.2)*	<0.04 *(<0.2)*
10-3405-02	0.15	0.07 *(0.5)*	0.22 *(1.5)*	<0.04 *(<0.2)*	0.19 *(1.3)*	0.73 *(4.9)*	<0.04 *(<0.3)*	<0.04 *(<0.3)*
Mean transfer factors:		*0.65*	*1.15*	*<0.2*	*1.3*	*4.35*	*<0.25*	*<0.25*

"<": the residue in the processed fraction was below LOQ and was set to LOQ for calculating processing factors.

Table 6.5.4.3-2: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in orange RACs and processed products (**processing into marmalade**) following application of BYI 02960 SL 200

Trial number	orange	stored fruit	marmalade
10-3405-01	0.26	0.16 *(0.6)*	0.05 *(0.2)*
10-3405-02	0.15	0.07 *(0.9)*	0.04 *(0.3)*
Mean transfer factors:		*0.75*	*0.25*

"<" the residue in the processed fraction was below LOQ and was set to LOQ for calculating processing factors.

Table 6.5.4.3.3: Summary of the total residues of BYI 02960 in mg/kg and transfer factors (in italics and parentheses) in orange RACs and processed products (**processing into oil**) following application of BYI 02960 SL 200

Trial number	orange	stored fruit	pulp	peel	washed peel	peel without oil	oil
10-3405-01	0.26	0.16 *(0.6)*	0.06 *(0.2)*	0.52 *(2.0)*	0.67 *(2.6)*	0.72 *(2.8)*	<0.04 *(<0.2)*
10-3405-02	0.15	0.11 *(0.7)*	<0.04 *(<0.3)*	0.24 *(1.6)*	0.31 *(2.1)*	0.57 *(3.8)*	<0.04 *(<0.3)*
Mean transfer factors:		*0.65*	*<0.25*	*1.8*	*2.35*	*3.3*	*<0.25*

"<" the residue in the processed fraction was below LOQ and was set to LOQ for calculating processing factors.

III. Conclusions

In order to determine "processing" factors for total residues of BYI 02960 from oranges into juice, marmalade, and oil, processing studies have been conducted.

Storage of oranges for 6-13 days at ambient conditions leads to mean processing factors of 0.65-0.75, indicating a reduction in total residues of BYI 2960 over the storage time. Washing does not lead to a reduction in residues, as indicated by a mean processing factor of 1.15 in washed fruit and <0.2 in washings. The processing factors of the total residue BYI 2960 for orange pulp (<0.25) and peel (1.8) clearly show that the main amount of residues is located in/on the orange peel.

Both the transfer factors for washed peel as well as peel without oil indicate an increase in total residues of BYI 02960. The findings show that residues are not extractable by water or steam extraction.

The mean total-residue "processing" factor for pasteurised juice was <0.25, 0.25 for marmalade, and <0.25 for oil. Typical industrial preparation steps for juice, marmalade, and oil production will result in a clear reduction of total residues of BYI 02960.

Diagram 6.5.4.3-1: Industrial "processing" of orange fruit into juice

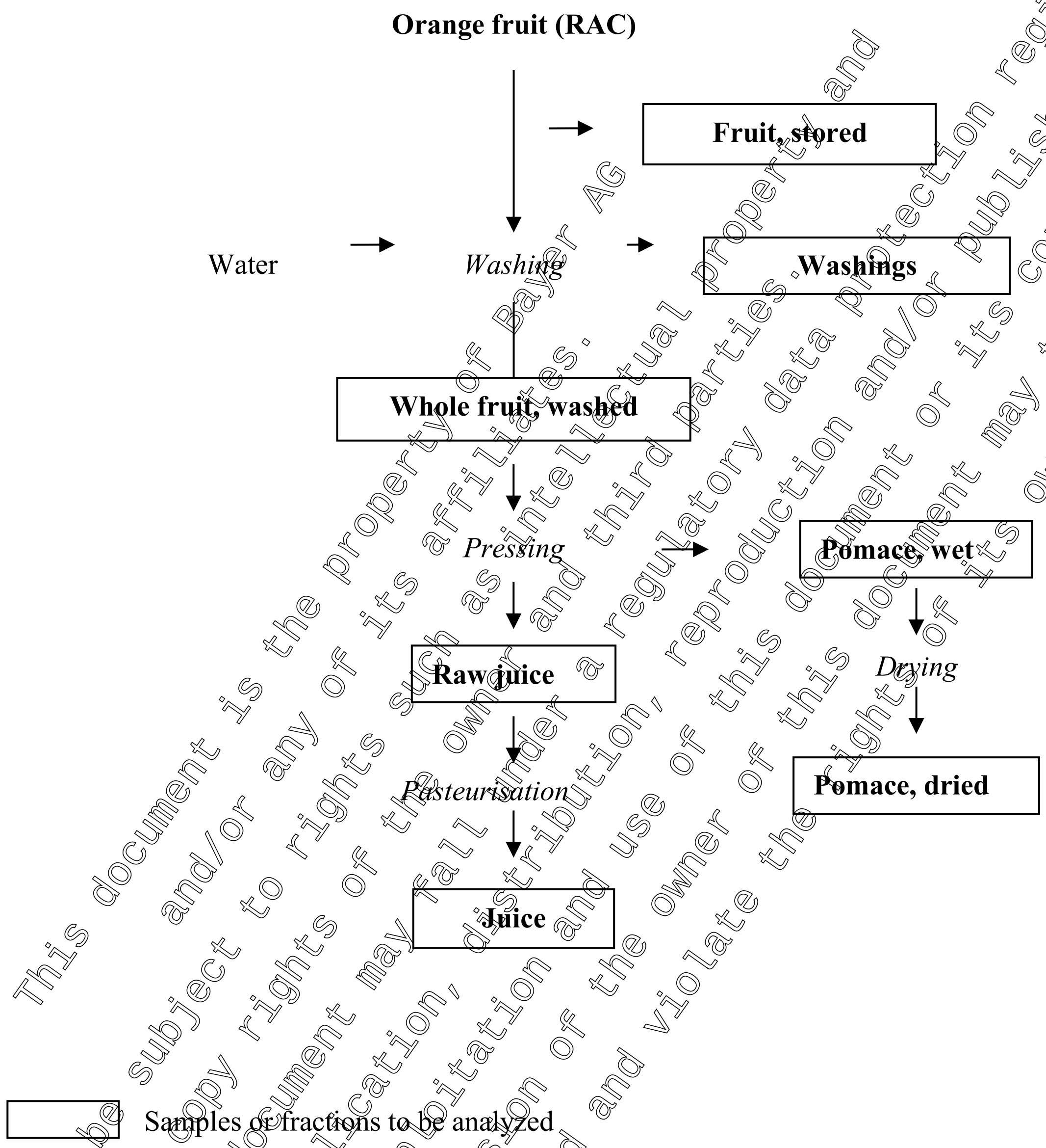
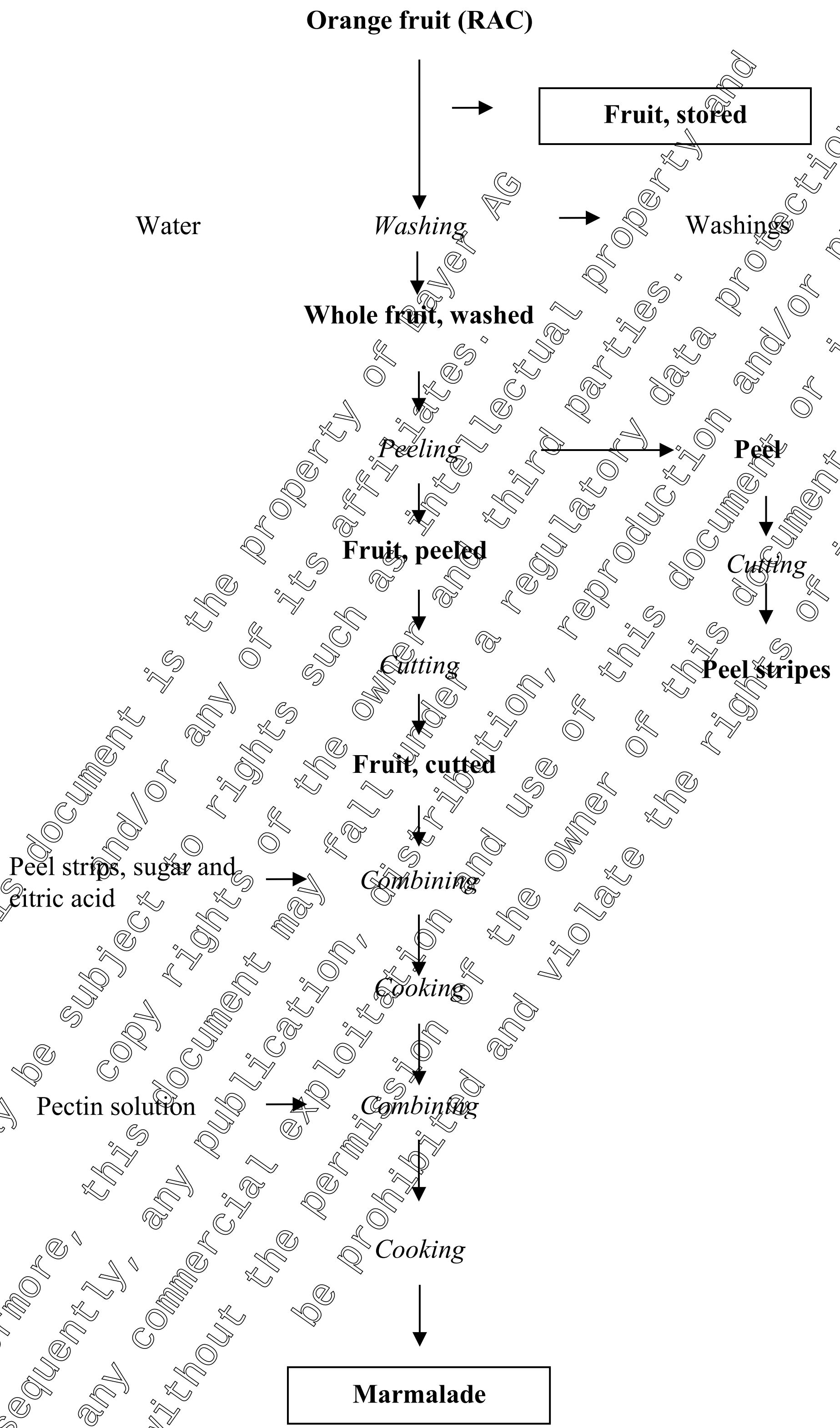


Diagram 6.5.4.3-2: Industrial "processing" of orange fruit into marmalade



Samples or fractions to be analyzed

Diagram 6.5.4.3-3: Industrial "processing" of orange fruit into oil

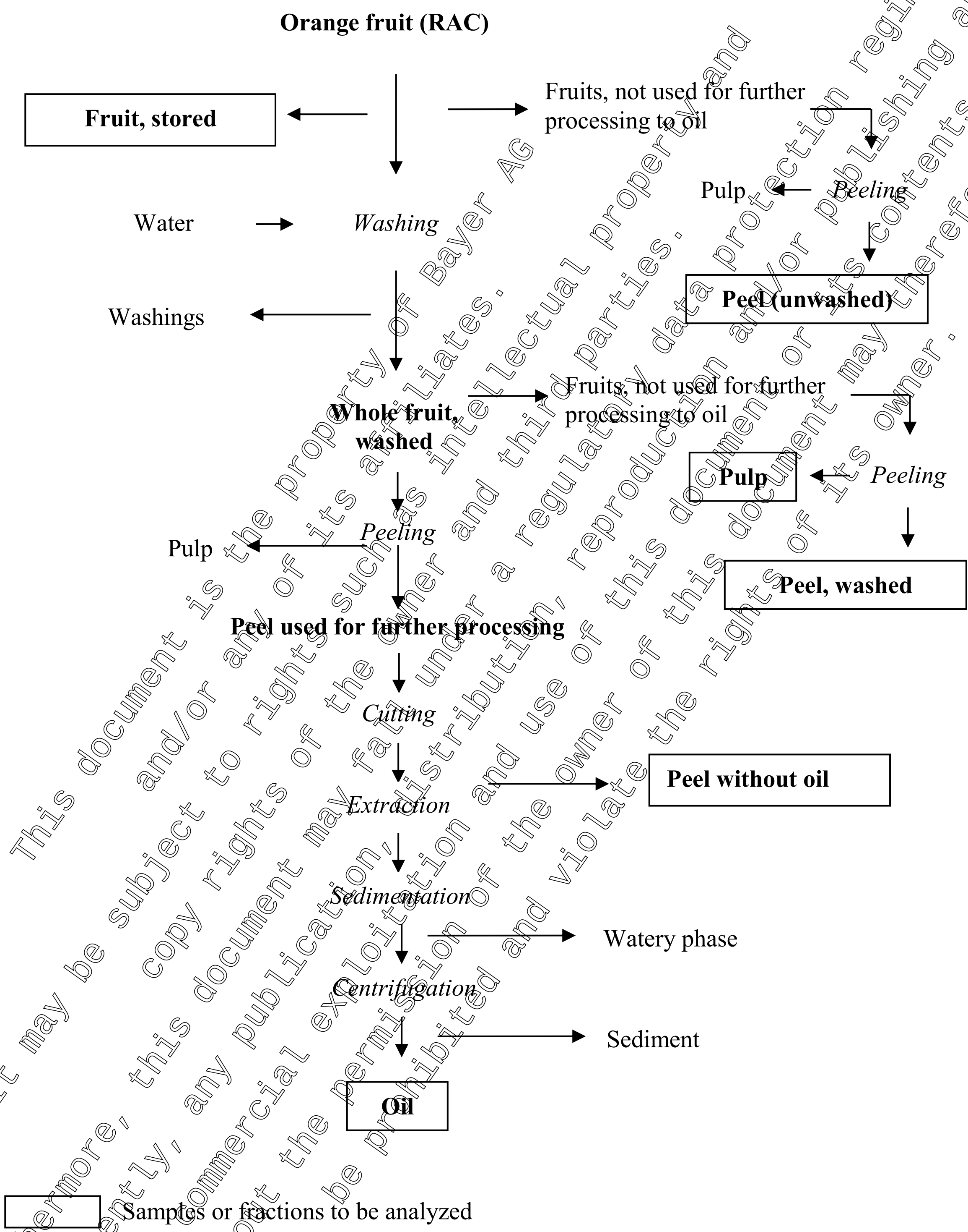


Table 6.5.4.3-4a: Application scenario in residue processing trials conducted in/on **orange trees** after spraying with BYI 02960 SL 200 in European fields

Study No. **(Trial No.) Country Location Region Year**	**Crop Variety**	**FL**	**Application**			**GS**	**PHI (days)**
			No.	**kg/ha (a.s.)**	**kg/hl (a.s.)**		
10-3405 (10-3405-01) Spain [redacted] EU-S 2010	orange Navelina	200 SL	1	0.375 (0.144 kg/(ha×m))	0.0375	81	29
10-3405 (10-3405-02) Spain [redacted] EU-S 2010	orange Navelina	200 SL	1	0.375 (0.125kg/(ha×m))	0.0375	83	29

FL=formulation
EU-S=southern European residue region
GS=growth stage (BBCH-code) at last treatment
PHI=pre-harvest interval

Table 6.5.4.3-4b: Results of residue processing trials conducted in/on **orange** after spraying with BYI 02960 SL 200 in southern European fields

Study No. (Trial No.) Country GLP	Portion analyzed	DALT (days)	Residues (mg/kg) expressed as BYI 02960 BYI 02960	DFA	BYI 02960-DFEAF	total residue of BYI 02960 calc.
10-3405 (10-3405-01) Spain GLP: yes	fruit (RAC)	29	0.21	0.03	<0.01	0.26
	pulp	29	<0.01	<0.02	<0.01	<0.04
	juice production					
	fruit, stored	29	0.17	0.04	<0.01	0.22
	whole fruit, washed	29	0.17	0.03	<0.01	0.21
	washings	29	<0.01	<0.02	<0.01	<0.04
	pomace, wet	29	0.29	0.04	<0.01	0.35
	pomace, dried	29	0.89	0.11	<0.01	1.0
	raw juice	29	<0.01	<0.02	<0.01	<0.04
	juice	29	<0.01	<0.02	<0.01	<0.04
	marmalade production					
	fruit, stored	29	0.12	0.03	<0.01	0.16
	marmalade	29	0.02	<0.02	<0.01	0.05
	oil production					
	fruit, stored	29	0.12	0.03	<0.01	0.16
	pulp	29	0.02	0.03	<0.01	0.06
	peel	29	0.46	0.04	<0.01	0.52
	peel washed	29	0.62	0.05	<0.01	0.67
	peel without oil	29	0.65	0.06	<0.01	0.72
	oil	29	<0.01	<0.02	<0.01	<0.04
10-3405 (10-3405-02) Spain GLP: yes	fruit (RAC)	29	0.12	0.02	<0.01	0.15
	pulp	29	<0.01	<0.02	<0.01	<0.04
	juice production					
	fruit, stored	29	0.04	<0.02	<0.01	0.07
	whole fruit, washed	29	0.19	0.02	<0.01	0.22
	washings	29	<0.01	<0.02	<0.01	<0.04
	pomace, wet	29	0.15	0.03	<0.01	0.19
	pomace, dried	29	0.63	0.09	<0.01	0.73
	raw juice	29	<0.01	<0.02	<0.01	<0.04
	juice	29	<0.01	<0.02	<0.01	<0.04
	marmalade production					
	fruit, stored	29	0.11	0.03	<0.01	0.14
	marmalade	29	0.01	<0.02	<0.01	0.04
	oil production					
	fruit, stored	29	0.08	<0.02	<0.01	0.11
	pulp	29	<0.01	<0.02	<0.01	<0.04
	peel	29	0.20	0.03	<0.01	0.24
	peel washed	29	0.27	0.03	<0.01	0.31
	peel without oil	29	0.51	0.05	<0.01	0.57
	oil	29	<0.01	<0.02	<0.01	<0.04

DALT=days after last treatment; RAC=raw agricultural commodity

Table 6.5.4.3-5: Recovery data for BYI 02960 in **orange** and **orange matrices**

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortifi-cation level** (mg/kg)	**Recovery (%)**				
						Individual recoveries	**Min**	**Max**	**Mean**	**RSD**
10-3405 (10-3405-01), to (10-3405-02) GLP: yes 2010	orange	fruit	BYI 02960	6	0.01	91; 93; 100; 102; 112; 114	91	114	102	9.3
				4	0.10	84; 88; 92; 94	84	94	90	5.0
				1	0.50	90	90	90		
				11	overall		84	114	96	10.0
			DFA	6	0.02	90; 93; 95; 97; 97; 101	90	101	96	4.0
				4	0.20	90; 91; 94; 95	90	95	93	2.6
				1	0.50	93	93	93		
				11	overall		90	101	94	3.5
			BYI 02960-DFEAF	6	0.01	88; 89; 89; 89; 94; 104	88	104	92	6.7
				4	0.10	82; 84; 87; 93	82	93	87	5.5
				1	0.50	96	96	96		
				11	overall		82	104	90	6.7
	orange	juice	BYI 02960	5	0.01	97; 99; 106; 109; 116	97	116	105	7.3
				3	0.50	81; 85; 94	81	94	87	7.7
				8	overall		81	116	98	12.1
			DFA	5	0.02	99; 103; 104; 105; 105	99	105	103	2.4
				3	0.50	90; 91; 92	90	92	91	1.1
				8	overall		90	105	99	6.7
			BYI 02960-DFEAF	5	0.01	79; 82; 84; 87; 92	79	92	85	5.9
				3	0.50	84; 84; 89	84	89	86	3.4
				8	overall		79	92	85	4.8
		marmalade	BYI 02960	5	0.01	104; 108; 109; 109; 112	104	112	108	2.7
				3	0.50	105; 111; 116	105	116	111*	5.0
				8	overall				109	3.5
			DFA	5	0.02	79; 81; 83; 84; 84	79	84	82	2.6
				3	0.50	71; 72; 73	71	73	72	1.4
				8	overall		71	84	78	7.1
			BYI 02960-DFEAF	5	0.01	98; 103; 108; 109; 113	98	113	106	5.5
				3	0.50	91; 101; 115	91	115	102	11.8
				8	overall				105	7.7

* This recovery was accepted since the RSD value was low and the individual recoveries were in the acceptable range.

Remark re. sample material *fruit*: also covers *whole fruit, washed*; *pulp*; and *stored fruit*
Remark re. sample material *juice*: also covers *raw juice* and *washings*

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Table 6.5.4.3-5 (cont'd): Recovery data for BYI 02960 in **orange** and **orange matrices**

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortifi-cation level** (mg/kg)	**Recovery (%)** **Individual recoveries**	**Min**	**Max**	**Mean**	**RSD**
10-3405 (10-3405-01), to (10-3405-02) GLP: yes 2010	orange	oil	BYI 02960	5	0.01	102; 104; 106; 107; 111	102	111	106	3.2
				3	0.50	92; 102; 103	92	103	99	6.1
				8	overall		92	111	103	5.3
			DFA	5	0.02	97; 101; 104; 105; 105	97	105	102	3.4
				3	0.50	96; 96; 101	96	101	98	3.0
				8	overall		96	105	101	3.9
			BYI 02960-DFEAF	5	0.01	98; 98; 98; 99; 100	98	100	99	0.9
				3	0.50	96; 96; 101	96	101	98	3.0
				8	overall		96	101	98	1.8
		peel	BYI 02960	5	0.01	84; 93; 100; 102; 111	84	111	98	10.3
				3	0.50	88; 89; 91	88	91	89	1.7
				2	1.0	79; 82	79	82	81	
				10	overall		79	111	92	10.8
			DFA	5	0.02	88; 91; 91; 95; 95	88	95	92	3.3
				3	0.50	83; 84; 85	83	85	84	1.2
				2	1.0	81; 83	81	83	82	
				10	overall		81	95	88	5.9
			BYI 02960-DFEAF	5	0.01	71; 79; 84; 89; 94	71	94	83	10.7
				3	0.50	87; 89; 94	87	94	90	4.0
				2	1.0	83; 93	83	93	88	
				10	overall		71	94	86	8.5
		pomace wet	BYI 02960	1	0.01	120	120	120		
				1	overall		120	120		
			DFA	1	0.02	97	97	97		
				1	overall		97	97		
			BYI 02960-DFEAF	1	0.01	100	100	100		
				1	overall		100	100		
		washings	BYI 02960	1	0.01	94	94	94		
				1	overall		94	94		
			DFA	1	0.02	98	98	98		
				1	overall		98	98		
			BYI 02960-DFEAF	1	0.01	90	90	90		
				1	overall		90	90		

Remark re. sample material *juice*: also covers *raw juice* and *washings*
Remark re. sample material *peel*: also covers *peel, washed*; *peel without oil*; *wet pomace*; and *dry pomace*

➢ US processing study

Report:	**KIIA 6.5.4.3/02, [redacted]; 2012**
Title:	BYI 02960 200 SL – Magnitude of the Residue in/on Orange Processed Commodities
Report No. & Document No.:	RARVY035, dated June 1, 2012. M-432186-01-2
Guidelines:	US: EPA Residue Chemistry Test Guidelines OPPTS 860.1520, Processed Food/Feed Canada: PMRA DACO 7.4.5, Processed Food/Feed OECD: Guidelines for the Testing of Chemicals, 508, Magnitude of the Residues in Processed Commodities, Adopted Oct. 3, 2008. OECD Guidance Document on Magnitude of the Pesticide Residues in Processed Commodities.
GLP	Yes

Two field trials were conducted to measure the magnitude of BYI 02960 residues in/on orange processed commodities following two broadcast foliar spray applications of BYI 02960 200 SL at 3X and 5X exaggerated application rates. BYI 02960 200 SL is a soluble concentrate formulation containing 200 g a.s./L.

BYI 02960 200 SL was applied to orange trees at rates and timings as shown in Table 6.5.4.3-6.

Table 6.5.4.6-6: Study Use Pattern for BYI 02960 200 SL on Orange

Trial Identification	Location (City, State, NAFTA Region, and Year)	End-use Product (Formulation)	Plot Name	Application						Tank Mix Adjuvants
				Method	Timing/Growth Stage (BBCH)	Actual Spray Volume GPA (L/ha)	Rate lb a.s./A (kg a.s./ha)	Retreatment Interval (days)	Total Rate lb a.s./A (kg a.s./ha)	
RV200-11PA	[redacted], CA Region 10 2011	BYI 02960 200 SL	TRT5X	Foliar Air-Blast	83 83	269 (2515) 269 (2515)	0.895 (1.00) 0.891 (0.999)	NA[a] 10	1.8 (2.0)	Dyne - Amic 0.25 % v/v
RV201-11PA	[redacted], CA Region 10 2011	BYI 02960 200 SL	TRT5X	Foliar Air-Blast	89 89	245 (2291) 250 (2337)	0.894 (1.00) 0.896 (1.00)	NA[a] 10	1.8 (2.0)	Dyne - Amic 0.25 % v/v

a NA = Not applicable

All applications were made using ground-based equipment. The additive, Dyne-Amic 0.25% v/v, was used in all applications.

Single composite orange whole fruit samples were harvested at a 1-day pre-harvest interval (PHI) from TRT5X plots. Single composite samples of orange whole fruit were harvested from the control plots on the same day the respective samples were harvested from the treated plots.

Triplicate subsamples of orange whole fruit, unwashed, the raw agricultural commodity (RAC) were removed. Unwashed peel was collected from a sub-sample of the RAC, then the remaining orange whole fruits were washed, (triplicate subsamples removed), washings collected (wash water), washed peel collected and the orange processed commodities of peel without oil, raw (fresh) juice, juice (pasteurized), oil, strain rest, pulp, wet pomace, dried pomace (drypomace/dried pulp), and marmalade generated.

The residue(s) of BYI 02960, DFA, and DFEAF were quantitated by HPLC-MS/MS using stable isotopically labeled internal standards standards. The individual analyte residues were summed to give a total BYI 02960 residue. Residue measurements below the analyte LOQ were summed into the total BYI 02960 residue value as the analyte LOQ value.

Findings

Concurrent recoveries of BYI 02960, DFA, and DFEAF were measured with each set of samples to verify method performance. All recoveries were corrected for any interferences in corresponding controls. The overall mean of the recoveries for each matrix was within the acceptable range of 70 to 110%, and the standard deviation values were below 20% (Table 6.5.4.3-7).

Table 6.5.4.6-7: Summary of Recoveries of BYI 02960 Residues from Orange RAC and Processed Commodities

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev (%)
Orange Whole Fruit Unwashed (RAC)	BYI 02960	0.010	7	96, 101, 94, 88, 88, 94, 90	93	5
		2.200[b]	3	88, 93, 112	98	13
	DFA	0.050	7	74, 74, 75, 85, 78, 79, 83	78	4
		2.200[b]	3	97, 103, 99	100	3
	DFEAF	0.010	7	83, 83, 100, 97, 98, 91, 99	93	7
		2.200[b]	3	97, 93, 88	93	4
Unwashed Peel	BYI 02960	0.010	3	113, 111, 105	110	5
		1.000	3	85, 82, 83	83	2
	DFA	0.050	3	105, 98, 92	98	6
		1.000	3	84, 88, 88	87	2
	DFEAF	0.010	3	93, 83, 96	91	7
		1.000	3	81, 88, 85	84	3
Orange Whole Fruit Washed	BYI 02960	1.000	3	90, 90, 89	90	1
	DFA	1.000	3	88, 87, 89	88	1
	DFEAF	1.000	3	86, 82, 79	82	4

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Table 6.5.4.6-7 (cont'd): Summary of Recoveries of BYI 02960 Residues from Orange RAC and Processed Commodities

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev (%)
Washings	BYI 02960	0.010	3	98, 98, 103	100	3
		1.000	3	90, 89, 93	90	2
	DFA	0.050	3	99, 98, 92	96	4
		1.000	3	103, 97, 102	101	3
	DFEAF	0.010	3	112, 85, 80	92	17
		1.000	3	87, 85, 86	86	1
Washed Peel	BYI 02960	1.500	3	90, 89, 88	89	1
		2.000	3	102, 107, 81	97	14
	DFA	1.500	3	87, 86, 94	89	5
		2.000	3	96, 97, 87	93	5
	DFEAF	1.500	3	94, 81, 87	87	6
		2.000	3	93, 89, 90	91	2
Peel Without Oil	BYI 02960	0.010	3	83, 92, 99	92	8
		1.000	3	92, 97, 88	92	4
	DFA	0.050	3	79, 84, 88	84	4
		1.000	3	90, 96, 104	97	7
	DFEAF	0.010	3	87, 77, 80	81	5
		1.000	3	86, 89, 102	93	9
Raw (Fresh) Juice	BYI 02960	0.010	3	95, 90, 100	95	5
		1.000	3	92, 90, 92	92	1
	DFA	0.050	3	85, 83, 88	85	3
		1.000	3	91, 88, 92	91	2
	DFEAF	0.010	3	95, 76, 78	83	10
		1.000	3	86, 88, 88	87	1
Juice (Pasteurized)	BYI 02960	0.010	3	78, 89, 94	87	8
		1.000	3	85, 87, 85	86	1
	DFA	0.050	3	78, 83, 74	78	5
		1.000	3	86, 89, 87	88	1
	DFEAF	0.010	3	80, 77, 99	85	12
		1.000	3	90, 85, 85	87	3
Oil	BYI 02960	0.010	3	104, 104, 113	107	6
		1.000	3	100, 98, 103	100	3
	DFA	0.050	3	108, 99, 102	103	5
		1.000	3	100, 102, 103	102	2
	DFEAF	0.010	3	114, 104, 107	109	5
		1.000	3	98, 93, 106	99	7
Strain Rest	BYI 02960	0.010	3	93, 89, 92	91	2
		1.000	3	88, 84, 91	87	4
	DFA	0.050	3	89, 76, 101	89	12
		1.000	3	94, 91, 93	93	1
	DFEAF	0.010	3	88, 111, 84	94	15
		1.000	3	96, 95, 103	98	4

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Table 6.5.4.6-7 (cont'd): Summary of Recoveries of BYI 02960 Residues from Orange RAC and Processed Commodities

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev (%)
Pulp	BYI 02960	0.010	3	101, 101, 99	100	1
		1.000	3	89, 88, 86	88	2
	DFA	0.050	3	87, 98, 88	91	6
		1.000	3	87, 87, 87	87	1
	DFEAF	0.010	3	77, 79, 87	81	6
		1.000	3	84, 86, 86	86	1
Wet Pomace	BYI 02960	0.010	3	103, 102, 104	103	1
		1.000	3	77, 87, 90	85	7
	DFA	0.050	3	82, 93, 86	87	6
		1.000	3	75, 88, 83	82	6
	DFEAF	0.010	3	76, 85, 109	90	17
		1.000	3	77, 86, 84	82	5
Dried Pomace (Dry Pomace/ Dried Pulp)	BYI 02960	0.010	3	86, 90, 81	86	4
		2.000	3	86, 87, 89	87	2
		3.000	3	84, 114, 97	98	15
	DFA	0.050	3	83, 79, 91	85	6
		2.000	3	77, 76, 80	78	2
		3.000	3	82, 82, 81	82	1
	DFEAF	0.010	3	95, 90, 90	92	3
		2.000	3	87, 88, 90	88	2
		3.000	3	86, 94, 86	89	5
Marmalade	BYI 02960	0.010	3	115, 91, 88	98	15
		1.000	3	92, 92, 91	92	1
	DFA	0.050	3	75, 77, 78	77	1
		1.000	3	82, 86, 79	82	4
	DFEAF	0.010	3	107, 109, 106	107	1
		1.000	3	92, 93, 96	94	2

a Mean Recovery = mathematical average of all recoveries.
b High recoveries were conducted to validate the method for citrus samples.

The freezer storage stability study indicates that BYI 02960 residues were stable in orange fruits as representative commodity (high acid content) during frozen storage for at least 18 months (556 days) prior to analyses. The maximum storage period of frozen samples in this study for BYI 02960 was 317 days. A summary of the storage conditions are shown in the Table 6.5.4.3-8.

Table 6.5.4.3-8: Summary of Storage Conditions for all Orange Commodities

Residue Component(s)	Matrix (RAC)	Average Storage Temperature (°C)[a]	Actual Storage Duration months (days)[b]	Interval of Demonstrated Storage Stability months (days)[c]
BYI 02960, DFA, DFEAF	Orange Whole Fruit Unwashed (RAC)	<0	10 (317)	18 (556)
BYI 02960, DFA, DFEAF	Unwashed Peel	<0	8 (261)	18 (556)

Table 6.5.4.3-8 (cont'd): Summary of Storage Conditions for all Orange Commodities

Residue Component(s)	Matrix (RAC)	Average Storage Temperature (°C)[a]	Actual Storage Duration months (days)[b]	Interval of Demonstrated Storage Stability months (days)[c]
BYI 02960, DFA, DFEAF	Orange Whole Fruit Washed	<0	8 (261)	18 (556)
BYI 02960, DFA, DFEAF	Washings	<0	8 (279)	18 (556)
BYI 02960, DFA, DFEAF	Washed Peel	<0	9 (272)	18 (556)
BYI 02960, DFA, DFEAF	Peel Without Oil	<0	8 (269)	18 (556)
BYI 02960, DFA, DFEAF	Raw (Fresh) Juice	<0	8 (266)	18 (556)
BYI 02960, DFA, DFEAF	Juice (Pasteurized)	<0	8 (259)	18 (556)
BYI 02960, DFA, DFEAF	Oil	<0	8 (261)	18 (556)
BYI 02960, DFA, DFEAF	Strain Rest	<0	8 (261)	18 (556)
BYI 02960, DFA, DFEAF	Pulp	<0	8 (264)	18 (556)
BYI 02960, DFA, DFEAF	Wet Pomace	<0	8 (267)	18 (556)
BYI 02960, DFA, DFEAF	Dried Pomace (Dry Pomace/Dried Pulp)	<0	9 (278)	18 (556)
BYI 02960, DFA, DFEAF	Marmalade	<0	9 (276)	18 (556)

a The average storage temperature reported is from the time of sample generation at the University Of [redacted] Food Technology Center through the last sample extraction. Samples were maintained in a laboratory freezer at all times except during preparation for sample analysis.

b The actual storage duration for the orange RAC is from the time of harvest through the last sample extraction for that matrix. The actual storage duration for all remaining commodities is from the time of commodity generation through the last sample extraction.

c [redacted], [redacted]. [redacted]. 2012. Storage stability of BYI 02960, difluoroacetic acid, and difluoroethyl-amino-furanone in plant matrices. Bayer CropScience Report No. RARVP046, amended version including 18-month data (KIIA 6.1.1/01).

The BYI 02960, DFA, DFEAF, and total BYI 02960 residue data for orange RAC and processed commodities are provided in Table 6.5.4.3-9.

Table 6.5.4.3-9: BYI 02960 Residue Data from Orange RAC and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg a.s./ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)	Total BYI 02960 Residue Processing Factor[b]	Average Processing Factor
RV200-11PA	Whole Fruit	NA[c]	NA[c]	1.8 (2.0)	1	0.306 0.247 0.626	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.31 0.25 0.63 Avg. 0.40	NA[c]	NA[c]
RV201-11PA	Whole Fruit	NA[c]	NA[c]	1.8 (2.0)	1	0.576 0.522 0.454	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.59 0.54 0.46 Avg. 0.53	NA[c]	
RV200-11PA	Whole Fruit	Un-Washed Peel	NA[c]	NA[c]	NA[c]	1.12 1.04 0.941	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	1.1 1.1 0.95 Avg. 1.1	2.8X	2.3X
RV201-11PA	Whole Fruit	Un-Washed Peel	NA[c]	NA[c]	NA[c]	0.868 0.866 0.826	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.90 0.89 0.85 Avg. 0.88	1.7X	
RV200-11PA	Whole Fruit	Washed Whole Fruit	NA[c]	NA[c]	NA[c]	0.515 0.416 0.355	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.52 0.42 0.36 Avg. 0.43	1.1X	<1X
RV201-11PA	Whole Fruit	Washed Whole Fruit	NA[c]	NA[c]	NA[c]	0.312 0.315 0.612	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.32 0.32 0.63 Avg. 0.43	<1X	

Table 6.5.4.3-9 (cont'd): BYI 02960 Residue Data from Orange RAC and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg a.s./ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)	Total BYI 02960 Residue Processing Factor[b]	Average Processing Factor
RV200-11PA	Whole Fruit	Wash-ings	NA[c]	NA[c]	NA[c]	0.020 0.018 0.020	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.025 0.023 0.025 Avg. 0.024	<1X	<1X
RV201-11PA	Whole Fruit	Wash-ings	NA[c]	NA[c]	NA[c]	0.026 0.024 0.025	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.030 0.029 0.030 Avg. 0.030	<1X	
RV200-11PA	Whole Fruit	Washed Peel	NA[c]	NA[c]	NA[c]	1.67 1.84 1.93	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	1.7 1.9 2.0 Avg. 1.9	4.8X	4X
RV201-11PA	Whole Fruit	Washed Peel	NA[c]	NA[c]	NA[c]	1.55 1.59 1.55	<0.050 0.052 <0.050	<0.010 <0.010 <0.010	1.6 1.6 1.6 Avg. 1.6	3.1X	
RV200-11PA	Whole Fruit	Peel Without Oil	NA[c]	NA[c]	NA[c]	0.935 0.818 0.999	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.95 0.83 1.0 Avg. 0.93	2.3X	2.1X
RV201-11PA	Whole Fruit	Peel Without Oil	NA[c]	NA[c]	NA[c]	0.949 1.01 1.00	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.98 1.1 1.0 Avg. 1.0	1.9X	
RV200-11PA	Whole Fruit	Raw (Fresh) Juice	NA[c]	NA[c]	NA[c]	0.017 0.014 0.014	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.021 0.019 0.019 Avg. 0.020	<1X	<1X
RV201-11PA	Whole Fruit	Raw (Fresh) Juice	NA[c]	NA[c]	NA[c]	0.011 0.012 0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.015 0.016 0.015 Avg. 0.016	<1X	

Table 6.5.4.3-9 (cont'd): BYI 02960 Residue Data from Orange RAC and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg a.s./ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)	Total BYI 02960 Residue Processing Factor[b]	Average Processing Factor
RV200-11PA	Whole Fruit	Juice	NA[c]	NA[c]	NA[c]	0.010 0.012 0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.014 0.016 0.015 Avg. 0.015	<1X	<1X
RV201-11PA	Whole Fruit	Juice	NA[c]	NA[c]	NA[c]	0.018 0.012 0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.027 0.017 0.015 Avg. 0.019	<1X	
RV200-11PA	Whole Fruit	Oil	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV201-11PA	Whole Fruit	Oil	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	
RV200-11PA	Whole Fruit	Strain Rest	NA[c]	NA[c]	NA[c]	0.013 0.013 0.014	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.018 0.017 0.018 Avg. 0.018	<1X	<1X
RV201-11PA	Whole Fruit	Strain Rest	NA[c]	NA[c]	NA[c]	0.016 0.014 0.014	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.020 0.019 0.018 Avg. 0.019	<1X	
RV200-11PA	Whole Fruit	Pulp	NA[c]	NA[c]	NA[c]	0.432 0.446 0.488	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.44 0.45 0.49 Avg. 0.46	1.2X	
RV201-11PA	Whole Fruit	Pulp	NA[c]	NA[c]	NA[c]	0.446 0.470 0.466	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.46 0.49 0.48 Avg. 0.48	<1X	1X

Table 6.5.4.3-9 (cont'd): BYI 02960 Residue Data from Orange RAC and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg a.s./ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Processing Factor
RV200-11PA	Whole Fruit	Wet Pomace	NA[c]	NA[c]	NA[c]	0.493 0.511 0.526	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.50 0.52 0.53 Avg. 0.52	1.3X	1.2X
RV201-11PA	Whole Fruit	Wet Pomace	NA[c]	NA[c]	NA[c]	0.536 0.575 0.524	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.56 0.60 0.54 Avg. 0.57	1.1X	
RV200-11PA	Whole Fruit	Dried Pomace (Dry Pomace /Dried Pulp	95	NA[c]	NA[c]	2.05 1.99 2.12	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	2.1 2.0 2.1 Avg. 2.1	5.3X	4.8X
RV201-11PA	Whole Fruit	Dried Pomace (Dry Pomace /Dried Pulp	91	NA[c]	NA[c]	2.01 1.98 2.10	0.126 0.092 0.092	0.014 <0.010 <0.010	2.2 2.1 2.2 Avg. 2.2	4.2X	
RV200-11PA	Whole Fruit	Marma-lade	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV201-11PA	Whole Fruit	Marma-lade	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	

a Total BYI 02960 residue is the sum of BYI 02960, DFA, and DFEAF residue in parent equivalents. Residue measurements below the analyte LOQ were summed into the Total BYI 02960 residue value as the analyte LOQ value. These totals represent the upper limit of what the residue levels might be.

b Total BYI 02960 Processing Factor = Average total BYI 02960 residue in processed sample/average total BYI 02960 residue in unprocessed (RAC) sample. Processing factors calculated to be less than 1X were reported as <1X.

c NA = Not applicable.

Conclusion

A summary of the calculated processing factors for orange processed commodities are shown in Table 6.5.4.3-10.

Following a five-fold (5X) exaggerated application of BYI 02960 to two separate trials of orange trees, the average total BYI 02960 residue did not concentrate (processing factor ≤1X) in orange, washed fruit, washings, raw (fresh) juice, juice (pasteurized), oil, strain rest, pulp, and marmalade. However, the residue did concentrate in orange dried pomace (dry pomace/dried pulp (4.8X), washed peel (4X), unwashed peel (2.3X), peel without oil (2.1X), and wet pomace (1.2X).

The processing factors determined for BYI 02960 total residue in this study are less than the theoretical concentration factors cited in the EPA Residue Chemistry Test Guideline OPPTS 860.1520 which lists factors of 3.3X for citrus peel, 1000X for citrus oil, and 2X for citrus juice.[13] Two separate citrus peel samples were taken, washed and unwashed. Although the unwashed peel sample was less then the EPA Test Guidelines listed above, the washed peel showed a slightly higher concentration at 4X.

The residue data and subsequent calculated processing factors provided in this report are suitable for regulatory purposes.

Table 6.5.4.3-10: Summary of Total BYI 02960 Processing Factors Calculated for Orange Processed Commodities

RAC	Processed Commodity	Average Total BYI 02960 Residue Processing Factor
Orange Whole Fruit (Unwashed)	Dried pomace (dry pomace/dried pulp)	4.8X
	Washed peel	4X
	Unwashed peel	2.3X
	Peel without oil	2.1X
	Wet pomace	1.2X
	Washed fruit, washings, raw (fresh) juice, juice (pasteurized, oil, strain rest, pulp, and marmalade	≤1X

IIA 6.5.4.4 Apple

Report:	**KIIA 6.5.4.4/01, [redacted] & [redacted]; 2012**
Title:	Determination of the residues of BYI 02960 in/on apple and the processed fractions (whole fruit, washed; washings; raw sauce; strain rest; sauce; pomace, wet; pomace, dried; raw juice; juice, retentate; peel; fruit peeled; fruit, dried) after spraying of BYI 02960 SL 200 in the field in Germany and Belgium
Report No. & Document No.:	10-3171, dated July 5, 2012 M-434004-02-1

Report:	**KIIA 6.5.4.4/02, [redacted] & [redacted]; 2012**
Title:	Determination of the residues of BYI 02960 in/on apple and the processed fractions (whole fruit, washed; washings; raw sauce; strain rest; sauce; pomace, wet; pomace, dried; raw juice; retentate and juice) after spraying of BYI 02960 SL 200 in the field in Italy and Spain
Report No. & Document No.:	10-3172, dated July 5, 2012 M-434006-01-2

Guidelines *(applies to both studies)*:	EU Council Directive 91/414/EEC – OECD Guideline for the Testing of Chemicals No. 508, Magnitude of the Pesticide Residues in Processed Commodities – EPA Ref. OPPTS 860.1520 SUPP
GLP *(applies to both studies)*:	yes (certified laboratory)

I. Materials and Methods

Due to the presence of measurable residues of BYI 02960 on harvested apples determined in samples from field residue trials performed according to the intended commercial use conditions (see point IIA 6.3.1.3) as well as to the nature of apple use (preparation and consumption patterns), investigations on the effects of basic processing have been conducted. Two trials were conducted in the northern European residue region, in Germany and Belgium, in order to determine the total residues of BYI 02960 in unprocessed apple fruits and then in the primary processed commodities juice, dried fruit, and apple sauce, as well as in intermediate fractions ([redacted] & [redacted], 2012; KIIA 6.5.4.4/01).

Two additional trials were conducted in the southern European residue region, in Italy and Spain, in order to determine the total residues of BYI 02960 in unprocessed apple fruits and in the primary processed commodities apple sauce and juice ([redacted] & [redacted], 2012; KIIA 6.5.4.4/02).

The field trials were conducted as part of studies 10-2171 and 10-2172 (cf. KIIA 6.3.1.3/01 and /03 for details). BYI 02960 SL 200 was sprayed twice at an application rate of 75 g a.s./(ha×m) and a water volume of 500 L/(ha×m). The final application was conducted at a pre-harvest interval of 14 days.

After processing (described below), residue analysis was performed according to method 01304 as used in the RAC trials themselves (for more information, cf. points IIA 6.3.1.3 and IIA 4.3). The limits of quantitation were 0.01 mg/kg (BYI 02960 and DFEAF) and 0.02 mg/kg (DFA), expressed in parent compound equivalents, yielding a calculated total-residue LOQ of 0.04 mg/kg, in all matrices. Prior and parallel to the residue analysis, the method was validated by recovery experiments.

Processing procedures:
The washing and peeling of apple fruits was done using household practice. The preparation of juice, sauce, and dried fruit simulated industrial practice at a laboratory scale.

Juice preparation:
No damaged fruits were sorted out. Remaining stalks were removed where appropriate. The processing started in deep-frozen state. The fruits were washed for 1 to 2 min in lukewarm standing water and allowed to drain in a sieve to create the laboratory samples *whole fruit, washed* and *washings* (only in trial 10-3171-06). The washed fruits were crushed into mash in a cutter. The obtained frozen mash was warmed up to a minimum temperature of 10–15°C and subsequently pressed to obtain the laboratory samples *raw juice* and *pomace, wet*. The remaining part of the sample material wet pomace was dried at about 100°C until the water content was at approx. 10% to obtain the laboratory sample *pomace, dried*.

The remaining raw juice was enzymated by heating the juice for about 5 min at 90°C and for a further 5 min at 45°C. Afterwards, the juice was stored overnight at room temperature. Then, the juice was "fined" coarsely and subsequently filtered, yielding clear juice. The obtained retentate was taken as laboratory sample *retentate*. The Brix values of the filtrate were determined.

Thereafter, the filtered juice was pasteurised and collected in fractions. The first fractions had lower Brix values than the filtrate, because they were mixed with water still present in the heat exchanger. These fractions were rejected. Only fractions with a similar Brix value compared to the filtrate were collected in a larger container; these constitute the sample *pasteurised juice*.

The process is illustrated in flow diagram 6.5.4.4-1.

Sauce preparation:
No damaged fruits were sorted out. Remaining stalks were removed where appropriate. The processing started in deep-frozen state. The fruits were washed for 1 to 2 min in lukewarm standing water and allowed to drain in a sieve to create the laboratory samples *whole fruit, washed* and *washings* (only in trial 10-3171-03 and study 10-3172).

The washed whole fruits were cut in small pieces and heated to 98-100°C after addition of approx. 125 mL water/kg fruit, in order to prevent enzymatic reactions as well as changes of colour and taste. The heating also facilitates the subsequent straining. The steaming time was approx. 20 min. After steaming, the pulp was passed through a strainer in order to obtain the laboratory samples *raw sauce* and *strain rest*.

The remaining raw sauce was mixed with sugar (w [sugar]=16.5%), filled into preserving cans, and pasteurized in an autoclave. After pasteurization, the preserving cans were emptied in a larger vessel and the sauce was mixed thoroughly to obtain the laboratory sample *apple sauce*.

The process is illustrated in flow diagram 6.5.4.4-2.

Processing of dried fruit (only study 10-3171):
No damaged fruits were sorted out. Remaining stalks were removed where appropriate. The processing started in deep-frozen state. The lightly defrosted apples were peeled, an aliquot of the obtained laboratory sample of *fruit, peeled* and the whole sample of *peel* was taken.

From the remaining sample of peeled fruit, the apple cores were removed. The prepared fruits were deep-frozen for further processing to prevent the loss of fruit water. Subsequently the deep-frozen fruits were cut into 5 to 7 mm slices.

To prevent enzymatic reactions, oxidation, and to maintain the vitamins, a treatment with sulphite solution (w=0.01%) and citric acid solution (w=0.01%) followed. The treated apple slices were thoroughly washed in standing lukewarm water. The washed apple slices were dried in a fan-assisted oven at 80°C until a water content of 10 to 30% was reached to obtain the laboratory sample *fruit, dried*.

The process is illustrated in flow diagram 6.5.4.4-3.

II. Findings

The validation of the sample materials apple juice and sauce was conducted within study 10-3171. A set of validation recoveries for the sample material apple fruit was performed within study 10-2172 (cf. KIIA 6.3.1.3/03 for details). Concurrent recoveries were obtained from samples of apple matrices (apple fruit; whole fruit, washed; strain rest; sauce; pomace, wet; and juice). The recoveries for the sample material fruit are also representative for whole fruit, washed; strain rest; pomace, wet; pomace, dried; retentate; peel; fruit, peeled; and fruit, dried. The sample material sauce is also representative for raw sauce. The sample material juice is also representative for washings and raw juice.

In apple fruit samples, recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg, 0.10 mg/kg, and 1.0 mg/kg (expressed in BYI 02960 equivalents); in apple juice and apple sauce, spiking levels were 0.01 and 0.10 mg/kg. Additional individual recoveries were obtained for wet pomace and strain rest at 1.0 mg/kg, and for washed fruit at the 0.1 and 1.0 mg/kg spiking levels. Mean recoveries for all matrices were 87-113%, with RSDs in the larger validations sets ($n > 2$) of 0.9-13.0%; n=1-9.

For DFA, concurrent recovery samples for apple fruit were spiked at levels of 0.02, 0.05, 0.20, 0.50, and 1.0 mg/kg (expressed in BYI 02960 equivalents); fortification levels in apple juice and apple sauce were 0.02 and 0.20 mg/kg. Additional individual recoveries were obtained for wet pomace and strain rest at 1.0 mg/kg, and for washed whole fruit at the 0.02 and 0.20 mg/kg spiking levels. Mean recoveries in all matrices were 82-117%, with RSDs in the larger validations sets ($n > 2$) of 1.0-8.6%; n=1-6.

A tabular summary of the recovery values is presented below in table 6.5.4.4-5.

The total residues of BYI 02960 (parent compound plus DFA and DFEAF) in the harvested fruits at day 14 ranged from 0.07-0.15 mg/kg, as summarized previously (cf. KIIA 6.3.1.3/01 and /03). These values were used for the calculation of "processing" factors.

● <u>Juice preparation</u>:

<u>Fruit, washed and washings</u>: In *fruit, washed,* levels of the total residue of BYI 02960 were found at 0.06 mg/kg and 0.16 mg/kg. The corresponding processing factors were 0.86 and 1.07 with a mean value of 0.97 (n=2). In *washing,* levels of the total residue of BYI 02960 were always < 0.04 mg/kg. Thus, washing of fruits does not not lead to a reduction of the total residue of BYI 02960.

<u>Raw juice, retentate, and juice</u>: In raw juice, retentate, levels of the total residue of BYI 02960 were from 0.05-0.13 mg/kg. The residue levels in juice were from 0.04-0.10 mg/kg. In raw juice, retentate, and juice, the mean processing factors were 0.82 (range: 0.70-1.0; n=4), 0.74 (range: 0.60-0.83; n=4), and 0.65 (0.57-0.75; n=4), respectively, indicating a reduction of total residues of BYI 02960 during juice processing.

<u>Pomace, wet; and pomace, dried</u>: Levels of the total residue of BYI 02960 were at 0.09-0.18 mg/kg for wet pomace and 0.24-0.59 mg/kg for dried pomace. The measured residue levels lead to mean "processing" factors of 1.34 (range: 1.20-1.50; n=4) for wet pomace and 3.68 (range: 3.43-3.93; n=4) for dried pomace.

Based on these values, it is evident that a large proportion of the residues concentrates in the pomace fraction. Drying of wet pomace also leads to higher residue concentrations in the processed fractions, due to water loss and subsequent higher residue/weight ratios.

● <u>Sauce preparation</u>:

<u>Whole fruit, washed and washings</u>: In *whole fruit, washed*, the levels of the total residue of BYI 02960 were from 0.06-0.16 mg/kg, and in washings, residues were <0.04 mg/kg. The measured residue levels lead to mean "processing" factors of 1.01 (range: 0.86-2.2; n=3) for washed whole fruit, and <0.41 (range: <0.27-<0.57; n=3) for washings, indicating that washing does not affect the residue situation.

<u>Raw sauce, sauce, and strain rest</u>: In raw sauce, levels of the total residue of BYI 02960 were from 0.07-0.14 mg/kg; the residue levels in sauce were in a similar range, from 0.06-0.11 mg/kg. The measured residue levels lead to mean "processing" factors of 0.98 (range: 0.93-1.0, n=4) for raw sauce, and 0.81 (range: 0.73-0.86; n=4) for sauce. In strain rest, levels of the total residue of BYI 02960 were considerably higher, at 0.08-0.21 mg/kg, leading to a mean "processing" factor of 1.36 (range: 1.14-1.58; n=4).

Based on these values, it is evident that a larger proportion of the total residues of BYI 02960 concentrates in the strain rest fraction. Only a limited reduction of the total residue of BYI 02960 is evident for sauce.

● Processing of dried fruit:

Fruit, peeled; and peel: In peeled fruit (before drying), the residue level of the total residue of BYI 02960 was 0.06 mg/kg. In peel, the residue level was considerably higher, at 0.41 mg/kg. The measured residue levels lead to mean "processing" factors of 0.6 for peeled fruit and 4.10 for peel.

Fruit, dried: The residue level of the total residue of BYI 02960 in dried fruit was 0.18 mg/kg. The measured residue levels lead to a mean "processing" factor of 1.80.

Based on these values, it is evident that a large proportion of the residues concentrates in the peel fraction. Drying of peeled fruit also leads to higher residue concentrations in the processed fractions, due to water loss and subsequent higher residue/weight ratios.

The transfer factors for the total residues of BYI 02960 for juice, sauce, and dried fruit production are summarized below in table 6.5.4.4-1 to 6.5.4.4-3, respectively. All trial data are summarised further below in table 6.5.4.4-4a & b and in greater detail in the Tier 1 summary forms.

Table 6.5.4.4-1: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in apple RACs and processed products of **juice processing** following application of BYI 02960 SL 200

Trial number	**apple fruit (RAC)**	**whole fruit, washed**	**washings**	**pomace, wet**	**pomace, dried**	**raw juice**	**retentate**	**juice**
10-3171-03 Germany	0.10	-*	-*	0.15 *(1.50)*	0.37 *(3.70)*	0.07 *(0.70)*	0.06 *(0.60)*	0.06 *(0.60)*
10-3171-06 Belgium	0.12	0.16 *(1.33)*	<0.04 *(<0.33)*	0.16 *(1.33)*	0.44 *(3.67)*	0.12 *(1.00)*	0.10 *(0.83)*	0.09 *(0.75)*
10-3172-03 Italy	0.07	-*	-*	0.09 *(1.29)*	0.24 *(3.43)*	0.05 *(0.71)*	0.05 *(0.71)*	0.04 *(0.57)*
10.3172-06 Spain	0.15	-*	-*	0.18 *(1.20)*	0.59 *(3.93)*	0.13 *(0.87)*	0.12 *(0.80)*	0.10 *(0.67)*
Mean transfer factors:		*1.33*	*<0.33*	*1.34*	*3.68*	*0.82*	*0.74*	*0.65*

* sample was taken within another processing procedure

"<" the residue in the processed fraction was below LOQ and was set to LOQ for calculating processing factors.

Table 6.5.4.4-2: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in apple RACs and processed products of **sauce processing** following application of BYI 02960 SL 200

Trial number	apple fruit (RAC)	whole fruit, washed	washings	raw sauce	strain rest	sauce
10-3171-03 Germany	0.10	0.11 *(1.10)*	<0.04 *(<0.40)*	0.10 *(1.00)*	0.13 *(1.30)*	0.08 *(0.80)*
10-3171-06 Belgium	0.12	-*	-*	0.12 *(1.00)*	0.19 *(1.58)*	0.10 *(0.83)*
10-3172-03 Italy	0.07	0.06 *(0.86)*	<0.04 *(<0.57)*	0.07 *(1.00)*	0.08 *(1.14)*	0.06 *(0.86)*
10.3172-06 Spain	0.15	0.16 *(1.07)*	<0.04 *(<0.27)*	0.14 *(0.93)*	0.21 *(1.41)*	0.11 *(0.73)*
Mean transfer factors:		*1.01*	*<0.41*	*0.98*	*1.36*	*0.81*

* sample was taken within another processing procedure

"<" the residue in the processed fraction was below LOQ and was set to LOQ for calculating processing factors.

Table 6.5.4.4-3: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in apple RACs and processed products of **dried fruit processing** following application of BYI 02960 SL 200

Trial number	apple fruit (RAC)	peel	fruit, peeled	fruit, dried
10-3171-03 Germany	0.10	0.41 *(4.10)*	0.06 *(0.6)*	0.18 *(1.80)*
10-3171-06 Belgium	0.12	-**	-**	-**
Mean transfer factors:		*4.10*	*0.6*	*1.80*

** no processing of dried fruit was performed in trial 10-3171-06

III. Conclusions

In order to determine "processing" factors for total residues of BYI 02960 from apple fruit to juice, sauce, and dried fruit, processing studies have been conducted.

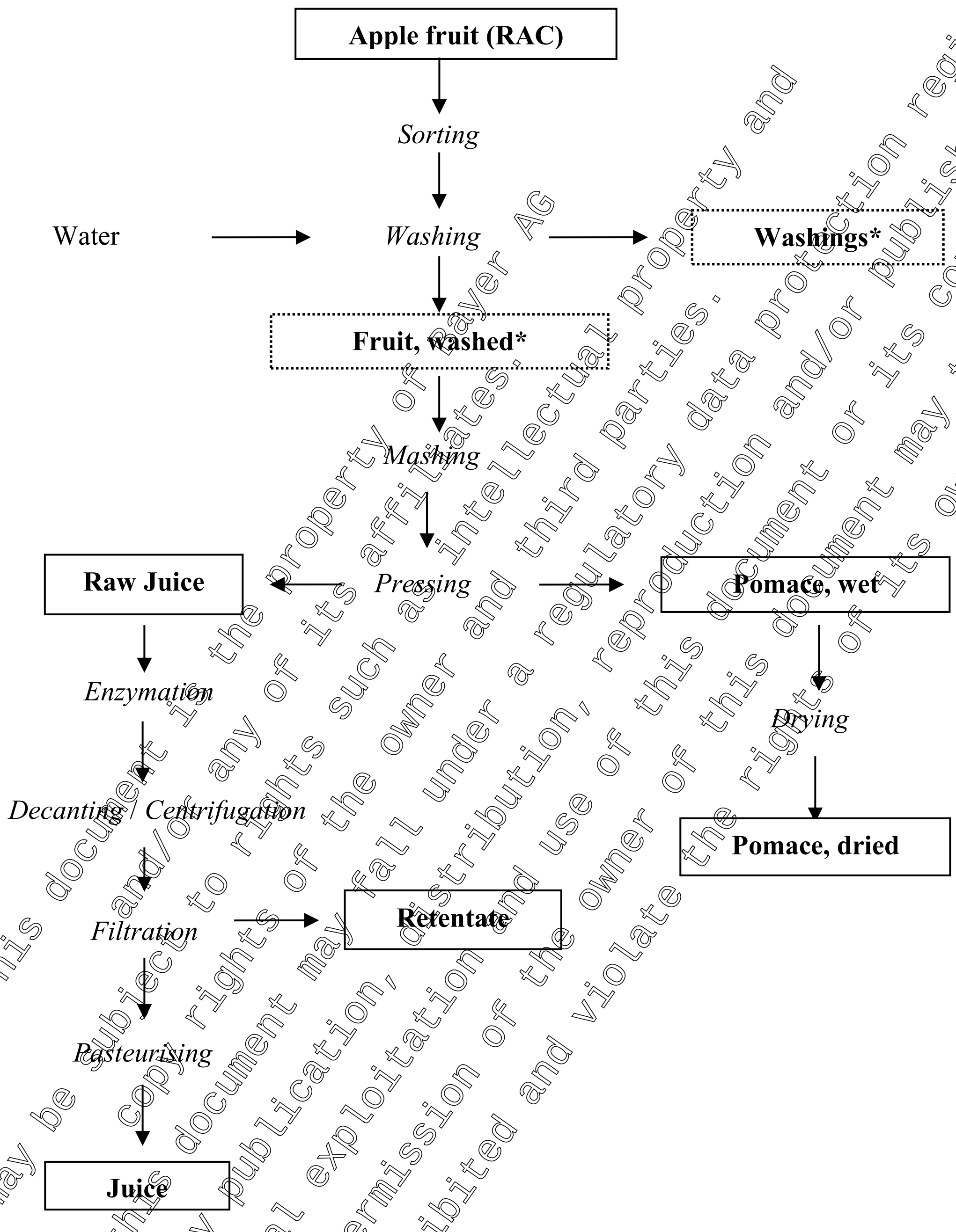
During juice production, the mean value of total residue "processing" factors was of 0.65 for juice and 1.34 and 3.68 for wet and dried pomace, respectively.

During sauce production, the mean value of total residue "processing" factors was 0.98 for raw sauce, 1.36 for strain rest, and 0.81 for sauce.

During dried fruit production the total residue "processing" factor was 1.80 for dried fruit. Peeling fruits before drying is of high consequence, with mean "processing" factors of 0.6 for peeled fruit and 4.10 for peel.

Typical household preparation steps (peeling of fruits before consumption) or typical industrial processes (preparation of juice, sauce) will result in lower total residues of BYI 02960 than in the RAC itself, as the main portion of the residues is in/on the peel. However, preparation of dried fruit or dried pomace results in higher residue concentrations in the processed fraction, due to water loss and subsequent higher residue/weight ratios.

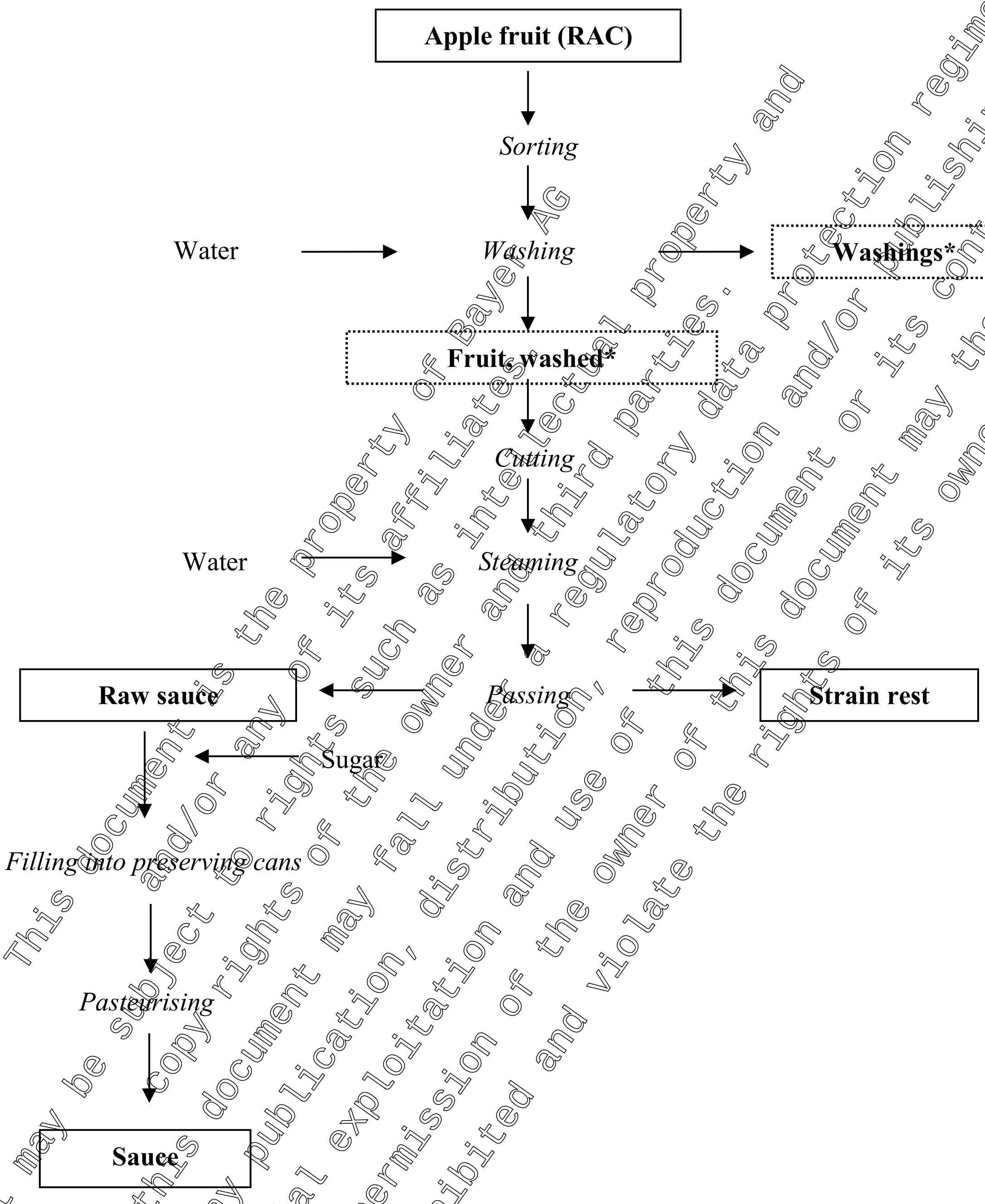
Diagram 6.5.4.4-1: Industrial "processing" of apple fruits into juice



Samples or fractions to be analyzed

*Samples or fractions to be analyzed only in trial 10-3171-06

Diagram 6.5.4.4-2: Industrial "processing" of apple fruits into sauce



Samples or fractions to be analyzed

* Samples or fractions to be analyzed only in trial 10-3171-03 and study 10-3172

Diagram 6.5.4.4-3: Industrial "processing" of apple fruits into dried fruits (only study 10-3171)

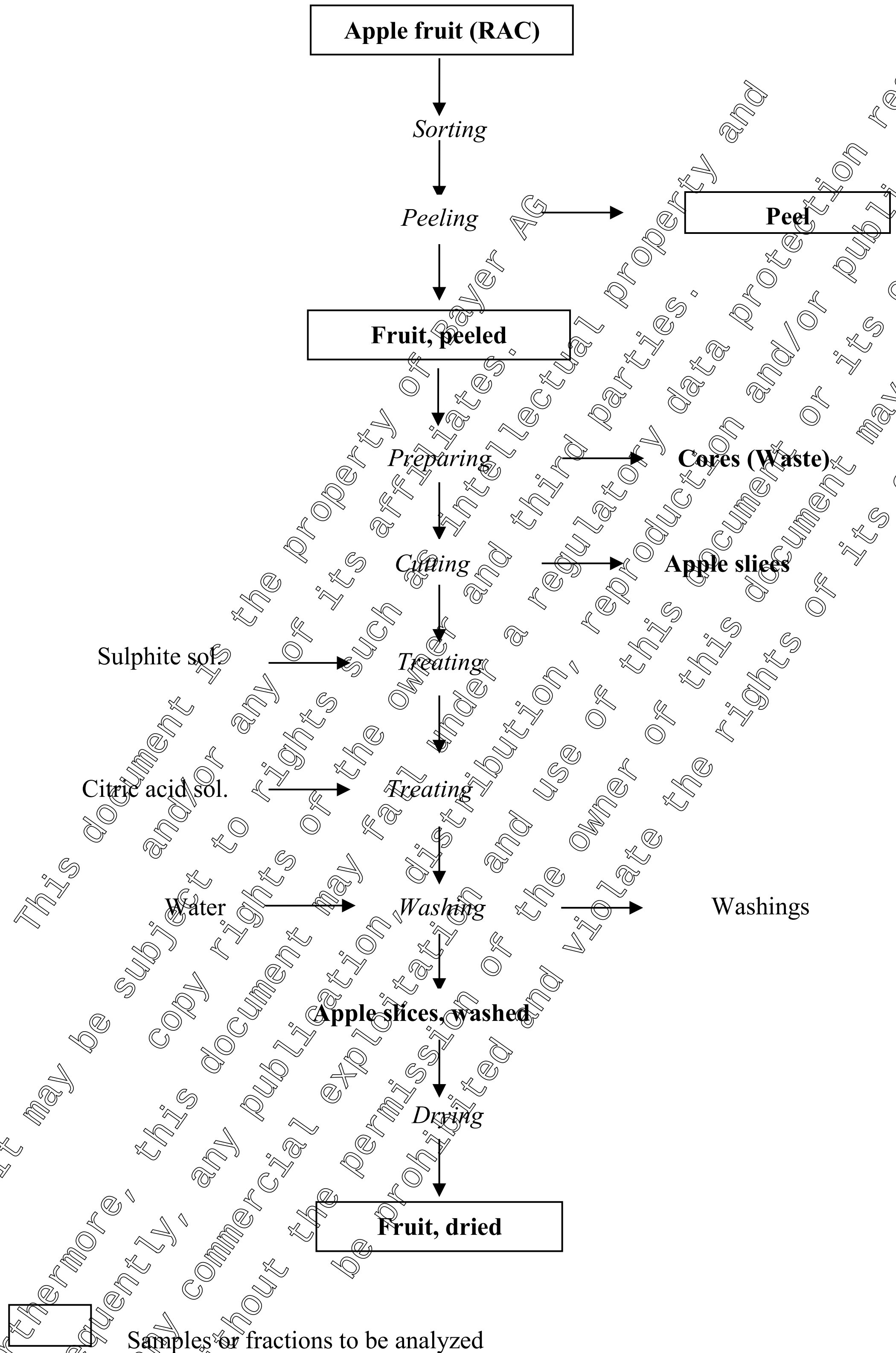


Table 6.5.4.4-4a: Application scenario in residue processing trials conducted in/on **apple** after spraying with BYI 02960 SL 200 in European fields*

Study No. **(Trial No.) Country Location Region Year**	**Crop Variety**	**FL**	**Application**			**GS**	**PHI (days)**
			No.	**kg/ha (a.s.)**	**kg/hl (a.s.)**		
10-3171 (10-3171-03) Germany [redacted] EU-N 2010	apple Jonagold	200 SL	2	0.15 (0.075 kg/(ha×m))	0.015	81	14
10-3171 (10-3171-06) Belgium [redacted] EU-N 2010	apple Elstar	200 SL	2	0.169 (0.075 kg/(ha×m))	0.0150	85	14
10-3172 (10-3172-03) Italy [redacted] EU-S 2010	apple Fuji	200 SL	2	0.15 (0.075 kg/(ha×m))	0.015	83	14
10-3172 (10-3172-06) Spain [redacted] EU-S 2010	apple Galaxia	200 SL	2	0.188 (0.075 kg/(ha×m))	0.015	81	14

FL=formulation GS=growth stage (BBCH-code) at last treatment
EU-N=northern Europe EU-S=southern Europe

* The field part of study 10-3171 was conducted in study 10-2171, and of study 10-3172 in study 10-2172.

Table 6.5.4.4-4b: Results of residue processing trials conducted in/on **apple** after spraying with BYI 02960 SL 200 in European fields

Study No. (Trial No.) Country GLP	Portion analyzed	DALT (days)	Residues (mg/kg) expressed as BYI 02960 BYI 02960	DFA	BYI 02960-DFEAF	total residue of BYI 02960 calc.
10-3171 (10-3171-03) Germany GLP: yes	fruit (RAC)	14	0.07	<0.02	<0.01	0.10
	sauce preparation					
	whole fruit, washed	14	0.08	<0.02	<0.01	0.11
	washings	14	<0.01	<0.02	<0.01	<0.04
	raw sauce	14	0.07	<0.02	<0.01	0.10
	strain rest	14	0.10	<0.02	<0.01	0.13
	sauce	14	0.05	<0.02	<0.01	0.08
	juice preparation					
	pomace, wet	14	0.12	<0.02	<0.01	0.15
	pomace, dried	14	0.34	<0.02	<0.01	0.37
	raw juice	14	0.04	<0.02	<0.01	0.07
	retentate	14	0.03	<0.02	<0.01	0.06
	juice	14	0.03	<0.02	<0.01	0.06
	processing into dried fruit					
	peel	14	0.38	0.02	<0.01	0.41
	fruit, peeled	14	0.03	<0.02	<0.01	0.06
	fruit, dried	14	0.14	0.03	<0.01	0.18
10-3171 (10-3171-06) Belgium GLP: yes	fruit	14	0.09	<0.02	<0.01	0.12
	sauce preparation					
	raw sauce	14	0.09	<0.02	<0.01	0.12
	strain rest	14	0.16	<0.02	<0.01	0.19
	sauce	14	0.07	<0.02	<0.01	0.10
	juice preparation					
	whole fruit, washed	14	0.13	<0.02	<0.01	0.16
	washings	14	<0.01	<0.02	<0.01	<0.04
	pomace, wet	14	0.13	<0.02	<0.01	0.16
	pomace, dried	14	0.41	0.02	<0.01	0.44
	raw juice	14	0.09	<0.02	<0.01	0.12
	retentate	14	0.07	<0.02	<0.01	0.10
	juice	14	0.06	<0.02	<0.01	0.09

DALT=days after last treatment; RAC = raw agricultural commodity

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Table 6.5.4.4-4b (cont'd): Results of residue processing trials conducted in/on **apple** after spraying with BYI 02960 SL 200 in European fields

Study No. (Trial No.) Country GLP	Portion analyzed	DALT (days)	Residues (mg/kg) expressed as BYI 02960 BYI 02960	DFA	BYI 02960-DFEAF	total residue of BYI 02960 calc.
10-3172 (10-3172-03) Italy GLP: yes	fruit (RAC)	14	0.04	<0.02	<0.01	0.07
	sauce preparation					
	whole fruit, washed	14	0.03	0.02	<0.01	0.06
	washings	14	<0.01	<0.02	<0.01	<0.04
	raw sauce	14	0.04	0.02	<0.01	0.07
	strain rest	14	0.05	0.02	<0.01	0.08
	sauce	14	0.03	<0.02	<0.01	0.06
	juice preparation					
	pomace, wet	14	0.06	<0.02	<0.01	0.09
	pomace, dried	14	0.20	0.03	<0.01	0.24
	raw juice	14	0.02	<0.02	<0.01	0.05
	retentate	14	0.02	<0.02	<0.01	0.05
	juice	14	0.01	<0.02	<0.01	0.04
10-3172 (10-3172-06) Spain GLP: yes	fruit (RAC)	14	0.10	0.04	<0.01	0.15
	sauce preparation					
	whole fruit, washed	14	0.11	0.04	<0.01	0.16
	washings	14	<0.01	<0.02	<0.01	<0.04
	raw sauce	14	0.09	0.04	<0.01	0.14
	strain rest	14	0.17	0.03	<0.01	0.21
	sauce	14	0.07	0.03	<0.01	0.11
	juice preparation					
	pomace, wet	14	0.13	0.03	<0.01	0.18
	pomace, dried	14	0.49	0.09	<0.01	0.59
	raw juice	14	0.08	0.04	<0.01	0.13
	retentate	14	0.07	0.04	<0.01	0.12
	juice	14	0.06	0.03	<0.01	0.10

DALT=days after last treatment, RAC = raw agricultural commodity

Table 6.5.4.4-5: Recovery data for BYI 02960 in **apple** and **apple matrices**

Study **Trial No. Plot No. GLP Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortifi-cation level** (mg/kg)	**Recovery (%)** Individual recoveries	Min	Max	Mean	RSD
*10-3171** (10-3171-03) and (10-3171-06) GLP: yes 2010	apple	fruit	BYI 02960	9	0.01	89; 90; 94; 94; 96; 99; 99; 100; 107	89	107	96	5.8
				5	0.10	88; 90; 94; 96; 99	88	99	93	4.8
				6	1.0	76; 88; 90; 92; 94; 101	76	101	90	9.2
				20	overall		76	107	94	7.0
			DFA	6	0.02	87; 88; 89; 92; 96; 100	87	100	92	5.5
				3	0.05	83; 90; 93	83	93	89	5.8
				1	0.20	92	92	92	92	
				4	0.50	90; 91; 93; 96	90	96	93	2.9
				6	1.0	73; 82; 83; 88; 91; 93	73	93	85	8.6
				20	overall		73	100	90	6.6
			BYI 02960-DFEAF	9	0.01	75; 81; 85; 86; 87; 88; 89; 91; 95	75	95	86	6.7
				5	0.10	69; 92; 94; 96; 97	69	97	90	13.0
				6	1.0	70; 83; 90; 94; 96; 100	70	100	89	12.3
				20	overall		69	100	88	9.9
		whole fruit, washed	BYI 02960	1	0.01	93	93	93	93	
				1	0.10	86	86	86	86	
				2	overall		86	93	90	
			DFA	1	0.02	97	97	97	97	
				1	0.20	87	87	87	87	
				2	overall		87	97	92	
			BYI 02960-DFEAF	1	0.01	91	91	91	91	
				1	0.10	83	83	83	83	
				2	overall		83	91	87	
		strain rest	BYI 02960	1	1.0	80	80	80	80	
				1	overall		80	80	80	
			difluoroacetic acid	1	1.0	76	76	76	76	
				1	overall		76	76	76	
			BYI 02960-DFEAF	1	1.0	75	75	75	75	
				1	overall		75	75	75	

* These recovery determinations were performed during the conduct of the studies 10-3171 and 10-3172. Therefore, recoveries presented for study 10-3171 are also valid for study 10-3172.

Remark re. fruit: also covers *whole fruit, washed*; *strain rest*; *pomace, wet*; *pomace, dried*; *retentate*; *peel*; *fruit, peeled*; and *fruit, dried*
Remark re. sauce: also covers *raw sauce*
Remark re. juice: also covers *washings* and *raw juice*

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Table 6.5.4.4-5 (cont'd): Recovery data for BYI 02960 in **apple** and **apple matrices**

Study **Trial No. Plot No. GLP Year**	**Crop**	**Portion analyzed**	**a.s./metabolite**	**n**	**Fortification level** (mg/kg)	**Recovery (%)** Individual recoveries	**Min**	**Max**	**Mean**	**RSD**
*10-3171** (10-3171-03) and (10-3171-06) GLP: yes 2010	apple	sauce	BYI 02960	5	0.01	99; 100; 102;102; 104	99	104	101	1.9
				3	0.10	96; 98; 99	96	99	98	1.6
				8	overall		96	104	100	2.6
			DFA	5	0.02	88; 89; 90; 93; 93	88	93	91	2.5
				3	0.20	80; 82; 84	80	84	82	2.4
				8	overall		80	93	87	5.6
			BYI 02960-DFEAF	5	0.01	90; 102; 103; 108; 114	90	114	103	8.6
				3	0.10	95; 100; 106	95	106	100	5.5
				8	overall		90	114	102	7.3
		pomace, wet	BYI 02960	1	1.0	94	94	94		
				1	overall		94	94		
			DFA	1	1.0	82	82	82		
				1	overall		82	82		
			BYI 02960-DFEAF	1	1.0	85	85	85		
				1	overall		85	85		
		juice	BYI 02960	5	0.01	105; 110; 112; 114; 114	105	114	111	3.4
				3	0.10	114; 115; 116	114	116	115	0.9
				8	overall		105	116	113	3.2
			DFA	5	0.02	112; 113; 114; 116; 120	112	120	115	2.7
				3	0.20	116; 116; 118	116	118	117	1.0
				8	overall		112	120	116	2.3
			BYI 02960-DFEAF	5	0.01	100; 101; 104; 108; 109	100	109	104	3.9
				3	0.10	107; 107; 109	107	109	108	1.1
				8	overall		100	109	106	3.4

* These recovery determinations were performed during the conduct of the studies 10-3171 and 10-3172. Therefore, recoveries presented for study 10-3171 are also valid for study 10-3172.

Remark re. fruit: also covers *whole fruit, washed*; *strain rest*; *pomace, wet*; *pomace, dried*; *retentate*; *peel*; *fruit, peeled*; and *fruit, dried*
Remark re. sauce: also covers *raw sauce*
Remark re. juice: also covers *washings* and *raw juice*

IIA 6.5.4.5 Peach

Report:	**KIIA 6.5.4.5/01, [redacted], [redacted]; 2012**
Title:	Determination of the residues of BYI 02960 in/on peach and the processed fractions (whole fruit, washed; washings; peel; fruit peeled and preserve) after spraying of BYI 02960 SL 200 in the field in Spain and Italy
Report No. & Document No.:	10-3216, dated October 8, 2012 M-439376-01-1
Guidelines:	– EU Council Directive 91/414/EEC – EC Guidance working document 7029/VI/95 rev.5 – EU Guidance Working Document 7035/VI/95 rev. 5 – OECD Guideline for the Testing of Chemicals No. 508, Magnitude of the Pesticide Residues in Processed Commodities – EPA Ref. OPPTS 860.1520.SUPP
GLP:	yes (certified laboratory)

I. Materials and Methods

Due to the presence of measurable residues of BYI 02960 on harvested fruit samples from field residue trials performed according to the intended commercial use conditions as well as to the nature of the use of fruits and vegetables, investigations on the effects of processing have been conducted. The samples of peach (fruit) to be processed and reference raw agricultural commodity (RAC) samples originate from two supervised residue trials (10-2216-02, 10-2216-03) in the conduct of study 10-2216 (to be submitted later; data available on request). Among the supervised residue trials in that study conducted during the 2010 season, two (one each in Spain and Italy) yielded samples used for processing purposes in the study reported here, 10-3216. Samples for processing were taken in order to determine the total residues of BYI 02960 in unprocessed peach fruit and then in the primary processed product preserved fruit (=canned fruit), as well as in intermediate fractions ([redacted] & [redacted], 2012; KIIA 6.5.4.5/01).

In the field trials, BYI 02960 SL 200 was sprayed twice with an interval of 14 days at an application rate of approx. 75 g a.s./(ha×m) and a water volume of 500 L/ha. The last application was conducted at a pre-harvest interval of 14 days.

After processing (described below), residue analysis was performed according to method 01304 (for more information, cf. IIA 4.3). The limits of quantitation were 0.01 mg/kg (BYI 02960 and DFEAF) and 0.02 mg/kg (DFA), expressed in parent compound equivalents, yielding a calculated total-residue LOQ of 0.04 mg/kg, in all matrices. Prior and parallel to the residue analysis, the method was validated by recovery experiments.

<u>Processing procedure:</u>
The processing of peach samples was designed to simulate procedures of peach fruit into preserved (=canned) fruit.

Peach fruit was washed, peeled, and depitted. Depitted fruit was sterilized at 92°C-94°C for approx. 1-2 min. The total time of the sterilization cycles including heating and cooling was: 21-29 min. The process is illustrated in flow diagram 6.5.4.5-1.

II. Findings

The validation of the sample materials peach fruit, peel, and preserve was conducted within study 10-3216. Concurrent recoveries of BYI 02960 and its metabolites DFA and DFEAF were obtained from samples of peach matrices (peach fruit, peel, preserve, and washed whole fruit). The recoveries for the sample materials *fruit* and *whole fruit, washed* are also representative for the sample materials *washings* and *fruit, peeled*.

Concurrent recovery samples for parent compound and DFEAF were spiked at levels of 0.01 and 0.50 mg/kg (expressed in BYI 02960 equivalents) for peach fruit, at levels of 0.01 and 0.10 mg/kg for peel, preserve, and washed whole fruit, and additionally at 1.0 mg/kg for peel. Mean recoveries in all matrices were 73-112%, with RSDs in the larger validations sets (n > 2) of 1.7-18.4%; n=1-5.

For DFA, concurrent recovery samples for of peach matrices were spiked at levels of 0.02, and 0.50 mg/kg (expressed in BYI 02960 equivalents) for peach fruit, at levels of 0.02 and 0.20 mg/kg for peel, preserve, and washed whole fruit, and additionally at 1.0 mg/kg for peel. Mean recoveries in all matrices were 93-112%, with RSDs in the larger validations sets (n > 2) of 1.5-12.3%; n=1-5.

A tabular summary of the recovery values is presented below in table 6.5.4.5-3.

The total residues of BYI 02960 (parent compound plus DFA and DFEAF) in the harvested peaches fruit at day14 ranged from 0.14-0.26 mg/kg. These values were used for the calculation of "processing" factors.

● Preserve production:

Whole fruit, washed: The levels of the total residue of BYI 02960 in *whole fruit, washed* were from 0.11-0.28 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.95 (range: 0.8-1.1, n=2), showing that washing of fruit does not relevantly affect the residue situation for the total residue of BYI 02960.

Washings: The levels of the total residue of BYI 02960 in *washings* were from 0.04-0.06 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.25 (range: 0.2-0.3, n=2).

Peel: In peel, the levels of the total residue of BYI 02960 were 0.24-0.92 mg/kg. The measured residue levels lead to a mean "processing" factor of 2.6 (range: 1.7-3.5, n=2), showing a concentration of the total residues of BYI 02960 on peel.

Fruit, peeled: The levels of the total residue of BYI 02960 in *fruit, peeled* were from 0.06-0.14 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.45 (range: 0.4-0.5, n=2), showing a reduction of the residue level of the total residue of BYI 02960 during peeling of peach fruit.

Preserve: The levels of the total residue of BYI 02960 in *preserve* were from 0.08-0.11 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.5 (range: 0.4-0.6, n=2), showing a reduction of the residue level of the total residue of BYI 02960 during peach preserve production.

The transfer factors for the total residues of BYI 02960 are summarized below in table 6.5.4.5-1. All trial data are summarised further below in table 6.5.4.5-2a & b and in greater detail in the Tier 1 summary forms.

Table 6.5.4.5-1: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in peach RACs and processed products (**processing into preserve**) following application of BYI 02960 SL 200

Trial number	peach fruit	whole fruit, washed	washings	peel	fruit, peeled	preserve
10-3216-02	0.14	0.11 *(0.8)*	0.04 *(0.3)*	0.24 *(1.7)*	0.06 *(0.4)*	0.08 *(0.6)*
10-3216-03	0.26	0.28 *(1.1)*	0.06 *(0.2)*	0.92 *(3.5)*	0.14 *(0.5)*	0.11 *(0.4)*
Mean transfer factors:		*0.95*	*0.25*	*2.6*	*0.45*	*0.5*

III. Conclusions

In order to determine "processing" factors for total residues of BYI 02960 from peach fruit into preserved fruit (=canned fruit), processing studies have been conducted. The mean value of total residue "processing" factors for preserve was 0.5. These findings show that typical preparation steps for preserve production will result in lower total residues of BYI 02960 than in the RAC itself. The relevant processing step which results in reduction of total residues of BYI 02960 is the peeling of the fruit, while washing does not relevantly affect the residue level.

Diagram 6.5.4.5-1: “processing" of peach – preparation of preserve

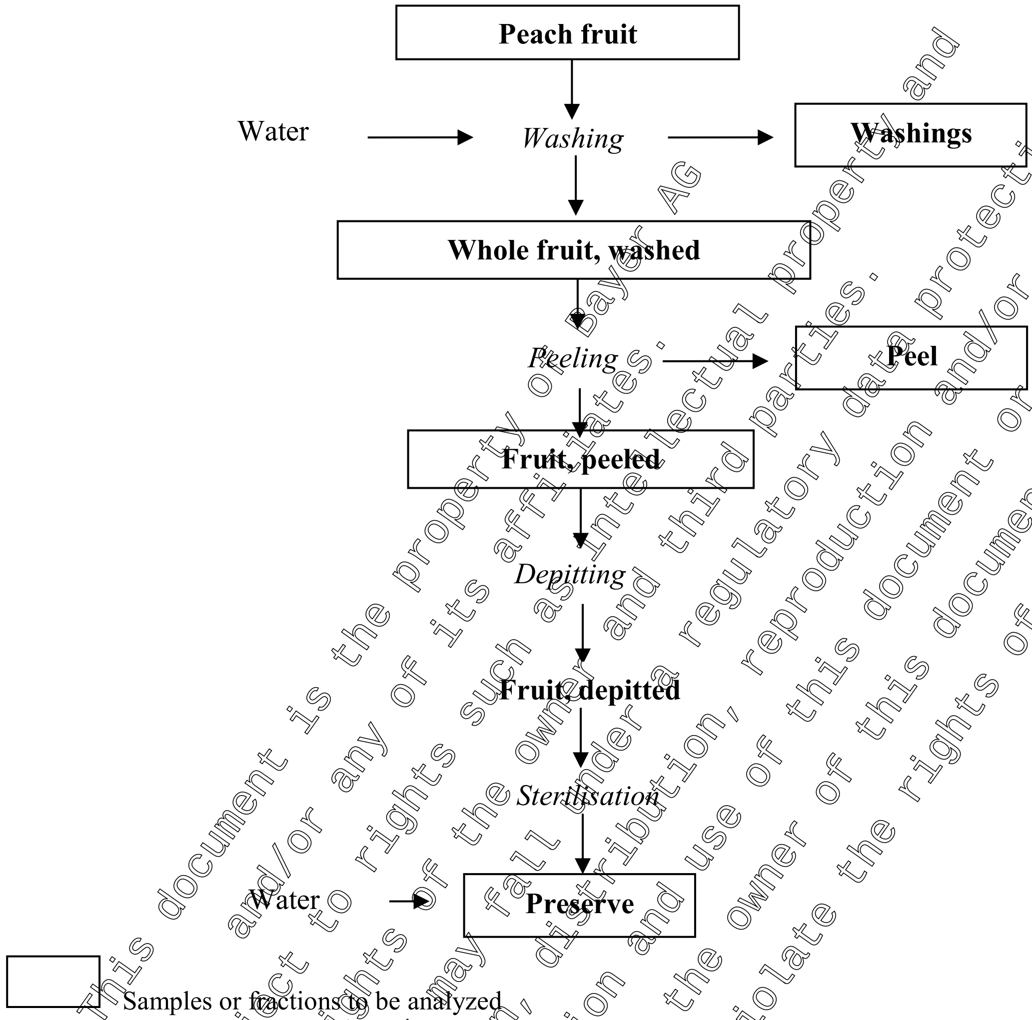

Table 6.5.4.5-2a: Application scenario in residue processing trials conducted in/on **peach** after spraying with BYI 02960 SL 200 in southern European fields*

Study No. **(Trial No.) Country Location Region Year**	**Crop Variety**	**FL**	**Application**			**GS**	**PHI (days)**
			No.	**kg/ha (a.s.)**	**kg/hl (a.s.)**		
10-3216 (10-3216-02) Spain [redacted] Sevilla EU-S 2010	peach Transvalia	200 SL	2	0.13 (0.075 kg/(ha×m))	0.015	81	14
10-3216 (10-3216-03) Italy [redacted] EU-S 2010	peach Flaminia	200 SL	2	0.15 (0.075 kg/(ha×m))	0.015	81	14

FL=formulation GS=growth stage (BBCH-code) at last treatment
EU-S=southern Europe
* The field part of study 10-3216 was conducted in study 10-2216.

Table 6.5.4.5-2b: Results of residue processing trials conducted in/on **peach** after spraying with BYI 02960 SL 200 in European fields*

Study No. **(Trial No.) Country** **GLP**	**Portion analyzed**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
			BYI 02960	**DFA**	**BYI 02960-DFEAF**	**total residue of BYI 02960 calc.**
10-3216 (10-3216-02) Spain GLP: yes	peach fruit (RAC)	14	0.09	0.04	<0.01	0.14
	Preserve production					
	whole fruit, washed	14	0.05	0.05	<0.01	0.11
	washings	14	0.01	<0.02	<0.01	0.04
	peel	14	0.16	0.06	<0.01	0.24
	fruit peeled	14	0.02	0.03	<0.01	0.06
	preserve	14	0.03	0.03	<0.01	0.08
10-3216 (10-3216-03) Italy GLP: yes	peach fruit (RAC)	14	0.20	0.05	<0.01	0.26
	Preserve production					
	whole fruit, washed	14	0.21	0.06	<0.01	0.28
	washings	14	0.03	<0.02	<0.01	0.06
	peel	14	0.84	0.07	<0.01	0.92
	fruit peeled	14	0.08	0.05	<0.01	0.14
	preserve	14	0.07	0.03	<0.01	0.11

DALT=days after last treatment; RAC = raw agricultural commodity

* The field part was conducted within study 10-2216.

Table 6.5.4.5-3: Recovery data for BYI 02960 in **peach** and **peach matrices**

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortifi-cation level** (mg/kg)	**Recovery (%)**				
						Individual recoveries	**Min**	**Max**	**Mean**	**RSD**
10-2216 (10-2216-01) to (10-2216-04) GLP: yes 2010	peach	fruit	BYI 02960	5	0.01	92; 94; 100; 102; 105	92	105	99	5.5
				3	0.50	92; 94; 98	92	98	95	3.2
				8	overall		92	105	97	5.0
			DFA	5	0.02	90; 92; 92; 94; 103	90	103	94	5.4
				3	0.50	91; 91; 97	91	97	93	3.7
				8	overall		90	103	94	4.6
			BYI 02960-DFEAF	5	0.01	84; 88; 99; 100; 101	84	101	94	8.3
				3	0.50	71; 71; 78	71	78	73	5.5
				8	overall		71	101	87	14.6
10-3216 (10-3216-01) to (10-3216-04) GLP: yes 2010	peach	peel	BYI 02960	4	0.01	111; 111; 112; 115	111	115	112	1.7
				3	0.10	105; 106; 109	105	109	107	2.0
				1	1.0	93	93	93		
				8	overall		93	115	108	6.3
			DFA	5	0.02	111; 111; 112; 113; 115	111	115	112	1.5
				3	0.20	110; 113; 113	110	113	112	1.5
				1	1.0	90	90	90		
				9	overall		90	115	110	6.9
			BYI 02960-DFEAF	5	0.01	102; 103; 104; 114; 114	102	114	107	5.6
				3	0.10	98; 103; 104	98	104	102	3.2
				1	1.0	97	97	97		
				9	overall		97	114	104	5.8

Remark re. fruit: also covers *washings* and *peeled fruit*

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Table 6.5.4.5-3 (cont'd): Recovery data for BYI 02960 in **peach** and **peach matrices**

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortifi-cation level** (mg/kg)	**Recovery (%)** Individual recoveries	Min	Max	Mean	RSD
10-3216 (10-3216-01) to (10-3216-04) GLP: yes 2010	peach	preserve	BYI 02960	5	0.01	82; 115; 115; 116; 118	82	118	109	14.0
				3	0.10	103; 109; 117	103	117	110	6.4
				8	overall		82	118	109	11.1
			DFA	5	0.02	84; 110; 111; 115; 116	84	116	107	12.3
				3	0.20	104; 109; 114	104	114	109	4.6
				8	overall		84	114	108	9.6
			BYI 02960-DFEAF	5	0.01	67; 103; 107; 108; 111	67	111	99	18.4
				3	0.10	101; 112; 116	101	116	110	7.1
				8	overall		67	116	103	14.9
		whole fruit, washed	BYI 02960	1	0.01	108	108	108		
				1	0.10	105	105	105		
				2	overall		105	108	107	
			DFA	1	0.02	107	107	107		
				1	0.20	111	111	111		
				2	overall		107	111	109	
			BYI 02960-DFEAF	1	0.01	108	108	108		
				1	0.10	109	109	109		
				2	overall		108	109	109	

Remark re. *whole fruit, washed*: also covers *washings* and *peeled fruit*

IIA 6.5.4.6 Grape

Report:	**KIIA 6.5.4.6/01, [redacted], [redacted] & [redacted]; 2012**
Title:	Determination of the residues of BYI 02960 in/on grape and the processed fractions (pomace, grape; must; wine at bottling; wine at first taste test; juice, pasteurised; jelly; washings; raisin waste; raisin) after spraying of BYI 02960 SL 200 in the field in Germany
Report No. & Document No.:	10-3406, dated July 4, 2012 M-433545-01-1
Guidelines:	– EU Council Directive 91/414/EEC – EC Guidance working document 7029/VI/95 rev.5 – EU Guidance Working Document 7035/VI/95 rev. 5 – OECD Guideline for the Testing of Chemicals No. 508, Magnitude of the Pesticide Residues in Processed Commodities – EPA Ref. OPPTS 860.1520 SUPP
GLP:	yes (certified laboratory)

I. Materials and Methods

Due to the presence of measurable residues of BYI 02960 on harvested grapes determined in samples from field residue trials performed according to the intended commercial use conditions (see point IIA 6.3.1.4) as well as to the nature of grape use (preparation and consumption patterns), investigations on the effects of industrial processing have been conducted. Four trials were conducted in the northern European residue region, all in Germany, in order to determine the total residues of BYI 02960 in unprocessed bunches of grapes and in the destemmed fruit itself ("berries") and then in the primary processing products wine, juice, raisins, and jelly, as well as in intermediate fractions ([redacted], [redacted] & [redacted], 2012; KIIA 6.5.4.6/01).

In the field trials, BYI 02960 SL 200 was sprayed once at an application rate of approx. 300 g a.s./ha and a water volume of 800 L/ha. The application was conducted at a pre-harvest interval of 14 days. The application scheme reflected an overdosing (approx. 3× higher than the envisaged EU worst case) in a spray application scheme, in order to ensure that detectable residues would be found in the relevant raw commodities at harvest, thus allowing elucidation of processing factors.

After processing (described below), residue analysis was performed according to method 01304 (for more information, cf. IIA 4.3). The limits of quantitation were 0.01 mg/kg (BYI 02960 and DFEAF) and 0.02 mg/kg (DFA), expressed in parent compound equivalents, yielding a calculated total-residue LOQ of 0.04 mg/kg, in all matrices. Prior and parallel to the residue analysis, the method was validated by recovery experiments.

<u>Processing procedures</u>:
Grape "processing" was designed to simulate industrial procedures of bunches of grapes into juice and wine as well as jelly and raisins.

<u>Juice preparation</u>:
Unwashed grapes were crushed in a grape mill (crusher) and pressed to extract the liquid. A specimen of *pomace, grape* was taken. After clarification, a specimen of *must* was taken. Subsequently, the

must (raw juice) was pasteurised (at 83-87°C for approx. 2 min). A specimen of *juice, pasteurised* was taken.

Vinification:
Pure culture yeast and nutrient salt were added to the raw juice to start the fermentation. After termination of the fermentation and clarification, $K_2S_2O_5$ (SO_2) was added and the intermediate was transferred into new vessels, leaving the sediment in the original vessel. Subsequent to this first transfer (racking), bentonite was added to absorb the proteins. Upon completion of the clarification, the second transfer of wine was carried out and $K_2S_2O_5$ (SO_2) was added. The young wine was filtered through filter pads after a resting time (clarification). *Wine at bottling* (young wine) was sampled. A portion of the remaining young wine was bottled for maturation and taken as an intermediate sample for wine at first taste test (white wine). The intermediate was stored at 5-12°C for approx. 6.5 months. After maturation time, *wine at first taste test* (white wine) was sampled for analysis.

Jelly production:
For the production of jelly, raw juice and gelling sugar were mixed and heated up. After approx. 4 min cooking time, lemon juice was added and mixed with the cooked product. After cooling down, specimens of *jelly* were taken.

Raisin production:
Bunches of grapes were manually washed in tap water for three minutes. The ratio of water to fruit was approx. 1:1. The water covered the fruit. A specimen of washings was taken. Washed grape bunches were put in boiling water for 8-10 seconds and afterwards they were manually washed (3 min) with cold tap water in a vessel. The ratio of water to fruit was again approx. 1:1. The water covered the bunch of grapes. Then the bunches were dried in an oven (approx. 66-74°C) for approx. 24 hours, until a moisture content of 10-14% was achieved. After drying, raisins were manually removed from the stalks. Specimens of *raisin* and *raisin waste* (stalks) were sampled.

The processes are illustrated in flow diagrams 6.5.4.6-1 – 6.5.4.6-6.

II. Findings

The validation of the sample materials bunch of grape, jelly, raisin, and wine at bottling was conducted within study 10-3406. Concurrent recoveries were obtained from samples of grape matrices (bunches of grapes, pomace, wine at bottling, jelly, and raisin). The recoveries for the sample material *bunch of grape* are also representative for *berry*. The sample material *jelly* is also representative for *must* and *juice*. The sample material *raisin* is also representative for *raisin waste*. The sample material *wine at bottling* is also representative for *wine at first taste test*.

In all mentioned matrices, recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg and 0.10 mg/kg, as well as at 2.0 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries for all matrices were 64-106%, with RSDs in the larger validations sets (n > 2) of 0.6-16.7%; n=1-5.

For DFA, concurrent recovery samples for grape matrices (bunches of grapes, pomace, wine at bottling, jelly, and raisin) were spiked at levels of 0.02, 0.20, and 2.0 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries in all matrices were 61-96%, with RSDs in the larger validations sets (n > 2) of 0.6-7.0%; n = 1-5.

A tabular summary of the recovery values is presented below in table 6.5.4.6-4.

The total residues of BYI 02960 (parent compound plus DFA and DFEAF) in the harvested bunches of grape at day14 ranged from 0.40-0.68 mg/kg. For the sample material berry, the total residues of BYI 02960 harvested at day14 ranged from 0.23-0.56 mg/kg. Residues in/on berries were generally in the same concentration range as for bunch of grapes, with the exception of trial 10-3406-04 where the total residues of BYI 02960 in/on bunch of grapes were 0.48 mg/kg and 0.23 mg/kg in/on berries. Residue values from bunches of grapes were used for the calculation of "processing" factors.

● Juice production:

Pomace, grape: The levels of the total residue of BYI 02960 in grape pomace were from 0.71-1.1 mg/kg. The measured residue levels lead to a mean "processing" factor of 1.7 (range: 1.6-1.8, n=4), showing an accumulation of total residues of BYI 02960 in pomace.

Must: The levels of the total residue of BYI 02960 in must were from 0.22-0.36 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.67 (range: 0.46-0.85, n=4), showing a reduction of the residue level of the total residue of BYI 02960 for must during the juice production.

Juice, pasteurised: In *juice, pasteurised*, levels of the total residue of BYI 02960 were 0.34 mg/kg in both processed specimens. The measured residue levels lead to a mean "processing" factor of 0.68 (range: 0.50-0.85, n=2), showing a reduction of the residue level of the total residue of BYI 02960 during juice production. The results show that clarification and pasteurisation of must do not affect the residue level of the total residue of BYI 02960.

● Vinification:

Wine at first taste test: In *wine at first taste test*, the levels of the total residue of BYI 02960 were 0.16-0.23 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.42 (range: 0.24-0.56, n=4), showing a reduction of the residue level of the total residue of BYI 02960 during wine production.

Wine at bottling: In *wine at bottling*, the levels of the total residue of BYI 02960 were 0.21-0.32 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.56 (range: 0.31-0.78, n=4), showing a reduction of the residue level of the total residue of BYI 02960 during wine production.

In comparison to results obtained for must production, there is no apparent additional reduction in total residues of BYI 02960 during vinification, showing that the main reduction is achieved by the separation of the grape pomace.

● Jelly production:

The levels of the total residue of BYI 02960 in jelly were from 0.12-0.16 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.31 (range: 0.22-0.40, n=2), showing a reduction of the residue level of the total residue of BYI 02960 during jelly production. The process of jelly production leads to an additional reduction of residues in comparison to must production.

● Raisin production:

Raisin: The level of the total residue of BYI 02960 in raisins was 1.4 mg/kg in both trials. The measured residue level lead to a mean "processing" factor of 2.5 (range: 2.1-2.5, n=2), showing an accumulation during the production of raisins.

Raisin waste: The level of the total residue of BYI 02960 in raisin waste was 1.3-1.5 mg/kg. The measured residue level lead to a mean "processing" factor of 2.5 (range: 2.2-2.7, n=2), showing the same accumulation of the total residues of BYI 02960 in raisin waste (stalks) as for raisins themselves.

Washings: In washings of bunches of grapes during the processing of raisins, the levels of the total residue of BYI 02960 were 0.06 mg/kg in both samples analyzed. The measured residue levels lead to a mean "processing" factor of 0.11 (range: 0.09-0.13, n=2), showing a reduction of the residue level of the total residue of BYI 02960 for bunches of grape during the washing process.

The transfer factors for the total residues of BYI 02960 are summarized below in table 6.5.4.6-1 to 6.5.4.6-2. All trial data are summarised further below in table 6.5.4.6-3a & b and in greater detail in the Tier 1 summary forms.

Table 6.5.4.6-1: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in grape RACs and processed products (**processing into juice and wine**) following application of BYI 02960 SL 200

Trial number	bunch of grapes	pomace, grape	must	juice, pasteurised	wine at first taste test	wine at bottling
10-3406-01	0.40	0.72 *(1.8)*	0.34 *(0.85)*	0.34 *(0.85)*	0.21 *(0.53)*	0.28 *(0.70)*
10-3406-02	0.41	0.71 *(1.7)*	0.35 *(0.85)*	-*	0.23 *(0.56)*	0.32 *(0.78)*
10-3406-03	0.68	1.1 *(1.6)*	0.36 *(0.53)*	0.34 *(0.50)*	0.16 *(0.24)*	0.21 *(0.31)*
10-3406-04	0.48	0.81 *(1.7)*	0.22 *(0.46)*	-*	0.16 *(0.33)*	0.22 *(0.46)*
Mean transfer factors:		*1.7*	*0.67*	*0.68*	*0.42*	*0.56*

* Processing of juice was not conducted in this trial.

Table 6.5.4.6-2: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in grape RACs and processed products (**processing into jelly and raisins**) following application of BYI 02960 SL 200

Trial number	**bunch of grapes**	**jelly**	**washings**	**raisin waste**	**raisin**
10-3406-01	0.40	0.16 *(0.40)*	-*	-*	-*
10-3406-02	0.41	-*	-*	-*	-*
10-3406-03	0.68	0.12 *(0.22)*	0.06 *(0.09)*	1.5 *(2.2)*	1.4 *(2.1)*
10-3406-04	0.48	-*	0.06 *(0.13)*	1.3 *(2.7)*	1.4 *(2.9)*
Mean transfer factors:		*0.31*	*0.11*	*2.5*	*2.5*

* Processing of this product was not conducted in this trial.

III. Conclusions

In order to determine "processing" factors for total residues of BYI 02960 from bunches of grapes into juice and wine as well as jelly and raisins, processing studies have been conducted. The mean total residue "processing" factor for pasteurised juice was 0.68, and 0.56 to wine at bottling. For the production of jelly and raisins, the mean total residue "processing" factors were 0.31 and 2.5, respectively. Typical industrial preparation steps for juice, wine, and jelly production will result in lower total residues of BYI 02960 than in the RAC itself, while production of raisins results in a concentration of total residues of BYI 02960.

Diagram 6.5.4.6-1: Industrial "processing" of grape – pasteurized juice (white grapes)

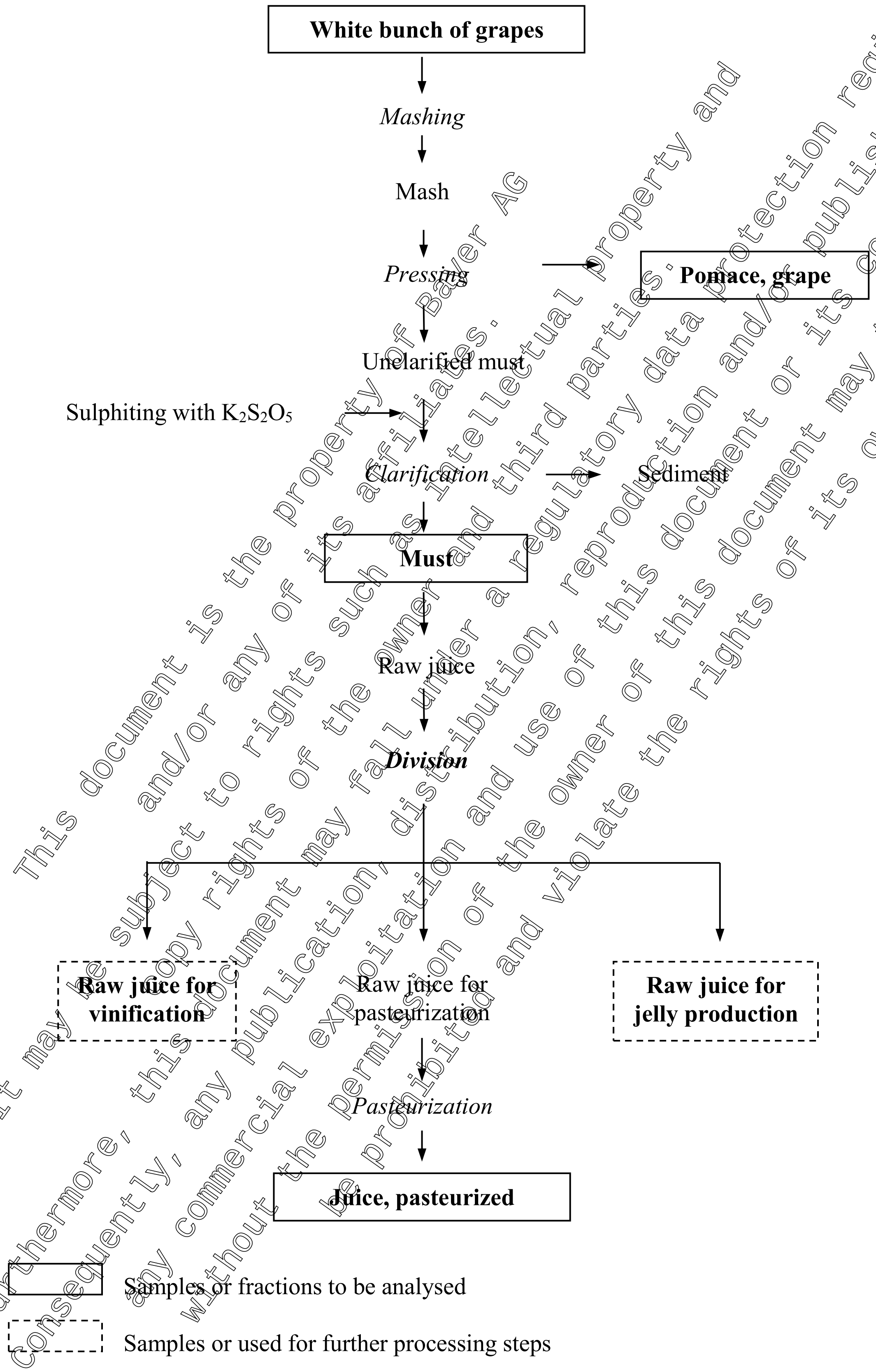


Diagram 6.5.4.6-2: Industrial "processing" of wine (white grapes)

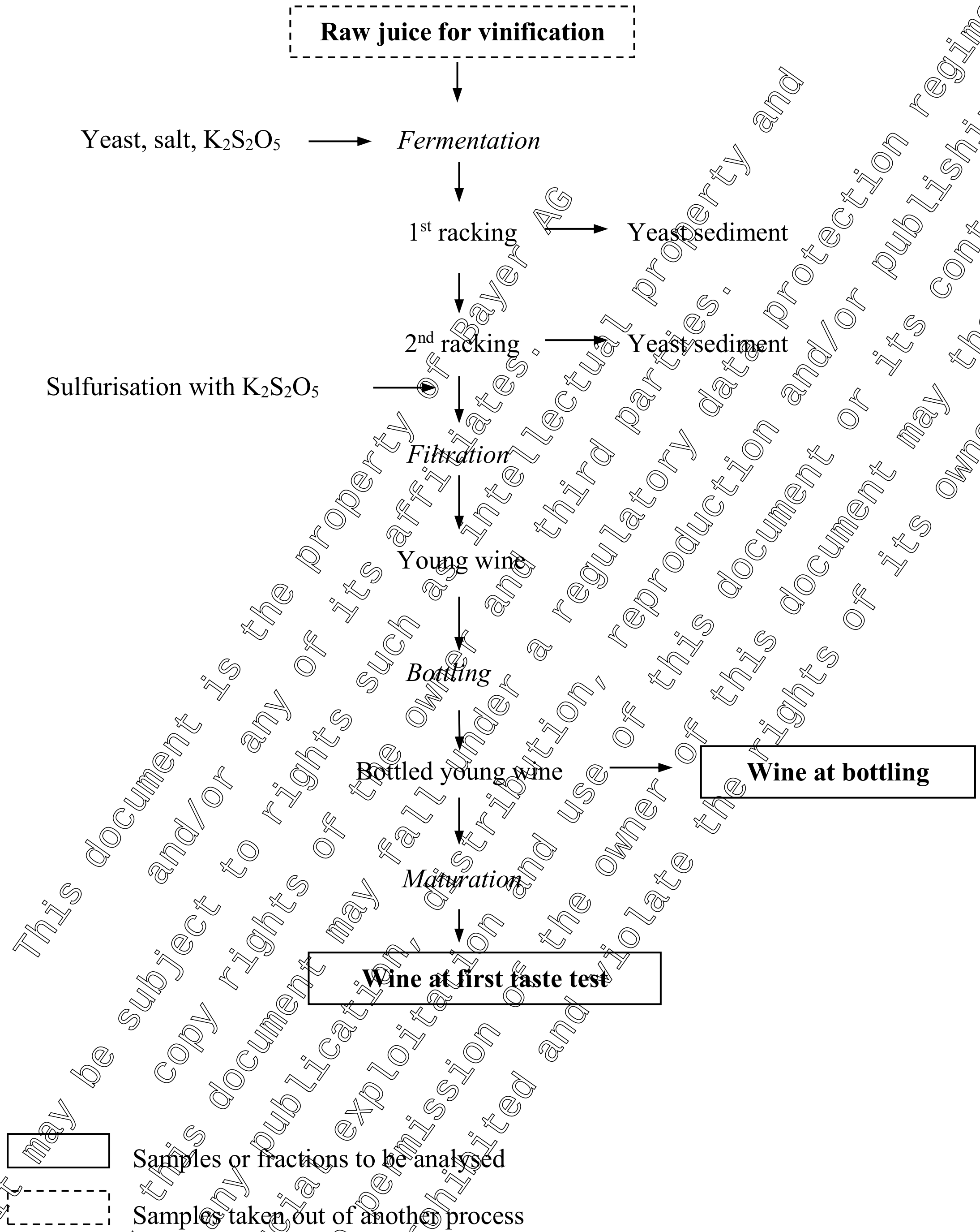


Diagram 6.5.4.6-3: Industrial "processing" of grape – jelly (white and red grapes)

Raw juice for jelly production

Gelling sugar →

↓

Heating

Lemon juice →

↓

Cooling down

↓

Jelly

Samples or fractions to be analyzed

Samples taken out of another process

Diagram 6.5.4.6-4: Industrial "processing" of grape –raisin processing (white grapes)

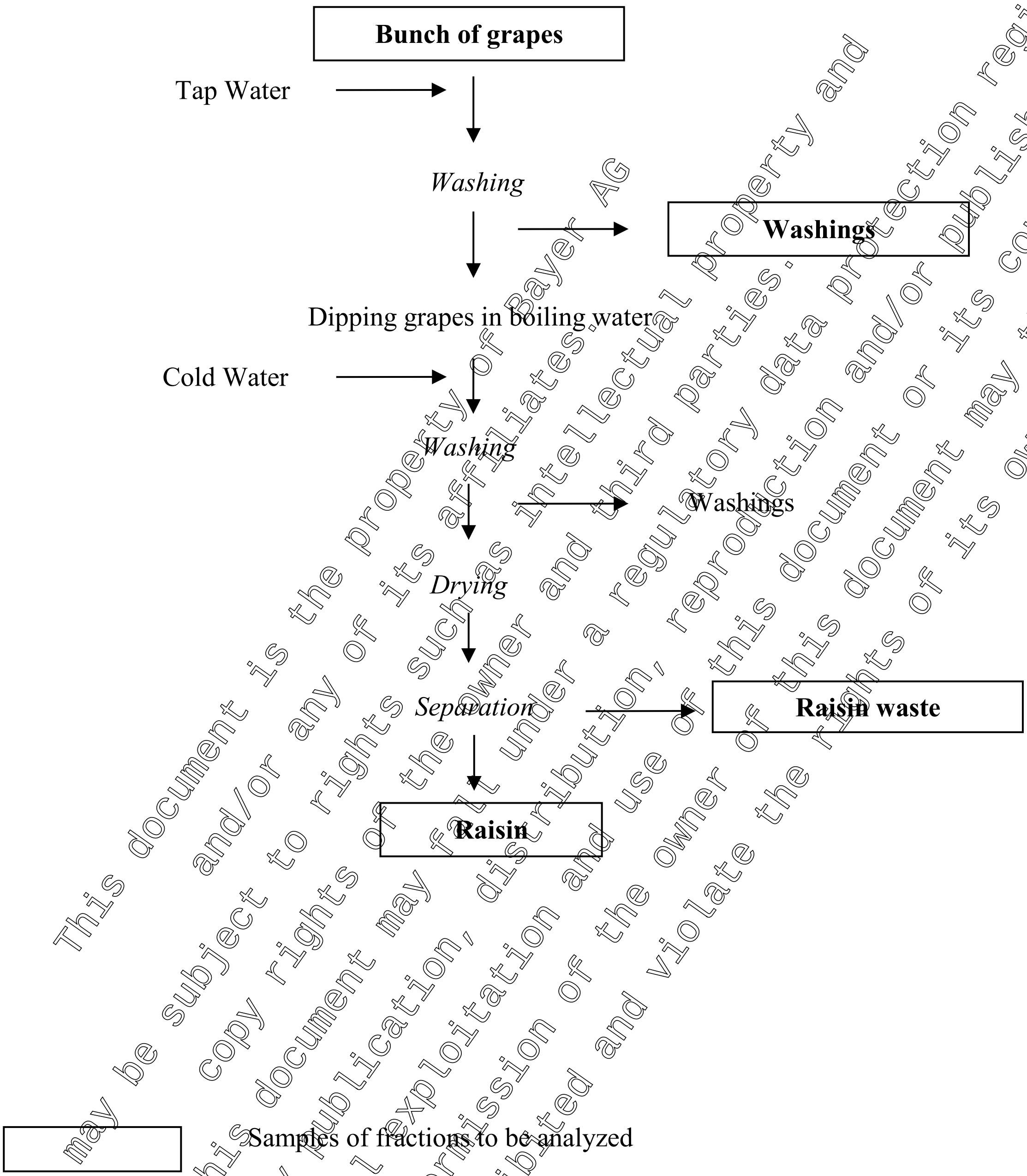
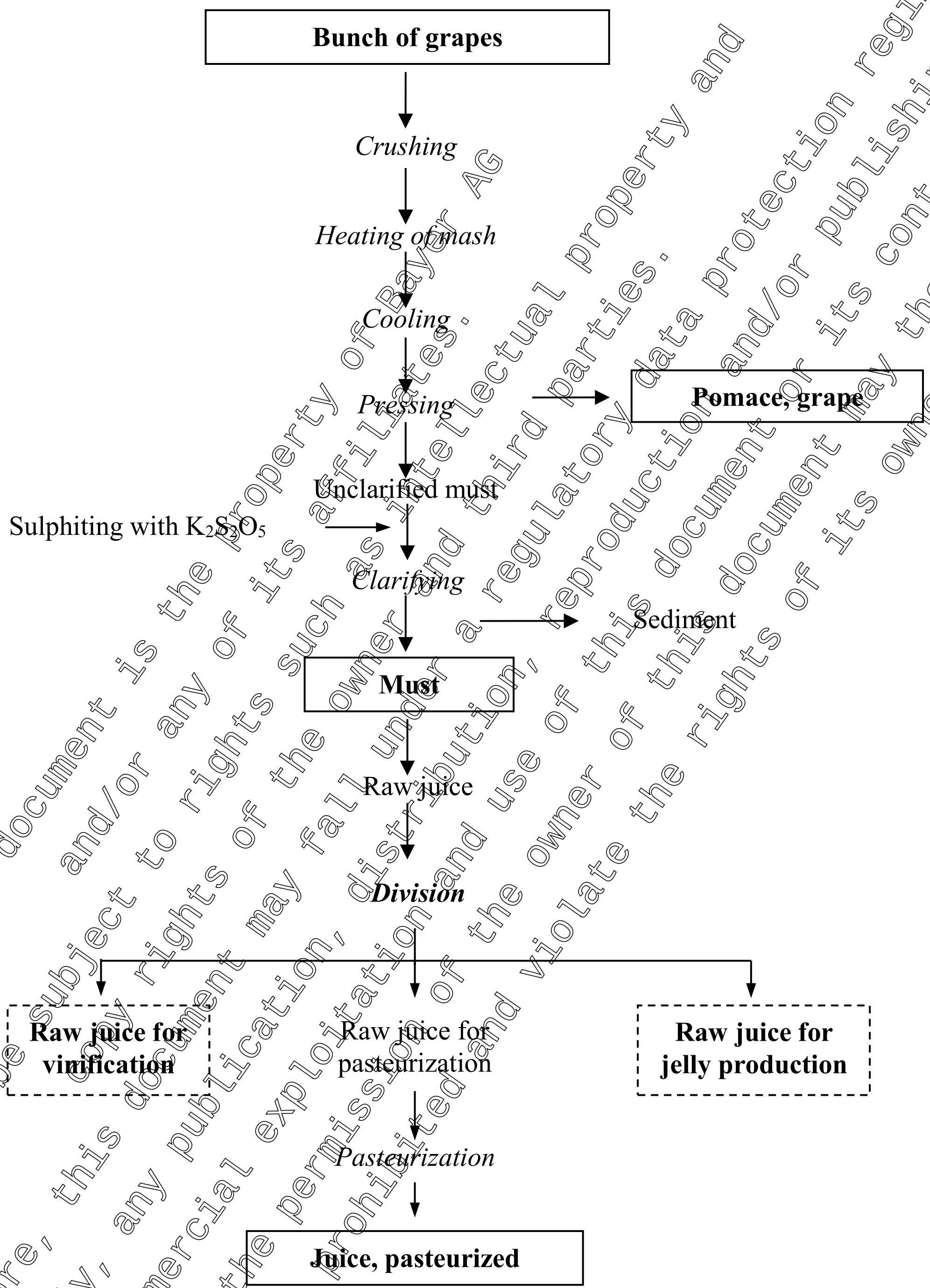


Diagram 6.5.4.6-5: Industrial "processing" of grape –pasteurized juice (red grapes)



Samples or fractions to be analyzed

Samples or used for further processing steps

Diagram 6.5.4.6-6: Industrial "processing" of grape – wine (red grapes)

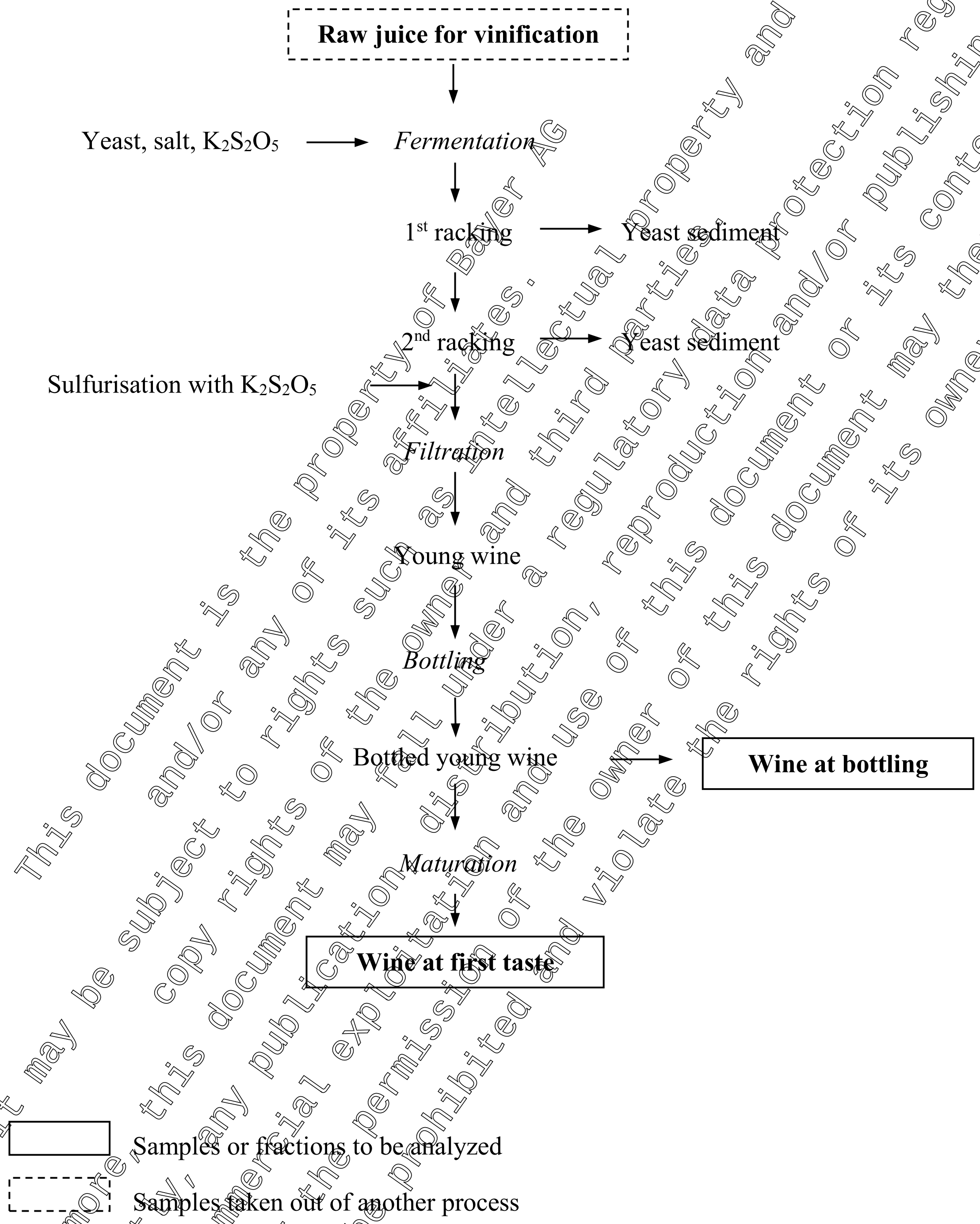


Table 6.5.4.6-3a: Application scenario in residue processing trials conducted in/on **grape** after spraying with BYI 02960 SL 200 in European fields

Study No. **(Trial No.) Country Location Region Year**	**Crop Variety**	**FL**	**Application**			**GS**	**PHI (days)**
			No.	**kg/ha (a.s.)**	**kg/hl (a.s.)**		
10-3406 (10-3406-01) Germany [redacted] EU-N 2010	grape Blauer Spaetbur-gunder (red variety)	200 SL	1	0.30	0.038	85	14
10-3406 (10-3406-02) Germany [redacted] EU-N 2010	grape Blauer Spaetbur-gunder (red variety)	200 SL	1	0.30	0.038	85	14
10-3406 (10-3406-03) Germany [redacted] EU-N 2010	grape Riesling (white variety)	200 SL	1	0.30	0.038	81	14
10-3406 (10-3406-04) Germany [redacted] EU-N 2010	grape Mueller-Thurgau (white variety)	200 SL	1	0.30	0.038	83	14

FL=formulation GS=growth stage (BBCH-code) at last treatment
EU-N=northern European residue region

Table 6.5.4.6-3b: Results of residue processing trials conducted in/on **grape** after spraying with BYI 02960 SL 200 in European fields

Study No. **(Trial No.) Country GLP**	**Portion analyzed**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960** BYI 02960	DFA	BYI 02960-DFEAF	total residue of BYI 02960 calc.
10-3406 (10-3406-01) Germany GLP: yes	bunch of grapes (RAC)	14	0.36	0.03	<0.01	0.40
	berry	14	0.34	0.02	0.01	0.38
	processing into juice and wine					
	pomace, grape	14	0.69	<0.02	<0.01	0.72
	must	14	0.31	0.03	<0.01	0.34
	juice, pasteurised	14	0.31	0.03	<0.01	0.34
	wine at bottling	14	0.24	0.03	<0.01	0.28
	wine at first taste test	14	0.18	0.02	<0.01	0.21
	processing into jelly					
	jelly	14	0.13	<0.02	<0.01	0.16
10-3406 (10-3406-02) Germany GLP: yes	bunch of grapes (RAC)	14	0.38	<0.02	<0.01	0.41
	berry	14	0.45	<0.02	<0.01	0.48
	processing into wine					
	pomace, grape	14	0.68	<0.02	<0.01	0.71
	must	14	0.32	<0.02	<0.01	0.35
	wine at bottling	14	0.29	<0.02	<0.01	0.32
	wine at first taste test	14	0.20	<0.02	<0.01	0.23
10-3406 (10-3406-03) Germany GLP: yes	bunch of grapes (RAC)	14	0.63	0.03	<0.01	0.68
	berry	14	0.52	0.03	<0.01	0.56
	processing into juice and wine					
	pomace, grape	14	1.0	0.02	<0.01	1.1
	must	14	0.32	0.04	<0.01	0.36
	juice, pasteurised	14	0.29	0.04	<0.01	0.34
	wine at bottling	14	0.17	0.03	<0.01	0.21
	wine at first taste test	14	0.12	0.03	<0.01	0.16
	processing into jelly					
	jelly	14	0.12	<0.02	<0.01	0.15

DALT=days after last treatment, RAC = raw agricultural commodity

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Table 6.5.4.6-3b (cont'd): Results of residue processing trials conducted in/on **grape** after spraying with BYI 02960 SL 200 in European fields

Study No. **(Trial No.) Country GLP**	**Portion analyzed**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
			BYI 02960	**DFA**	**BYI 02960-DFEAF**	**total residue of BYI 02960 calc.**
10-3406 (10-3406-04) Germany GLP: yes	bunch of grapes (RAC)	14	0.45	<0.02	<0.01	0.48
	berry	14	0.20	<0.02	<0.01	0.23
	processing into wine					
	pomace, grape	14	0.78	<0.02	<0.01	0.81
	must	14	0.19	<0.02	<0.01	0.22
	wine at bottling	14	0.19	<0.02	<0.01	0.22
	wine at first taste test	14	0.13	<0.02	<0.01	0.16
	processing into raisin					
	washings	14	0.03	<0.02	<0.01	0.06
	raisin waste	14	1.2	0.05	<0.01	1.3
	raisin	14	1.3	0.03	<0.01	1.4

DALT=days after last treatment; RAC = raw agricultural commodity

Table 6.5.4.6-4: Recovery data for BYI 02960 in **grape** and **grape matrices**

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortification level** (mg/kg)	**Recovery (%)** Individual recoveries	Min	Max	Mean	RSD
10-3406 (10-3406-01) to (10-3406-04) GLP: yes 2010	grape	bunch of grapes	BYI 02960	5	0.01	71; 79; 80; 82; 84	71	84	79	6.3
				3	0.10	78; 81; 82	78	82	80	2.6
				1	2.0	94	94	94	94	
				9	overall		71	94	81	7.5
			DFA	5	0.02	85; 92; 93; 96; 103	85	103	94	7.0
				3	0.20	92; 93; 94	92	94	93	1.1
				1	2.0	86	86	86	86	
				9	overall		85	103	93	5.7
			BYI 02960-DFEAF	5	0.01	81; 86; 96; 100; 107	81	107	94	11.2
				3	0.10	84; 89; 97	84	97	90	7.3
				1	2.0	91	91	91	91	
				9	overall		81	107	92	9.1
		pomace	BYI 02960	5	0.01	60; 61; 61; 64; 76	60	76	64	10.3
				3	0.10	66; 68; 75	66	75	70	6.8
				1	2.0	87	87	87	87	
				9	overall		60	87	69	13.1
			DFA	5	0.02	81; 87; 88; 91; 92	81	92	88	4.9
				3	0.20	76; 83; 86	76	86	82	6.3
				1	2.0	79	79	79	79	
				9	overall		76	92	85	6.4
			BYI 02960-DFEAF	5	0.01	78;78; 82;88; 113	78	113	88	16.7
				3	0.10	86; 95; 101	86	101	94	8.0
				1	2.0	91	91	91	91	
				9	overall		78	113	90	12.7

Remark re. *bunch of grapes*: also covers the sample material *berry*

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Table 6.5.4.6-4 (cont'd): Recovery data for BYI 02960 in **grape** and **grape matrices**

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortifi-cation level** (mg/kg)	**Recovery (%)** Individual recoveries	**Min**	**Max**	**Mean**	**RSD**
10-3406 (10-3406-01) to (10-3406-04) GLP: yes 2010	grape	wine at bottling	BYI 02960	5	0.01	81; 81; 82; 83; 84	81	84	82	1.6
				3	0.10	79; 79; 83	79	83	80	2.9
				1	2.0	90	90	90	90	
				9	overall		79	90	82	4.0
			DFA	5	0.02	95; 96; 97; 97; 97	95	97	96	0.9
				3	0.20	92; 92; 93	92	93	92	0.6
				1	2.0	87	87	87	87	
				9	overall		87	97	94	3.6
			BYI 02960-DFEAF	5	0.01	101; 104; 105; 106; 116	101	116	106	5.3
				3	0.10	94; 96; 98	94	98	96	2.1
				1	2.0	92	92	92	92	
				9	overall		92	116	101	7.3
		jelly	BYI 02960	5	0.01	87; 89; 89; 89; 91	87	91	89	1.6
				3	0.10	89; 90; 90	89	90	90	0.6
				1	2.0	90	90	90	90	
				9	overall		87	91	89	1.3
			DFA	5	0.02	94; 94; 96; 97; 100	94	100	96	2.6
				3	0.20	84; 85; 86	84	86	85	1.2
				1	2.0	89	89	89	89	
				9	overall		84	100	92	6.3
			BYI 02960-DFEAF	5	0.01	97; 104; 105; 107; 108	97	108	104	4.2
				3	0.10	82; 87; 89	82	89	86	4.2
				1	2.0	88	88	88	88	
				9	overall		82	108	96	10.4

Remark re. *wine at bottling*: also covers *wine at first taste test*
Remark re. *jelly*: also covers *must* and *juice*

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Table 6.5.4.6-4 (cont'd): Recovery data for BYI 02960 in **grape** and **grape matrices**

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortifi-cation level** (mg/kg)	**Recovery (%)**				
						Individual recoveries	**Min**	**Max**	**Mean**	**RSD**
10-3406 (10-3406-01) to (10-3406-04) GLP: yes 2010	grape	raisin	BYI 02960	5	0.01	78; 79; 80;81; 85	78	85	81	3.4
				3	0.10	74; 76; 78	74	78	76	2.6
				2	2.0	90; 94	90	94	92	
				10	overall		74	94	82	7.8
			DFA	5	0.02	74; 77; 78;78; 80	74	80	77	2.8
				3	0.20	60; 61; 63	60	63	61	2.5
				1	2.0	86	86	86	86	
				9	overall		60	86	73	12.8
			BYI 02960-DFEAF	5	0.01	84; 84; 86; 103; 106	84	106	93	11.8
				3	0.10	99; 101; 103	99	103	101	2.0
				2	2.0	90; 93	90	93	92	
				10	overall		84	106	95	9.0

Remark re. *raisin*: also covers *raisin waste*

IIA 6.5.4.7 Sugar beet

Report:	**KIIA 6.5.4.7/01, [redacted] & [redacted]; 2012**
Title:	Determination of the residues of BYI 02960 in/on beet, sugar and processed fractions (body, washed; washings; pulp; raw juice; thin juice; cake, lime; thick juice; molasses; raw sugar; white sugar; pulp, extracted, wet; press liquor; pulp, extracted, pressed; pulp, extracted, dry; pulp, extracted, ensiled and refined sugar) after spraying and incorporation of BYI 02960 SL 200 in the field in Germany
Report No. & Document No.:	10-3408 dated October 18, 2012 M-439824-01-1
Guidelines:	– EU Council Directive 91/414/EEC – EC Guidance working document 7029/VI/95 rev.5 – EU Guidance Working Document 7035/VI/95 rev. 5 – OECD Guideline for the Testing of Chemicals No. 508, Magnitude of the Pesticide Residues in Processed Commodities – EPA Ref. OPPTS 860.1520.SUPP
GLP:	yes (certified laboratory)

I. Materials and Methods

Due to the presence of measurable residues of BYI 02960 on harvested root crops determined in samples from field rotational crop residue trials (cf. section 6.6.3.1) as well as to the nature of sugar-crop preparation and consumption patterns, investigations on the effects of industrial processing have been conducted. Two trials were conducted in the northern European residue region, both in Germany, in order to determine the total residues of BYI 02960 in unprocessed sugar beets and then in the primary processed products raw sugar and refined sugar, as well as in intermediate fractions ([redacted] & [redacted], 2012; KIIA 6.5.4.7/01).

In the field trials, BYI 02960 SL 200 was sprayed once at an application rate of approx. 360g a.s./ha and a water volume of 300 L/ha. The application was done on bare soil followed by incorporation into soil down to a depth of approx. 8 cm. The application scheme reflects an overdosing (approx. 3× higher than the envisaged EU worst case) in a spray application scheme, in order to ensure that detectable residues would be found in the relevant raw commodities at harvest, thus allowing elucidation of processing factors. Sugar beet (body) samples to be processed were sampled 181 days after the treatment (DALT 181) at commercial harvest (BBCH 49).

After processing (described below), residue analysis was performed according to method 01304 (for more information, cf. point IIA 4.3). The limits of quantitation were 0.01 mg/kg (BYI 02960 and DFEAF) and 0.02 mg/kg (DFA), expressed in parent compound equivalents, yielding a calculated total-residue LOQ of 0.04 mg/kg, in all matrices. Prior and parallel to the residue analysis, the method was validated by recovery experiments.

<u>Processing procedures:</u>
Sugar beet "processing" was designed to simulate industrial procedures of sugar beet into the sugar and related fractions (body, washed; washings; pulp; raw juice; cake, lime; thin juice; thick juice;

molasses; raw sugar; white sugar; refined sugar; pulp extracted, wet; press liquor; pulp extracted, pressed; pulp, extracted dry; and pulp extracted, ensiled).

Refined sugar processing:
Processing of sugar beet into refined sugar, white sugar, and molasses started with washing of the beets in a cylindrical beet washer, operating discontinuously. During the entire washing procedure, ordinary tap water was sprayed onto the beets. Subsequently, washed beets (body, washed) and wash water (washings) were sampled. The slicing process was carried out in a slicer. Sliced beet (pulp) was taken.

The extraction of the beets was performed in a DdS extraction trough as counter-current extraction. The denaturation temperature during the extraction process ranged from 72-75°C and the fresh tap water was warmed up to approx. 70°C. The extraction duration was 60-69 min. The temperature of the raw juice was approx. 43°C. Approx. 160 kg raw juice was achieved by the extraction of 100 kg sugar beets. After extraction, raw juice and wet pulp (pulp, extracted, wet) were sampled.

Samples of wet pulp were deep-frozen until further processing to "pulp, dry" and "pulp, ensiled" (see silage and dry pulp processing). The raw juice was purified according to the classical purification process using two-stage liming and two-stage carbonation. Cold pre-liming was carried out at a temperature between 35 and 42°C by adding lime milk stepwise (330 g calcium oxide/L) until a pH value of 6.6-11.2 was reached. Afterwards, the reaction was allowed to continue for approx. 10 min. The total lime milk quantity (up to 2% calcium oxide in the juice) was added and the juice was heated up to a temperature of approx. 85°C. After an interval of about 10 min (reaction time), the first carbonation was started. During this step, carbon dioxide was added until the pH-value of pre-liming (6.6-11.2) was reached. The carbonation temperature was at approx. 85°C.

Frame filter presses were used for the subsequent filtration process. The filtrate was heated up to approx. 95°C and carbon dioxide was added until the lime (CaO) content in the juice reached a minimum (optimum alkalinity, pH 9.2). Subsequently the filtration was carried out by means of frame filter presses. At the end of the process, thin juice and "cake, lime" (mixed sample from sludge of first carbonation and sludge of the second carbonation) were sampled.

The concentration of the thin juice was carried out in a single-stage evaporating plant at 80°C. The pressure in the heating chamber (calendria) amounted to -0.5 bar. After evaporation, thick juice was sampled. The thick juice was concentrated into the metastable supersaturation state at a pressure of approx. 0.3 bar. As soon as the desired supersaturation was reached, powdered sugar was injected as seed material. In order to maintain a constant supersaturation, thick juice was soaked in continuously. Subsequently crystallisation was finished and the massecuite was brought into the cooling crystalliser.

During this process, the massecuite from the evaporating crystallisation was cooled down to 23-42°C within 3 to 25 hours. The separation of crystal and syrup was done in a discontinuous centrifuge. No water was added. Syrup (molasses) and sugar (raw) were obtained and were sampled. After centrifuging, the sugar was dried in a drying chamber. Subsequently, white sugar was sampled.

For the purification, the raw sugar was mixed with distilled water (approx. 10% of raw sugar weight). The intermediate product was centrifuged and syrup and pure sugar were obtained from the separation. Pure sugar was dried in air. Subsequently, the air-dried sugar was sampled as refined sugar.

Silage and dry pulp processing:
The wet pulp used for the processing into silage and dry pulp was generated during the first processing of sugar beets into sugar and molasses. The wet pulp was stored frozen until the start of processing into silage and dry pulp.

After defrosting at room temperature, the wet pulp was pressed and separated into press water (press liquor) and into pressed pulp (pulp, extracted, pressed). Samples of both were taken.

One part of the pressed pulp (pulp, extracted, pressed) was dried in a drying chamber at 35°C until a moisture content of below 10% was reached. Dried pulp (pulp, extracted, dry) was sampled.

A further part of the pressed pulp (pulp, extracted, pressed) was frozen for further silage production. The pressed pulp was put in a special silage glass container (under pressure). Subsequently, the glass container was closed and stored at approx. 20-25°C for approx. 6 weeks. After this fermentation time, silage (pulp, extracted, ensiled) was sampled.

The processes are illustrated in flow diagrams 6.5.4.7-1 and 6.5.4.7-2.

II. Findings

Method validation experiments for sugar beet body were conducted in study 10-2240 (to be submitted later; can be provided upon request); validation of the sample materials molasses; pulp extracted, wet; raw sugar; and thick juice was done within the present study.

Concurrent recoveries were obtained from samples of sugar beet body, thick juice, molasses, and raw sugar. The recoveries for the sample material *body* are also representative for *body, washed* and *pulp*. Those for *thick juice* are also representative for *raw juice* and *thin juice*; those for *raw sugar* are also representative for *white sugar* and *refined sugar*; and those for *molasses* are also representative for *washings, lime cake,* and *press liquor*.

In all mentioned matrices, concurrent recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg and 0.10 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries for all matrices were 91-112%, with RSDs in the larger validations sets (n > 2) of 0.5-13.2%; n=2-5.

For DFA, concurrent recovery samples for sugar beet body and sugar beet matrices (molasses; pulp, extracted; raw sugar; and thick juice) were spiked at levels of 0.02 and 0.20 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries in all matrices were 61-111%, with RSDs in the larger validations sets (n > 2) of 0.9-4.4%; n=1-5.

A tabular summary of the recovery values is presented below in table 6.5.4.7-5.

The total residues of BYI 02960 (parent compound plus DFA and DFEAF) in the harvested sugar beet body at BBCH growth stage 49 were found at 0.07°mg/kg in the first trial. This value was used for the calculation of "processing" factors.

In the second trial, the total residues of BYI 02960 in the RAC sample sugar beet body of <0.04 mg/kg and in washed body of 0.11 mg/kg seem to show an increase due to washing. This result is not consistent with the process and there is no way of determining the definite reason for this discrepancy. Since residues were detected in the RAC sample of the first trial, and since residue values of all other samples of the second trial were comparable to or higher than the respective sample of the first trial, as well as due to the fact that the residue value detected in pulp is comparable to the residue value of "body, washed" in the second trial, it must be assumed that the RAC sample in the second trial was not completely representative, and thus contained residue levels lower than a truly representative sample would have. Therefore, for the second trial, the transfer factors were calculated using the sample material "body, washed".

● Processing of sugar beet into refined sugar and into dry pulp and silage:

Washing:
The levels of the total residue of BYI 02960 in washed body were from 0.06-0.11 mg/kg, and, in washings, <0.04°mg/kg in both trials. The measured residue levels lead to mean "processing" factors of 0.95 (range: 0.9-1.0, n=2) for "body, washed" and <0.5 (range: <0.4-<0.6, n=2) for washings.

The mean "processing" factors indicate that there is no relevant effect on levels of the total residue of BYI 02960 due to washing of sugar beet body.

Extraction:
In pulp the levels of the total residue of BYI 02960 were 0.07-0.10 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.95 (range: 0.9-1.0, n=2). In pulp extracted, wet and raw juice the levels of the total residue of BYI 02960 were <0.04 mg/kg and 0.06-0.08 mg/kg, respectively. The measured residue levels lead to a mean "processing" factor of <0.5 (range: <0.4-<0.6, n=2) for pulp extracted, wet and of 0.8 (range: 0.7-0.9, n=2) for raw juice.
The measured mean "processing" factor clearly show that residues of BYI 02960 are extracted into the raw juice during the extraction.

Juice purification:
In lime cake, the levels of the total residue of BYI 02960 were <0.04-0.04 mg/kg, and they were 0.05-0.08 mg/kg in thin juice. The measured residue levels lead to mean "processing" factors of <0.5 (range: <0.6-0.4, n=2) in lime cake and of 0.7 (range: 0.7, n=2) in thin juice, showing that purification does not lead to an obvious reduction of the residue level of the total residue of BYI 02960 in comparison to residues in raw juice.

Evaporation, crystallisation and cleaning:
In thick juice, the levels of the total residue of BYI 02960 were 0.13-0.35 mg/kg. The measured residue levels lead to a mean "processing" factor of 2.6 (range: 1.9-3.2, n=2), showing an increase of the level of the total residue of BYI 02960 after evaporation to thick juice.

In molasses, the levels of the total residue of BYI 02960 were 0.40-1.4 mg/kg. The measured residue levels lead to a mean "processing" factor of 9.2 (range: 5.7-12.7, n=2).

In raw sugar, white sugar, and refined sugar, the levels of the total residue of BYI 02960 were reduced to <0.04-0.06 mg/kg, <0.04-0.07 mg/kg, and <0.04 mg/kg (in both processed specimens), respectively. The measured residue levels lead to mean "processing" factors of <0.55 (range: <0.6-0.5, n=2) for raw sugar, of <0.6 (range: <0.6-0.6, n=2) for white sugar, and of <0.5 (range: <0.4-<0.6, n=2) for refined sugar.

The findings from centrifuging and crystallisation indicate that total residues of BYI 02960 may be almost completely separated from raw sugar and remain in the molasses. Drying of raw sugar to white sugar does not affect the residue level. Decolouring leads to total residues of BYI 02960 at <LOQ.

Processing into "dried pulp" and "pulp, extracted, ensiled":
As the total residues of BYI 02960 in "pulp, extracted, wet" were <0.04 mg/kg, no residues were present in the subsequent processed matrices. Therefore, for all processed pulp matrices, the mean "processing" factor was of <0.5. These findings indicate that the total residues of BYI 02960 are extracted into the raw juice.

The transfer factors for the total residues of BYI 02960 are summarized below in table 6.5.4.7-1 to 6.5.4.7-3. All trial data are summarised further below in table 6.5.4.7-4a & b and in greater detail in the Tier 1 summary forms.

Table 6.5.4.7-1: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in sugar beet RACs and processed products (**processing into refined sugar – part 1**) following application of BYI 02960 SL 200

Trial number	sugar beet body	body, washed	washings	pulp	raw juice	cake, lime	thin juice
10-3408-01	0.07	0.06 *(0.9)*	<0.04 *(<0.6)*	0.07 *(1.0)*	0.06 *(0.9)*	<0.04 *(<0.6)*	0.05 *(0.7)*
10-3408-02	<0.04*	0.11 *(1.0*)*	<0.04 *(<0.4)*	0.10 *(0.9)*	0.08 *(0.7)*	0.04 *(0.4)*	0.08 *(0.7)*
Mean transfer factors:		*0.95*	*<0.5*	*0.95*	*0.8*	*<0.5*	*0.7*

* the transfer factors were calculated based on the residue results of sample material *body, washed*.
"<" the residue in the processed fraction was below LOQ and was set to LOQ for calculating processing factors.

Table 6.5.4.7-2: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in sugar beet RACs and processed products (**processing into refined sugar – part 2**) following application of BYI 02960 SL 200

Trial number	sugar beet body	body, washed	thick juice	molasses	raw sugar	white sugar	refined sugar
10-3408-01	0.07	0.06 *(0.9)*	0.13 *(1.9)*	0.40 *(5.7)*	<0.04 *(<0.6)*	<0.04 *(<0.6)*	<0.04 *(<0.6)*
10-3408-02	<0.04*	0.11 *(1.0*)*	0.35 *(3.2)*	1.4 *(12.7)*	0.06 *(0.5)*	0.07 *(0.6)*	<0.04 *(<0.4)*
Mean transfer factors:		*0.95*	*2.6*	*9.2*	*0.55*	*<0.6*	*<0.5*

* the transfer factors were calculated based on the residue results of sample material *body, washed*
"<" the residue in the processed fraction was below LOQ and was set to LOQ for calculating processing factors.

Table 6.5.4.7-3: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in sugar beet RACs and processed products (**processing into dry pulp and silage**) following application of BYI 02960 SL 200

Trial number	sugar beet body	body washed	pulp, extracted, wet	press liquor	pulp, extracted, pressed	pulp, extracted, dry	pulp, extracted, ensiled
10-3408-01	0.07	0.06 *(0.9)*	<0.04 *(<0.6)*	<0.04 *(<0.6)*	<0.04 *(<0.6)*	<0.04 *(<0.6)*	<0.04 *(<0.6)*
10-3408-02	<0.04*	0.11 *(1.0*)*	<0.04 *(<0.4)*	<0.04 *(<0.4)*	<0.04 *(<0.4)*	<0.04 *(<0.4)*	<0.04 *(<0.4)*
Mean transfer factors:		*0.95*	*<0.5*	*<0.5*	*<0.5*	*<0.5*	*<0.5*

* the transfer factors were calculated based on the residue results of sample material *body, washed*.
"<" the residue in the processed fraction was below LOQ and was set to LOQ for calculating processing factors.

III. Conclusions

In order to determine "processing" factors for total residues of BYI 02960 from sugar beet into raw and refined sugar and into silage, processing studies have been conducted.

As the total residues of BYI 02960 in wet extracted pulp were <0.04 mg/kg no residues were present in the subsequent processed matrices. Therefore, for all processed pulp matrices, the mean "processing" factor was of <0.5. These findings indicate that the total residues of BYI 02960 are extracted into the raw juice.

The mean value of total residue "processing" factors for refined sugar was <0.5, indicating an "elimination" of the total residues of BYI 02960 from the end product, refined sugar, during sugar production. The main step in the reduction of residues is found in the separation of raw sugar and molasses.

Diagram 6.5.4.7-1: Industrial "processing" of sugar beet into refined sugar

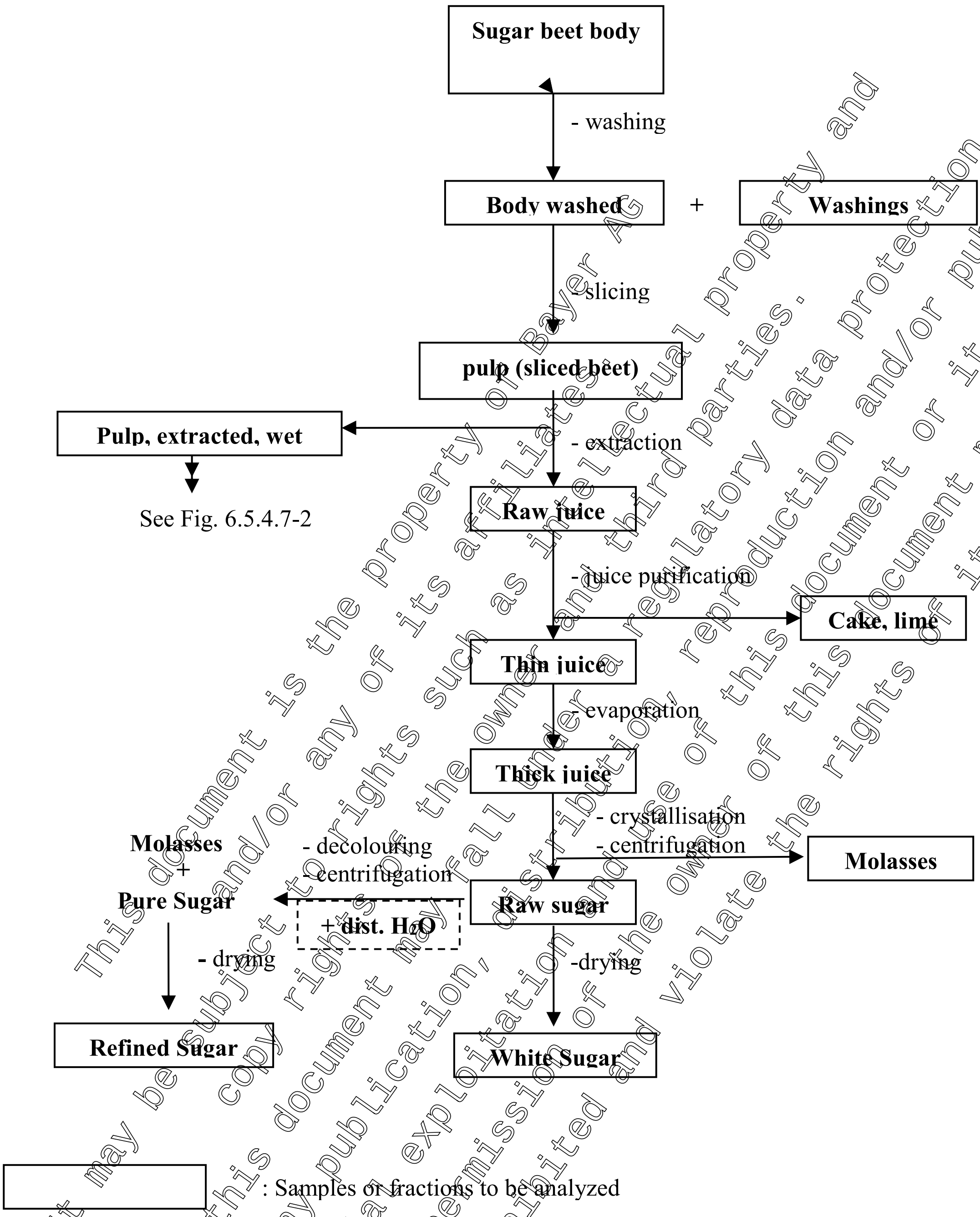
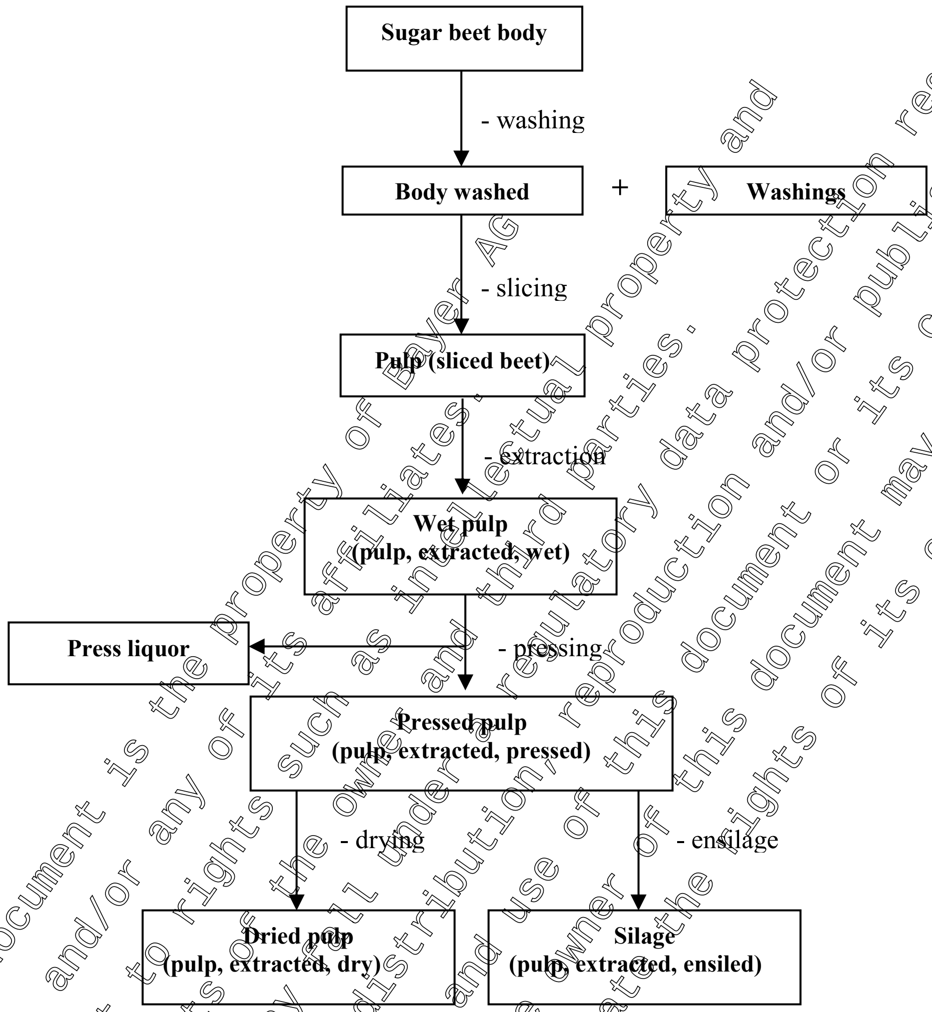


Diagram 6.5.4.7-2: Industrial "processing" of sugar beet into dry pulp and silage



: Samples or fractions to be analyzed

The first three processing steps correspond to the first three steps of figure 6.5.4.7-1. The processing process was divided into two flow charts for reasons of clarity.

Table 6.5.4.7-4a: Application scenario in residue processing trials conducted in/on **sugar beet** after spraying with BYI 02960 SL 200 in northern European fields

Study No. **(Trial No.) Country Location** **Region Year**	**Crop Variety**	**FL**	**Application**		
			No.	**kg/ha (a.s.)**	**kg/hl (a.s.)**
10-3408 (10-3408-01) Germany [redacted] EU-N 2010	beet, sugar ST-Neuga 01-2010	200 SL	1	0.36	0.12
10-3408 (10-3408-02) Germany D[redacted] EU-N 2010	beet, sugar ST-Neuga 01-2010	200 SL	1	0.36	0.12

FL=formulation GS=growth stage (BBCH-code) at last treatment
EU-N=northern European residue region
The application on bare soil was followed by incorporation into soil down to a depth of approx. 8 cm

Table 6.5.4.7-4b: Results of residue processing trials conducted in/on **sugar beet** after spraying with BYI 02960 SL 200 in European fields

Study No. **(Trial No.) Country** **GLP**	**Portion analyzed**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
			BYI 02960	**DFA**	**BYI 02960-DFEAF**	**total residue of BYI 02960 calc.**
10-3408 (10-3408-01) Germany GLP: yes	body (RAC)	181	<0.01	0.05	<0.01	0.07
	production of refined sugar					
	body, washed	181	<0.01	0.04	<0.01	0.06
	washings	181	<0.01	<0.02	<0.01	<0.04
	pulp	181	<0.01	0.05	<0.01	0.07
	raw juice	181	<0.01	0.04	<0.01	0.06
	thin juice	181	<0.01	0.03	<0.01	0.05
	cake, lime	181	<0.01	<0.02	<0.01	<0.04
	thick juice	181	<0.01	0.11	<0.01	0.13
	molasses	181	0.02	0.37	<0.01	0.40
	raw sugar	181	<0.01	<0.02	<0.01	<0.04
	white sugar	181	<0.01	<0.02	<0.01	<0.04
	refined sugar	181	<0.01	<0.02	<0.01	<0.04
	production of dried pulp and silage					
	pulp, extracted, wet	181	<0.01	<0.02	<0.01	<0.04
	press liquor	181	<0.01	<0.02	<0.01	<0.04
	pulp, extracted, pressed	181	<0.01	<0.02	<0.01	<0.04
	pulp, extracted, dry	181	<0.01	<0.02	<0.01	<0.04
	pulp, extracted, ensiled	181	<0.01	<0.02	<0.01	<0.04

DALT = days after last treatment; RAC = raw agricultural commodity

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Table 6.5.4.7-4b (cont'd): Results of residue processing trials conducted in/on **sugar beet** after spraying with BYI 02960 SL 200 in European fields

Study No. **(Trial No.) Country** **GLP**	**Portion analyzed**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
			BYI 02960	**DFA**	**BYI 02960-DFEAF**	**total residue of BYI 02960 calc.**
10-3408 (10-3408-02) Germany GLP: yes	body (RAC)#	181	<0.01	<0.02	<0.01	<0.04**
	production of refined sugar					
	body, washed	181	<0.01	0.09	<0.01	0.11**
	washings	181	<0.01	<0.02	<0.01	<0.04
	pulp	181	<0.01	0.08	<0.01	0.10
	raw juice	181	<0.01	0.06	<0.01	0.08
	thin juice	181	<0.01	0.06	<0.01	0.08
	cake, lime	181	<0.01	0.02	<0.01	0.04
	thick juice	181	<0.01	0.33	<0.01	0.35
	molasses	181	<0.01	1.4	<0.01	1.4
	raw sugar	181	<0.01	0.04	<0.01	0.06
	white sugar	181	<0.01	0.05	<0.01	0.07
	refined sugar	181	<0.01	<0.02	<0.01	<0.04
	production of dried pulp and silage					
	pulp, extracted, wet	181	<0.01	<0.02	<0.01	<0.04
	press liquor	181	<0.01	<0.02	<0.01	<0.04
	pulp, extracted, pressed	181	<0.01	<0.02	<0.01	<0.04
	pulp, extracted, dry	181	<0.01	<0.02	<0.01	<0.04
	pulp, extracted, ensiled	181	<0.01	<0.02	<0.01	<0.04

DALT = days after last treatment; RAC = raw agricultural commodity

\# The retain sample of this examination sample was analyzed and confirmed the results of the examination sample.

** The residue values determined for the RAC (body) and for *body, washed* in trial 10-3408-02 seem to show an increase due to washing. This result is not consistent with the process and there is no way of determining the definite reason for this discrepancy. It must be assumed that the RAC sample was not completely representative and thus contained residue levels lower than a truly representative sample would have. Though every effort is made to ensure representative sampling and the sampling procedure is, occasional non-representative samples cannot entirely be excluded due to the nature of the test system and the "true life" field conditions.

Table 6.5.4.7-5: Recovery data for BYI 02960 in **sugar beet** and **sugar beet matrices**

Study No. **Trial No. GLP Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortification level** (mg/kg)	**Recovery (%)** Individual recoveries	Min	Max	Mean	RSD
10-3408 (10-3408-01) and (10-3408-02) GLP: yes 2010	sugar beet	body	BYI 02960	3	0.01	92; 95; 99	92	99	95	3.7
				2	0.10	90; 92	90	92	91	
				5	overall		90	99	94	3.7
			DFA	1	0.02	98	98	98		
				2	0.05	90; 90	90	90	90	
				2	0.50	92; 92	92	92	92	
				5	overall		90	98	92	3.6
			BYI 02960-DFEAF	3	0.01	85; 92; 98	85	98	92	7.1
				2	0.10	96; 97	96	97	97	
				5	overall		85	98	94	5.7
		thick juice	BYI 02960	5	0.01	100; 103; 107; 109; 118	100	118	107	6.4
				3	0.10	110; 113; 114	110	114	112*	1.9
				8	overall		100	118	109	5.4
			DFA	5	0.02	69; 71; 72; 73; 74	69	74	72	2.7
				3	0.20	61; 62; 61	61	62	61*	0.9
				8	overall		61	74	68*	8.3
			BYI 02960-DFEAF	5	0.01	94; 96; 100; 101; 102	94	102	99	3.5
				3	0.10	103; 108; 112	103	112	108	4.2
				8	overall		94	112	102	5.8

* These mean recovery values were accepted since the individual recoveries were in the acceptable range of 60 to 120% and the RSD values were below 20%.

Remark re. *body*: also covers *body, washed* and *pulp*

Remark re. *thick juice*: also covers *raw juice* and *thin juice*

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Table 6.5.4.7-5 (cont'd): Recovery data for BYI 02960 in **sugar beet** and **sugar beet matrices**

Study No. **Trial No.** **GLP Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortification level** (mg/kg)	**Recovery (%)** Individual recoveries	Min	Max	Mean	RSD
10-3408 (10-3408-01) and (10-3408-02) GLP: yes 2010	sugar beet	molasses	BYI 02960	5	0.01	105; 110; 111; 114; 116	105	116	111*	3.8
				4	0.10	85; 109; 113; 115	85	115	106	13.2
				9	overall		85	116	109	8.7
			DFA	5	0.02	108; 109; 110; 110; 120	108	120	111*	4.4
				4	0.20	89; 92; 95; 95	89	95	93	3.1
				9	overall		89	120	103	10.2
			BYI 02960-DFEAF	5	0.01	87; 99; 100; 105; 114	87	114	101	9.7
				4	0.10	96; 104; 106; 107	96	107	103	4.8
				9	overall		87	114	102	7.5
		raw sugar	BYI 02960	5	0.01	104; 108; 109; 110; 115	104	115	109	3.6
				3	0.10	106; 108; 111	106	111	108	2.3
				8	overall		104	115	109	3.0
			DFA	5	0.02	84; 86; 86; 90; 93	84	93	88	4.1
				3	0.20	86; 88; 91	86	91	88	2.8
				8	overall		84	93	88	3.5
			BYI 02960-DFEAF	5	0.01	99; 102; 105; 107; 115	99	115	106	5.7
				3	0.10	109; 109; 110	109	110	109	0.5
				8	overall		99	115	107	4.7

* These mean recovery values were accepted since the individual recoveries were in the acceptable range of 60 to 120% and the RSD values were below 20%.

Remark re. *molasses*: also covers *washings*, *lime cake* and *press liquor*.

Remark re. *raw sugar*: also covers *white sugar* and *refined sugar*

IIA 6.5.4.8 Tomato

Report:	**KIIA 6.5.4.8/01, [redacted] & [redacted]; 2012**
Title:	Determination of the residues of BYI 02960 in/on tomato and the processed fractions (whole fruit, washed; washings; strain rest; raw juice; juice; raw puree; puree; paste; peel; peeling water; fruit peeled; preserve and tomato, dried) after spraying of BYI 02960 SL 200 in the field in southern France, Italy, Spain and Portugal
Report No. & Document No.:	10-3186, dated March 8, 2012 M-427003-01-1
Guidelines:	EU Council Directive 91/414/EEC – OECD Guideline for the Testing of Chemicals No. 508, Magnitude of the Pesticide Residues in Processed Commodities – EPA Ref. OPPTS 860.1520.SUPP
GLP:	yes (certified laboratory)

I. Materials and Methods

Due to the presence of measurable residues of BYI 02960 on harvested tomato fruit determined in samples from field residue trials performed according to the intended commercial use conditions (see point IIA 6.3.1.5), as well as to the nature of tomato use (preparation and consumption patterns), investigations on the effects of basic processing have been conducted. Four trials were conducted in the southern European residue region, in France, Italy, Spain, and Portugal, in order to determine the total residues of BYI 02960 in unprocessed tomato fruit and then in the primary processing products juice, puree, paste, preserve (=canned fruit), and dried fruit, as well as in intermediate fractions ([redacted] & [redacted], 2012; KIIA 6.5.4.8/01).

The field trials were conducted as part of study 10-2186 (cf. KIIA 6.3.1.5/01 for details). BYI 02960 SL 200 was sprayed twice at an application rate of approx. 125 g a.s./ha and a water volume of 600-1000 L/ha. The final application was conducted at a pre-harvest interval of 3 days.

After processing (described below), residue analysis was performed according to method 01304 as used in the RAC trials themselves (for more information, cf. points IIA 6.3.1.5 and IIA 4.3). The limits of quantitation were 0.01 mg/kg (BYI 02960 and DFEAF) and 0.02 mg/kg (DFA), expressed in parent compound equivalents, yielding a calculated total-residue LOQ of 0.04 mg/kg, in all matrices. Prior and parallel to the residue analysis, the method was validated by recovery experiments.

Tomato processing:
The washing and peeling of tomatoes was done using household practice. The preparation of juice, preserve, puree, paste, and dried fruit simulated industrial practice at a laboratory scale.

Juice production:
All tomatoes were in a good condition and no damaged fruits were sorted out. The processing started in deep-frozen state. The tomatoes were washed in luke-warm standing water by moving them around slowly. After washing, the fruits were allowed to drain in a sieve. An aliquot of each laboratory sample of "washings" and "whole fruit, washed" was taken.

The remaining washed tomatoes were cut with a knife into small pieces. The cut tomatoes were heated after addition of 100 mL water/kg tomatoes to 80–100°C, in order to prevent enzymatic reactions. After this blanching process, the tomato pulp was passed through a strainer to separate raw juice and strain rest. Sodium chloride (0.5-0.7% [w/w]) was added to the raw juice. An aliquot of the laboratory sample of raw juice was taken.

One part of the remaining raw juice was used for the processing into preserves. Another portion of the remaining raw juice was filled into 1/1 preserving cans and was pasteurised. After pasteurisation, an aliquot of the laboratory sample juice was taken.

The process is illustrated in flow diagram 6.5.4.8-1.

Production of preserve (canned fruit):
The deep-frozen tomatoes were washed in warm standing water by moving them around slowly. After a few minutes the peel could be taken off with a kitchen knife. Aliquots of the laboratory samples peel, peeling water, and "fruit, peeled" were taken.

After addition of raw juice, a part of the remaining peeled tomatoes (ratio fruit/juice=1/0.86) was filled into 1/1 preserving cans and pasteurized. After pasteurization, the tomato preserve was minced with a hand mixer. An aliquot of the obtained laboratory sample of tomato preserve was taken.

The process is illustrated in flow diagram 6.5.4.8-2.

Production of dried fruit:
The deep-frozen tomatoes were washed in luke-warm standing water by moving them around slowly. After washing, the fruits were allowed to drain in a sieve. The washed tomatoes were cut in half with a knife. The cut tomatoes were put with the cut surface face up onto a baking tray. The tomato halves were sprinkled with salt (8 g/kg tomato) and were then dried in a fan-assisted oven at 90–95°C over a period of 9 hours. The sample of "fruit, dried" was taken.

The process is illustrated in flow diagram 6.5.4.8-3.

Production of puree and paste:
The deep-frozen tomatoes were washed in luke-warm standing water by moving them around slowly. After washing, the fruits were allowed to drain in a sieve. The washed tomatoes were cut with a knife into small pieces. The cut tomatoes were heated with the addition of 100 mL water/kg tomatoes to 80-100°C, in order to prevent enzymatic reactions. After this blanching process, the tomato pulp was passed through a strainer to separate raw juice and strain rest. Sodium chloride (0.5-0.7% [w/w]) was

added to the obtained tomato raw juice, which was then split for the concentration into raw puree and raw paste.

For the preparation of raw puree, an aliquot of the raw juice was concentrated (100 mbar, 52–60°C, 3-12 h) while stirring to obtain raw puree (dry matter: 12–20%). An aliquot of raw puree was filled into 1/1 preserving cans and pasteurised to obtain the processed commodity tomato puree.

For the preparation of raw paste, an aliquot of the raw juice was concentrated (100 mbar, 55–60°C, 13-40 h) while stirring to obtain raw paste (dry matter: 24–29%). An aliquot of raw paste was filled into 1/1 preserving cans and pasteurised. After pasteurisation, the obtained laboratory sample of tomato paste was taken.

The process is illustrated in flow diagram 6.5.4.8-4.

II. Findings

The validation of the sample materials tomato peel, peeling water, puree, and raw juice was conducted within the present study. The validation of the sample material tomato fruit was conducted during the main validation of method 01304 as well as in study 10-2190 (for more information, cf. points IIA 4.3 and IIA 6.3.1.5/03).

Concurrent recoveries of BYI 02960 and its metabolites DFA and DFEAF were obtained from samples of tomato matrices (tomato fruit, juice, puree, peel, and peeling water). The recoveries for the sample material *fruit* are also representative for *whole fruit, washed* and *fruit, peeled*. The sample material *peel* is also representative for the sample materials *strain rest* and *fruit, dried*; the sample material *peeling water* is also representative for *washings*; the sample material *puree* is also representative for *raw puree*, *preserve*, and *paste*; and the sample material *raw juice* is also representative for *juice*.

In tomato fruit samples, recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg, 0.10 mg/kg, and 0.50 mg/kg (expressed in BYI 02960 equivalents); in tomato peel, spiking levels were 0.01 mg/kg, 0.10 mg/kg, and 0.50 mg/kg. In tomato puree, raw juice, and peeling water, spiking levels were 0.01 mg/kg and 0.10 mg/kg. Mean recoveries for all matrices were 84-104%, with RSDs in the larger validation sets (n>2) of 0.6-10.9%, n=1-10.

For DFA, concurrent recovery samples for tomato fruit were spiked at levels of 0.02 mg/kg, 0.05 mg/kg, and 0.50 mg/kg (expressed in BYI 02960 equivalents); fortification levels in tomato peel were 0.02 mg/kg, 0.20 mg/kg, and 1.0 mg/kg. Fortification levels in tomato puree, raw juice, and peeling water were 0.02 mg/kg and 0.20 mg/kg. Mean recoveries in all matrices were 88-96%, with RSDs in the larger validation sets (n>2) of 1.2/6.2, n=1-7.

A tabular summary of the recovery values is presented below in table 6.5.4.8-6.

The total residues of BYI 02960 (parent compound plus DFA and DFEAF) in the harvested fruit at day 3 ranged from <0.04-0.11 mg/kg, as summarized previously (cf. KIIA 6.3.1.5/01). These values were used for the calculation of "processing" factors.

●Juice production:

Whole fruit, washed: The levels of the total residue of BYI 02960 in "whole fruit, washed" were from <0.04-0.11 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.94 (range: n.c-1.0, n=4), showing that washing of fruit does not relevantly affect the residue situation for the total residues of BYI 02960.

Washings: The levels of the total residue of BYI 02960 in washings were from <0.04-0.04 mg/kg. The measured residue levels lead to a mean "processing" factor of <0.48 (range: n.c.-0.50, n=4).

Raw juice: The levels of the total residue of BYI 02960 in raw juice were from <0.04-0.07 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.74 (range: n.c.-0.88, n=4).

Juice: The levels of the total residue of BYI 02960 in juice were found in the same range as for raw juice (<0.04-0.07 mg/kg), resulting in a mean "processing" factor of 0.70 (range: n.c.-0.71, n=4).

Based on these values, it is evident that the total residues of BYI 02960 are decreased in juice in comparison to tomato fruit RAC.

● Preserve (canned fruit) production:

Fruit, peeled: The levels of the total residue of BYI 02960 in "fruit, peeled" were from <0.04-0.07 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.66 (range: n.c-0.71, n=4).

Peel: The levels of the total residue of BYI 02960 in peel were from 0.05-0.20 mg/kg. The measured residue levels lead to a mean "processing" factor of 2.0 (range: >1.3.-2.1, n=4).

Based on the processing factors for fruit, peeled and peel, it is evident that a larger proportion of the total residues of BYI 02960 concentrates in the peel fraction.

Peeling water: The levels of the total residue of BYI 02960 in peeling water were from <0.04-0.04 mg/kg. The measured residue levels lead to a mean "processing" factor of <0.48 (range: n.c-0.57, n=4).

Preserve: The levels of the total residue of BYI 02960 in preserve were from <0.04-0.06 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.72 (range: n.c-0.86, n=4), showing that only peeling has a clear effect the residue situation for preserve production; further steps of processing do not lead to a residue reduction.

● Production of puree and paste:

Strain rest: The levels of the total residue of BYI 02960 in strain rest were from <0.04-0.08 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.91 (range: n.c-1.0, n=4), indicating that high amounts of the total residue of BYI 02960 remain in the strain rest.

Raw puree: The levels of the total residue of BYI 02960 in raw puree were from 0.05-0.17 mg/kg. The measured residue levels lead to a mean "processing" factor of 1.4 (range: >1.3.-1.5, n=4).

Puree: The levels of the total residue of BYI 02960 in puree were from 0.04-0.11 mg/kg. The measured residue levels lead to a mean "processing" factor of 1.3 (range: >1.0-1.5, n=4).

Paste: The levels of the total residue of BYI 02960 in paste were from 0.07-0.11 mg/kg. The measured residue levels lead to a mean "processing" factor of 1.7 (range: 1.6->1.8, n=2).

Based on the processing factors for raw puree, puree, and paste, it is evident that concentration of tomato juice into puree and paste leads to concentration of residues in these commodities in comparison to residues in tomato fruit RAC and tomato juice.

● Production of dried fruit:

Dried fruit: The residue levels in dried fruit were 0.08-0.12 mg/kg. The measured residue levels lead to a mean "processing" factor of 1.9 (range; 1.7->2.0, n=2) for dried fruit. Drying of tomato fruit leads to higher residue concentrations in the processed fractions, due to water loss and subsequent higher residue/weight ratios.

The transfer factors for the total residues of BYI 02960 for juice, preserve, puree, paste, and dried fruit production are summarized below in table 6.5.4.8-1 to 6.5.4.8-4. All trial data are summarised further below in tables 6.5.4-10a & b and in greater detail in the Tier 1 summary forms.

Table 6.5.4.8-1: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in tomato RACs and processed products of **juice processing** following application of BYI 02960 SL 200

Trial number	**tomato fruit (RAC)**	**whole fruit, washed**	**washings**	**raw juice**	**juice**
10-3186-01 France	<0.04	<0.04 *(n.c.)*	<0.04 *(n.c.)*	<0.04 *(n.c.)*	<0.04 *(n.c.)*
10-3186-02 Italy	0.08	0.08 *(1.0)*	0.04 *(0.50)*	0.07 *(0.88)*	0.06 *(0.75)*
10-3186-03 Spain	0.11	0.12 *(1.1)*	<0.04 *(<0.36)*	0.07 *(0.64)*	0.07 *(0.64)*
10-3186-04 Portugal	0.07	0.05 *(0.71)*	<0.04 *(<0.57)*	0.05 *(0.71)*	0.05 *(0.71)*
Mean transfer factors:		*0.94*	*<0.48*	*0.74*	*0.70*

n.c. = not calculated (residues both in the RAC and in the processing product are below LOQ, therefore no transfer factor can be calculated)

"<" the residue in the processed fraction was below LOQ and was set to LOQ for calculating processing factors.
">" the residue in the RAC sample was below LOQ and was set to LOQ for calculating processing factors.

Table 6.5.4.8-2: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in tomato RACs and processed products (**preserve processing**) following application of BYI 02960 SL 200

Trial number	**tomato fruit (RAC)**	**fruit, peeled**	**peel**	**peeling water**	**preserve**
10-3186-01 France	<0.04	<0.04 *(n.c.)*	0.05 *(>1.3)*	<0.04 *(n.c.)*	<0.04 *(n.c.)*
10-3186-02 Italy	0.08	0.05 *(0.63)*	0.16 *(2.0)*	0.04 *(0.50)*	0.06 *(0.75)*
10-3186-03 Spain	0.11	0.07 *(0.64)*	0.20 *(1.8)*	<0.04 *(<0.36)*	0.06 *(0.55)*
10-3186-04 Portugal	0.07	0.05 *(0.71)*	0.15 *(2.1)*	0.04 *(0.57)*	0.06 *(0.86)*
Mean transfer factors:		*0.66*	*2.0*	*<0.48*	*0.72*

n.c. = not calculated (residues both in the RAC and in the processing product are below LOQ, therefore no transfer factor can be calculated)

"<" the residue in the processed fraction was below LOQ and was set to LOQ for calculating processing factors.
">" the residue in the RAC sample was below LOQ and was set to LOQ for calculating processing factors.

Table 6.5.4.8-3: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in tomato RACs and processed products of (**puree and paste processing**) following application of BYI 02960 SL 200

Trial number	tomato fruit (RAC)	strain rest	raw puree	puree	paste
10-3186-01 France	<0.04	<0.04 *(n.c.)*	0.05 *(>1.3)*	0.04 *(>1.0)*	0.07 *(>1.8)*
10-3186-02 Italy	0.08	0.08 *(1.0)*	0.12 *(1.5)*	0.11 *(1.4)*	-*
10-3186-03 Spain	0.11	0.08 *(0.73)*	0.17 *(1.5)*	0.16 *(1.5)*	-*
10-3186-04 Portugal	0.07	0.07 *(1.0)*	0.09 *(1.3)*	0.09 *(1.3)*	0.11 *(1.6)*
Mean transfer factors:		*0.91*	*1.3*	*1.4*	*1.7*

* sample was not processed to paste in this trial

n.c. = not calculated (residues both in the RAC and in the processing product are below LOQ, therefore no transfer factor can be calculated)

"<" the residue in the processed fraction was below LOQ and was set to LOQ for calculating processing factors.

">" the residue in the RAC sample was below LOQ and was set to LOQ for calculating processing factors.

Table 6.5.4.8-4: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in tomato RACs and processed products (**dried fruit processing**) following application of BYI 02960 SL 200

Trial number	tomato fruit (RAC)	dried fruit
10-3186-01 France	<0.04	0.08 *(>2.0)*
10-3186-04 Portugal	0.07	0.12 *(1.7)*
Mean transfer factors:		*1.9*

"<" the residue in the processed fraction was below LOQ and was set to LOQ for calculating processing factors.

III. Conclusions

In order to determine "processing" factors for the total residues of BYI 02960 from tomato fruit to juice, preserve, peeled fruit, puree, paste, and dried tomato, processing studies have been conducted. For juice production, the mean total residue "processing" factor was 0.70 for juice and 0.94 for washed fruit. For preserve production, the mean total residue "processing" factor was 0.72 for preserve, 0.66 for peeled fruit, and 2.0 for peel. For puree and paste production, the total residue "processing" factor was 1.3 for puree and 1.7 for paste. For dried fruit production, the total residue "processing" factor was 1.9 for dried fruit.

Peeling of fruits before further processing will result in lower total residues of BYI 02960 than in the RAC sample of tomato fruit, as the main portion of the residues is located in/on the peel. However, subsequent concentration of juice into puree and paste or drying of the fruit will lead to concentration of the total residues of BYI 02960.

Diagram 6.5.4.8-1: Industrial "processing" of tomato fruit into juice

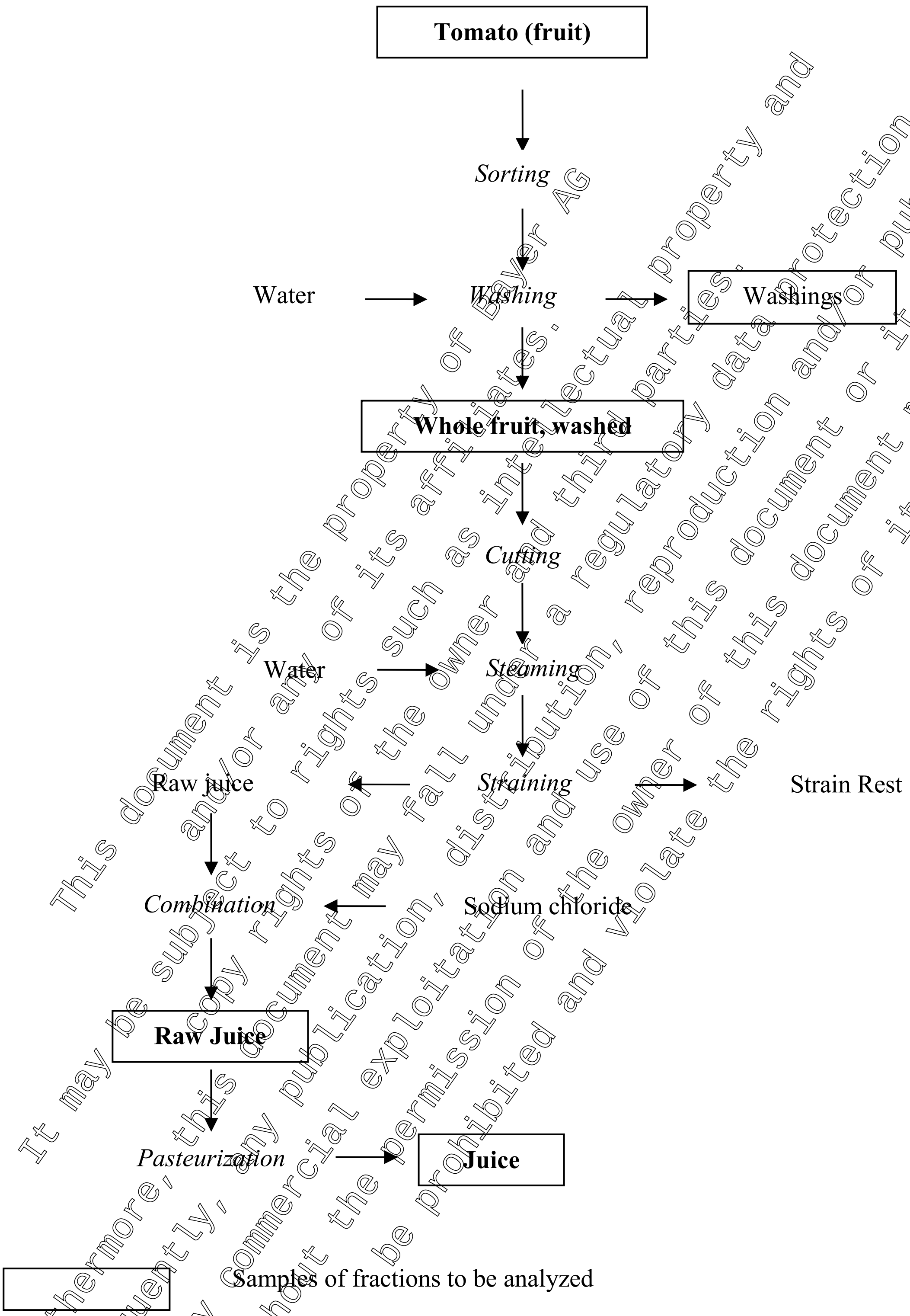

Diagram 6.5.4.8-2: Industrial "processing" of tomato fruit into preserve (=canned fruit)

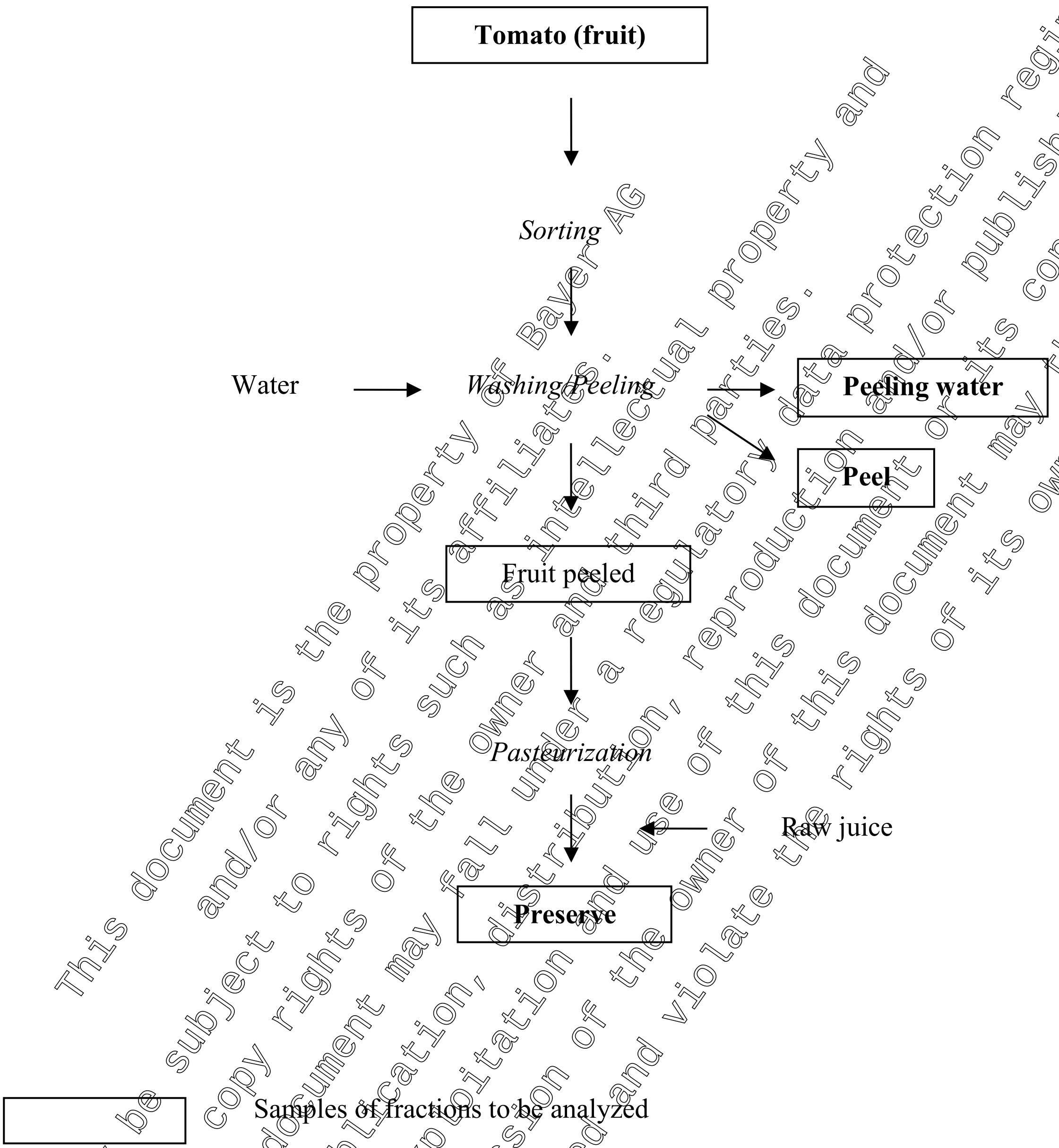

Diagram 6.5.4.8-3: Industrial "processing" of tomato fruit into dried fruit

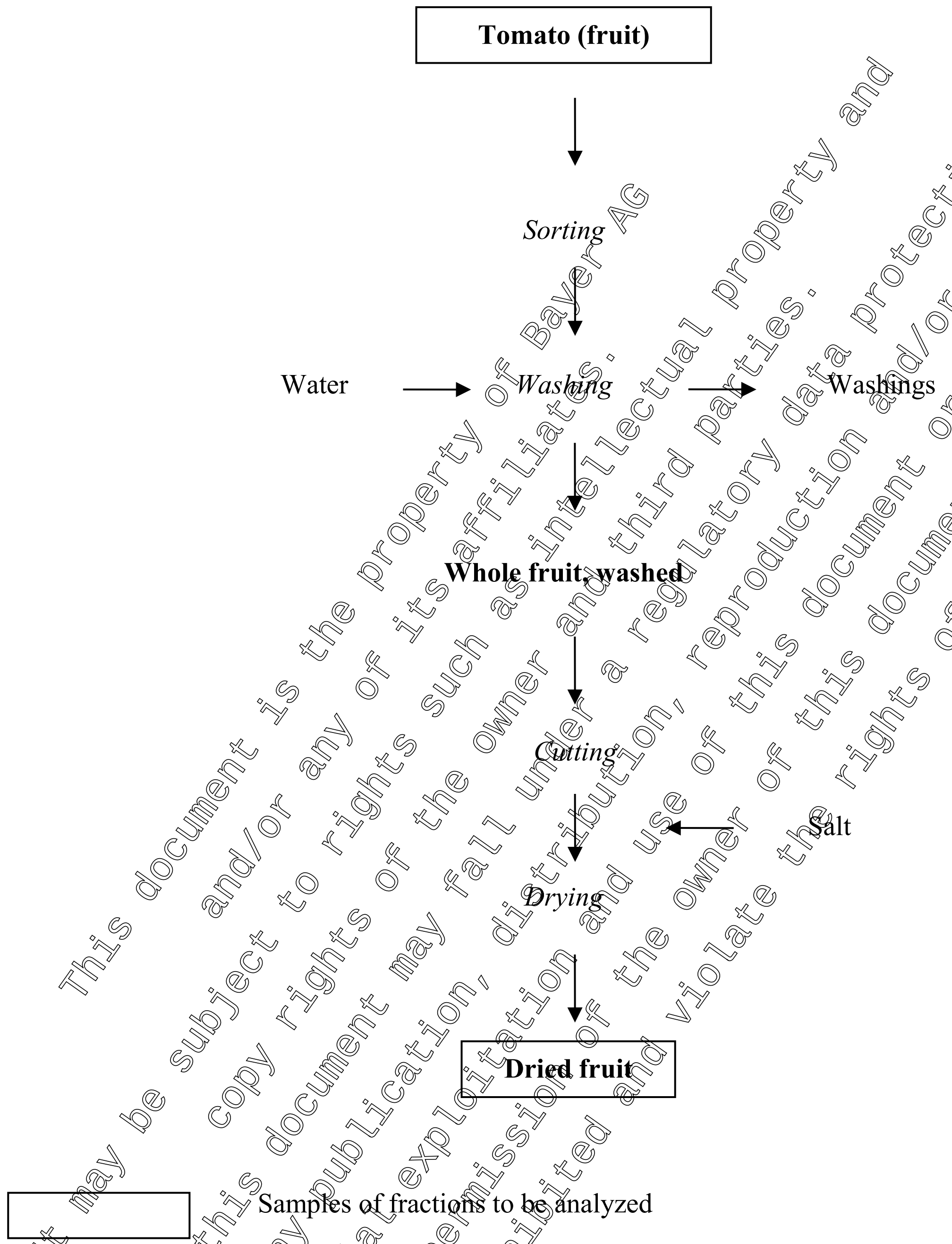

Diagram 6.5.4.8-4: Industrial "processing" of tomato fruit into puree and paste

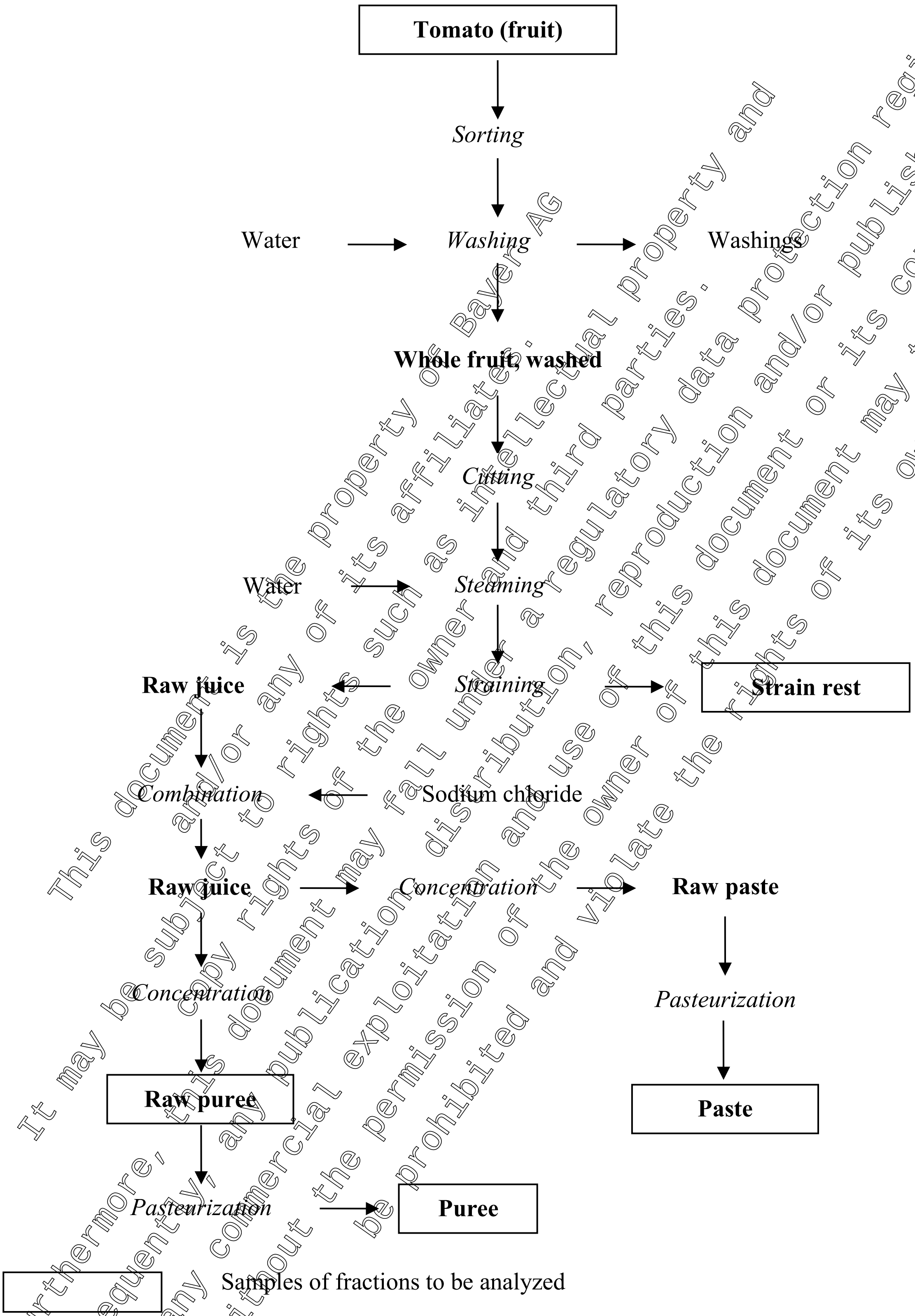

Table 6.5.4.8-5a: Application scenario in residue processing trials conducted in/on **tomato** after spraying with BYI 02960 SL 200 in European fields*

Study No. **(Trial No.) Country Location Region Year**	**Crop Variety**	**FL**	**Application No.**	**Application kg/ha (a.s.)**	**Application kg/hl (a.s.)**	**GS**	**PHI (days)**
10-3186 (10-3186-01) France [redacted] EU-S 2010	tomato Perfect Peel (Hybrid variety)	200 SL	2	0.125	0.0208	87	3
10-3186 (10-3186-02) Italy [redacted] EU-S 2010	tomato Missouri (Multiple use variety)	200 SL	2	0.125	0.0208	88	3
10-3186 (10-3186-03) Spain [redacted] EU-S 2010	tomato Malpica (Tomate de industria)	200 SL	2	0.125	0.0125	83	3
10-3186 (10-3186-04) Portugal [redacted] EU-S 2010	tomato H9144 Industry	200 SL	2	0.125	0.0179	88	3

FL=formulation GS=growth stage (BBCH-code) at last treatment
EU-S=southern European residue region

* The field part of these trials was conducted in study 10-2186

Table 6.5.4.8-5b: Results of residue processing trials conducted in/on **tomato** after spraying with BYI 02960 SL 200 in European fields

Study No. **(Trial No.) Country GLP**	**Crop Portion analyzed**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
			BYI 02960	**DFA**	**BYI 02960-DFEAF**	**total residue of BYI 02960 calc.**
10-3186 (10-3186-01) France GLP: yes	fruit (RAC)	3	<0.01	<0.02	<0.01	<0.04
	juice production					
	whole fruit, washed	3	<0.01	<0.02	<0.01	<0.04
	washings	3	<0.01	<0.02	<0.01	<0.04
	raw juice	3	<0.01	<0.02	<0.01	<0.04
	juice	3	<0.01	<0.02	<0.01	<0.04
	production of puree and paste					
	strain rest	3	<0.01	<0.02	<0.01	<0.04
	raw puree	3	0.01	0.03	<0.01	0.05
	puree	3	<0.01	0.02	<0.01	0.04
	paste	3	0.02	0.04	<0.01	0.07
	preserve production					
	peel	3	0.02	<0.02	<0.01	0.05
	peeling water	3	<0.01	<0.02	<0.01	<0.04
	fruit, peeled	3	<0.01	<0.02	<0.01	<0.04
	preserve	3	<0.01	<0.02	<0.01	<0.04
	production of dried fruit					
	fruit, dried	3	0.02	0.05	<0.01	0.08
10-3186 (10-3186-02) Italy GLP: yes	fruit (RAC)	3	0.05	<0.02	<0.01	0.08
	juice production					
	whole fruit, washed	3	0.05	<0.02	<0.01	0.08
	washings	3	0.01	<0.02	<0.01	0.04
	raw juice	3	0.04	<0.02	<0.01	0.07
	juice	3	0.03	<0.02	<0.01	0.06
	production of puree					
	strain rest	3	0.05	<0.02	<0.01	0.08
	raw puree	3	0.08	0.03	<0.01	0.12
	puree	3	0.07	0.03	<0.01	0.11
	preserve production					
	peel	3	0.13	<0.02	<0.01	0.16
	peeling water	3	0.01	<0.02	<0.01	0.04
	fruit, peeled	3	0.02	<0.02	<0.01	0.05
	preserve	3	0.03	<0.02	<0.01	0.06

DALT= days after last treatment; RAC = raw agricultural commodity

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Table 6.5.4.8-5b (cont'd): Results of residue processing trials conducted in/on **tomato** after spraying with BYI 02960 SL 200 in European fields

Study No. (Trial No.) Country GLP	Crop Portion analyzed	DALT (days)	Residues (mg/kg) expressed as BYI 02960			
			BYI 02960	DFA	BYI 02960-DFEAF	total residue of BYI 02960 calc.
10-3186 (10-3186-03) Spain GLP: yes	fruit (RAC)	3	<0.01	<0.02	<0.01	0.11
	juice production					
	whole fruit, washed	3	0.04	<0.02	<0.01	0.12
	washings	3	0.04	<0.02	<0.01	<0.04
	raw juice	3	0.05	<0.02	<0.01	0.07
	juice	3	0.11	<0.02	<0.01	0.07
	production of puree					
	strain rest	3	0.11	<0.02	<0.01	0.08
	raw puree	3	0.17	0.04	<0.01	0.17
	puree	3	<0.01	0.04	<0.01	0.16
	preserve production					
	peel	3	0.04	<0.02	<0.01	0.20
	peeling water	3	0.03	<0.02	<0.01	<0.04
	fruit, peeled	3	0.04	<0.02	<0.01	0.07
	preserve	3	0.02	<0.02	<0.01	0.06
10-3186 (10-3186-04) Portugal GLP: yes	fruit (RAC)	3	0.04	<0.02	<0.01	0.07
	juice production					
	whole fruit, washed	3	0.02	<0.02	<0.01	0.05
	washings	3	<0.01	<0.02	<0.01	<0.04
	raw juice	3	0.02	<0.02	<0.01	0.05
	juice	3	0.02	<0.02	<0.01	0.05
	production of puree and paste					
	strain rest	3	0.04	<0.02	<0.01	0.07
	raw puree	3	0.06	<0.02	<0.01	0.09
	puree	3	0.06	<0.02	<0.01	0.09
	paste	3	0.08	<0.02	<0.01	0.11
	preserve production					
	peel	3	0.12	<0.02	<0.01	0.15
	peeling water	3	0.01	<0.02	<0.01	0.04
	fruit, peeled	3	0.02	<0.02	<0.01	0.05
	preserve	3	0.03	<0.02	<0.01	0.06
	production of dried fruit					
	fruit, dried	3	0.08	0.03	<0.01	0.12

DALT = days after last treatment; RAC = raw agricultural commodity

Table 6.5.4.8-6: Recovery data for BYI 02960 in **tomato** and **tomato matrices**

Study No. **(Trial No.) GLP Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortifi-cation level** (mg/kg)	**Recovery (%)**				
						Individual recoveries	**Min**	**Max**	**Mean**	**RSD**
10-3186 (10-3186-01) to (10-3186-04) GLP: yes 2010	tomato	fruit	BYI 02960	10	0.01	93; 94; 94; 95; 97; 98; 98; 102; 104; 104	93	104	98	4.2
				3	0.10	83; 91; 91	83	91	88	5.2
				3	0.50	90; 98; 98	90	98	95	4.8
				16	overall		83	104	96	5.7
			DFA	7	0.02	87; 88; 90; 94; 96; 101; 101	87	101	94	6.2
				3	0.05	94; 95; 97	94	97	95	1.6
				6	0.50	83; 85; 89 ;90; 91; 92	83	92	88	4.0
				16	overall		83	101	92	5.7
			BYI 02960-DFEAF	10	0.01	73; 81; 82; 84; 86; 89; 89; 90; 91; 95	73	95	86	7.3
				3	0.10	83; 92; 93	83	93	89	6.2
				3	0.50	87; 92; 107	87	107	95	10.9
				16	overall		73	107	88	8.4
		raw juice	BYI 02960	5	0.01	92; 94; 97; 98; 99	92	99	96	3.0
				3	0.10	90; 93; 96	90	96	93	3.2
				8	overall		90	99	95	3.3
			DFA	5	0.02	92; 94; 94; 96; 97	92	97	95	2.1
				3	0.20	90; 91; 97	90	97	93	4.1
				8	overall		90	97	94	2.9
			BYI 02960-DFEAF	5	0.01	92; 93; 99; 99; 106	92	106	98	5.8
				3	0.10	89; 95; 96	89	96	93	4.1
				8	overall		89	106	96	5.5
		puree	BYI 02960	5	0.01	82; 83; 84; 85; 91	82	91	85	4.2
				3	0.10	79; 81; 84	79	84	81	3.1
				8	overall		79	91	84	4.2
			DFA	5	0.02	90; 92; 95; 96; 97	90	97	94	3.1
				3	0.20	88; 89; 93	88	93	90	2.9
				8	overall		88	97	93	3.6
			BYI 02960-DFEAF	5	0.01	88; 95; 95; 104; 106	88	106	98	7.6
				3	0.10	88; 88; 92	88	92	89	2.6
				8	overall		88	106	95	7.5

Remark re. sample material *fruit*: also covers *whole fruit, washed* and *fruit, peeled*
Remark re. sample material *raw juice*: also covers *juice*
Remark re. sample material *puree*: also covers *raw puree*, *preserve*, and *paste*

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Table 6.5.4.8-6 (cont'd): Recovery data for BYI 02960 in **tomato** and **tomato matrices**

Study No. **(Trial No.)** **GLP Year**	**Crop**	**Portion analyzed**	**a.s./ meta-bolite**	**n**	**Fortifi-cation level** (mg/kg)	**Recovery (%)**				
						Individual recoveries	**Min**	**Max**	**Mean**	**RSD**
10-3186 (10-3186-01) to (10-3186-04) GLP: yes 2010	tomato	peel	BYI 02960	5	0.01	90; 92; 95; 99; 106	90	106	96	6.6
				3	0.10	93; 94; 94	93	94	94	0.6
				1	1.0	85	85	85	85	
				9	overall		85	106	94	6.2
			DFA	5	0.02	88; 90; 90; 91; 92	88	92	90	1.6
				3	0.20	91; 96; 97	91	97	95	3.4
				1	1.0	81	81	81	81	
				9	overall		81	97	91	5.1
			BYI 02960-DFEAF	5	0.01	89; 95; 95; 98; 98	89	98	95	3.9
				3	0.10	94;98;98	94	98	97	2.4
				1	1.0	92	92	92	92	
				9	overall		89	98	95	3.4
		peeling water	BYI 02960	5	0.01	100; 101; 102; 104; 112	100	112	104	4.6
				3	0.10	96; 100; 100	96	100	99	2.3
				8	overall		96	112	102	4.6
			DFA	5	0.02	94; 96; 96; 97; 98	94	98	96	1.5
				3	0.20	93; 93; 95	93	95	94	1.2
				8	overall		93	98	95	1.9
			BYI 02960-DFEAF	5	0.01	91; 91; 93; 97; 99	91	99	94	3.9
				3	0.10	93; 95; 97	93	97	95	2.1
				8	overall		91	99	95	3.1

Remark re. sample material *peel*: also covers *strain rest* and *fruit, dried*
Remark re. sample material *peeling water*: also covers *washings*

IIA 6.5.4.9 Cucumber

Report:	**KIIA 6.5.4.9/01, [redacted] & [redacted]; 2012**
Title:	Determination of the residues of BYI 02960 in/on cucumber and the processed fractions (washings; whole fruit, washed; preserve; brine; and fruit, fermented) after spraying of BYI 02960 SL 200 in the field in France (south)
Report No. & Document No.:	10-3184, dated September 6, 2012 M-438180-01-1
Guidelines:	– EU Council Directive 91/414/EEC – OECD Guideline for the Testing of Chemicals No. 508, Magnitude of the Pesticide Residues in Processed Commodities – EPA Ref. OPPTS 860.1520.SUPP
GLP:	yes (certified laboratory)

I. Materials and Methods

Due to the presence of measurable residues of BYI 02960 on harvested cucumber/gherkin fruit determined in samples from field residue trials performed according to the intended commercial use conditions (see point IIA 6.3.1.7) as well as to the nature of cucumber/gherkin use (preparation and consumption patterns), investigations on the effects of basic processing have been conducted. Two trials were conducted in the southern European residue region, in France, in order to determine the total residues of BYI 02960 in unprocessed cucumber fruit and then in the primary processed commodities preserve and fermented fruit (both are varieties of pickles), as well as in intermediate fractions ([redacted] & [redacted], 2012; KIIA 6.5.4.9/01).

The field trials were conducted as part of study 10-2184 (cf. KIIA 6.3.1.7/01 for details). BYI 02960 SL 200 was sprayed twice at an application rate of approx. 125 g a.s./ha and a water volume of 550 L/ha. The final application was conducted at a pre-harvest interval of 2-3 days.

After processing (described below), residue analysis was performed according to method 01304 as used in the RAC trials themselves (for more information, cf. points IIA 6.3.1.7 and IIA 4.3). The limits of quantitation were 0.01 mg/kg (BYI 02960 and DFEAF) and 0.02 mg/kg (DFA), expressed in parent compound equivalents, yielding a calculated total-residue LOQ of 0.04 mg/kg, in all matrices. Prior and parallel to the residue analysis, the method was validated by recovery experiments.

<u>Cucumber processing</u>:
The processing of cucumber fruit into the processed fractions (washed commodities, washings, preserve, fermented fruit, and brine) simulated household practice at a laboratory scale.

<u>Processing of cucumber fruit into preserve</u>:
Fresh cucumbers were processed within 24 h after receipt in trial 10-3184-01 and within 4 days in trial 10-3184-04. Although storage was at refrigerator temperature, the cucumber fruit from trial 10-3184-04 was a bit withered when processing started. The cucumbers were soaked in water for 60–90 min to remove adhering dirt and to increase the turgor within the cells. After that, the cucumber fruits were washed by brushing. The sample materials "whole fruit, washed" and "washings" were taken.

Cucumber fruits were "scratched" with the intent to allow better absorption of brine and to avoid bursting of the fruit. Brine is composed of vinegar, salt, sugar, and spices. The prepared cucumbers and brine were filled into a preserving can in a ratio of approx. 1/1 to 1/2 (w/w).

The preserves were pasteurised (T=89°C; 20-23 min; F 0.71 to 0.80). After pasteurisation, the cucumbers were homogenised using a blender and filled in polystyrene boxes.

The process is illustrated in flow diagram 6.5.4.9-1.

<u>Processing of cucumber fruit into fermented cucumber (pickles)</u>:
Fresh cucumbers were processed within 24 h after receipt in trial 10-3184-01 and within 4 days in trial 10-3184-04. Although storage was at refrigerator temperature, the cucumber fruit from trial 10-3184-04 was a bit withered when processing started. Damaged cucumbers were sorted out, stems were removed. The cucumbers were soaked in water for 60-90 min to remove adhering dirt and to increase the turgor within the cells. After that, the cucumber fruits were washed by brushing.

Cucumber fruits were "scratched" with the intent to allow better absorption of brine and to avoid bursting of fruits. Spices and a 4% brine were added to the cucumbers (3-5 L brine/5 kg cucumbers).

Brine was filled into the pickling jar followed by a layer of herbs. Cucumbers were filled alternating in layers with herbs into the pickling jar. Finally more brine was added and the jar was closed.

The jar was stored at 21-23°C for 27-30 days. Within this time, the pH value and the acid value of the brine were controlled; the fermentation was finalised when a constant acid value was reached and the cucumbers became glassy inside. The fermented cucumbers were not homogenised using a blender before filling into polystyrene boxes.

The process is illustrated in flow diagram 6.5.4.9-2.

II. Findings

The validation of the sample material cucumber fruit was done in study 10-2189 (cf. KIIA 6.3.1.7/03 for details). The validation of the sample materials brine and washings was conducted within the present study.

Concurrent recoveries of BYI 02960 and its metabolites DFA and DFEAF were obtained from samples of cucumber matrices (cucumber fruit, brine, and washings). The recoveries for the sample material cucumber fruit are also representative for the sample materials *washed cucumber*, *fermented fruit*, and *preserve*.

In cucumber fruit samples, recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg, 0.02 mg/kg, 0.10 mg/kg, and 1.0 mg/kg (expressed in BYI 02960 equivalents); in cucumber brine and washings, spiking levels were 0.01 mg/kg and 0.10 mg/kg. Mean recoveries for all matrices were 91-113%, with RSDs in the larger validation sets (n>2) of 1.0-7.7%, n=1-6.

For DFA, concurrent recovery samples for cucumber fruit were spiked at levels of 0.02 mg/kg, 0.04 mg/kg, 0.10 mg/kg, 0.20 mg/kg, and 1.0 mg/kg (expressed in BYI 02960 equivalents); fortification levels in cucumber brine and washings were 0.02 mg/kg and 0.20 mg/kg. Mean recoveries in all matrices were 89-110%, with RSDs of 0.6-8.5%; n=1-6.

A tabular summary of the recovery values is presented below in table 6.5.4.9-3.

The total residues of BYI 02960 (parent compound plus DFA and DFEAF) in the harvested fruits at day 23 ranged from 0.10-0.17 mg/kg, as summarized previously (cf. KIIA 6.3.1.7/01). These values were used for the calculation of "processing" factors.

● <u>Preserve production</u>:

The residue levels in preserve ranged from 0.09-0.11 mg/kg. Residues in washed fruit ranged from 0.12-0.25 mg/kg, residues in washings were <0.04. Based on these values, it is evident that the total residues of BYI 02960 are lower in cucumber preserve in comparison to the cucumber fruit RAC. The measured residue levels lead to mean "processing" factors of 0.78 for preserve. The processing factor for washed fruit was calculated to be 1.34, indicating that washing of fruits does not not lead to a reduction of the total residue of BYI 02960. This assumption was supported by the fact that no residues > 0.04 mg/kg were detected in washings.

● <u>Production of fermented fruit</u>:

The residue levels in fermented fruit (= sour pickles) were from 0.06-0.09 mg/kg. In brine, residue levels were from 0.06-0.07 mg/kg. Based on these values, it is evident that the total residues of BYI 02960 are decreased in fermented fruit in comparison to the cucumber fruit RAC. The measured residue levels lead to mean "processing" factors of 0.57 for fermented fruit and 0.51 for brine.

The transfer factors for the total residues of BYI 02960 for preserve and fermented fruit production are summarized below in table 6.5.4.9-1. All trial data are summarised further below in tables 6.5.4.9-2a & b and in greater detail in the Tier 1 summary forms.

Table 6.5.4.9-1: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in cucumber RACs and processed products (processing into **preserve** and **fermented fruits**) following application of BYI 02960 SL 200

Trial number	cucumber fruit (RAC)	whole fruit, washed	washings	preserve	fruit, fermented	brine
10-3184-01 France	0.17	0.25 *(1.47)*	<0.04 *(<0.24)*	0.11 *(0.65)*	0.09 *(0.53)*	0.07 *(0.41)*
10-3184-04 France	0.10	0.12 *(1.20)*	<0.04 *(<0.40)*	0.09 *(0.90)*	0.06 *(0.60)*	0.06 *(0.60)*
Mean transfer factors:		*1.34*	*<0.32*	*0.78*	*0.57*	*0.51*

"<" the residue in the processed fraction was below LOQ and was set to LOQ for calculating processing factors.

III. Conclusions

In order to determine "processing" factors for total residues of BYI 02960 from cucumber fruits to preserve and fermented fruits – each product is a type of "pickle" – processing studies have been conducted. For preserve production, the mean total residue "processing" factor was 0.78 for preserve. Washing of fruits does not not lead to a reduction of the total residue of BYI 02960. For fermented fruit production, the mean total residue "processing" factor was 0.57 for fermented fruit and 0.51 for brine.

Preservation and fermentation of cucumber fruit both lead to a decrease in total residues of BYI 02960 in comparison to cucumber fruit RACs.

Diagram 6.5.4.9-1: Household "processing" of cucumber fruit into preserve

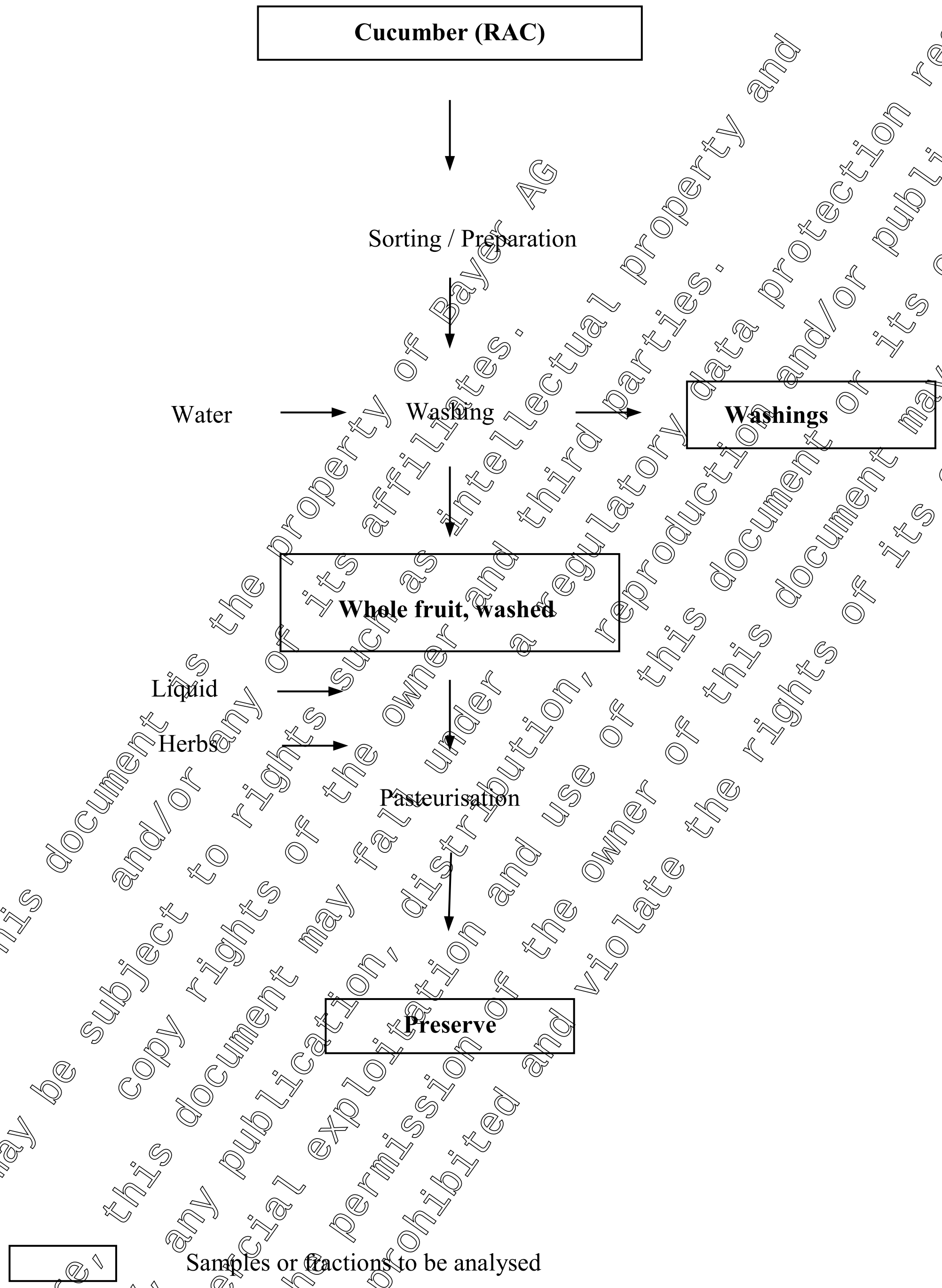

Diagram 6.5.4.9-2: Household "processing" of cucumber fruit into fermented fruit

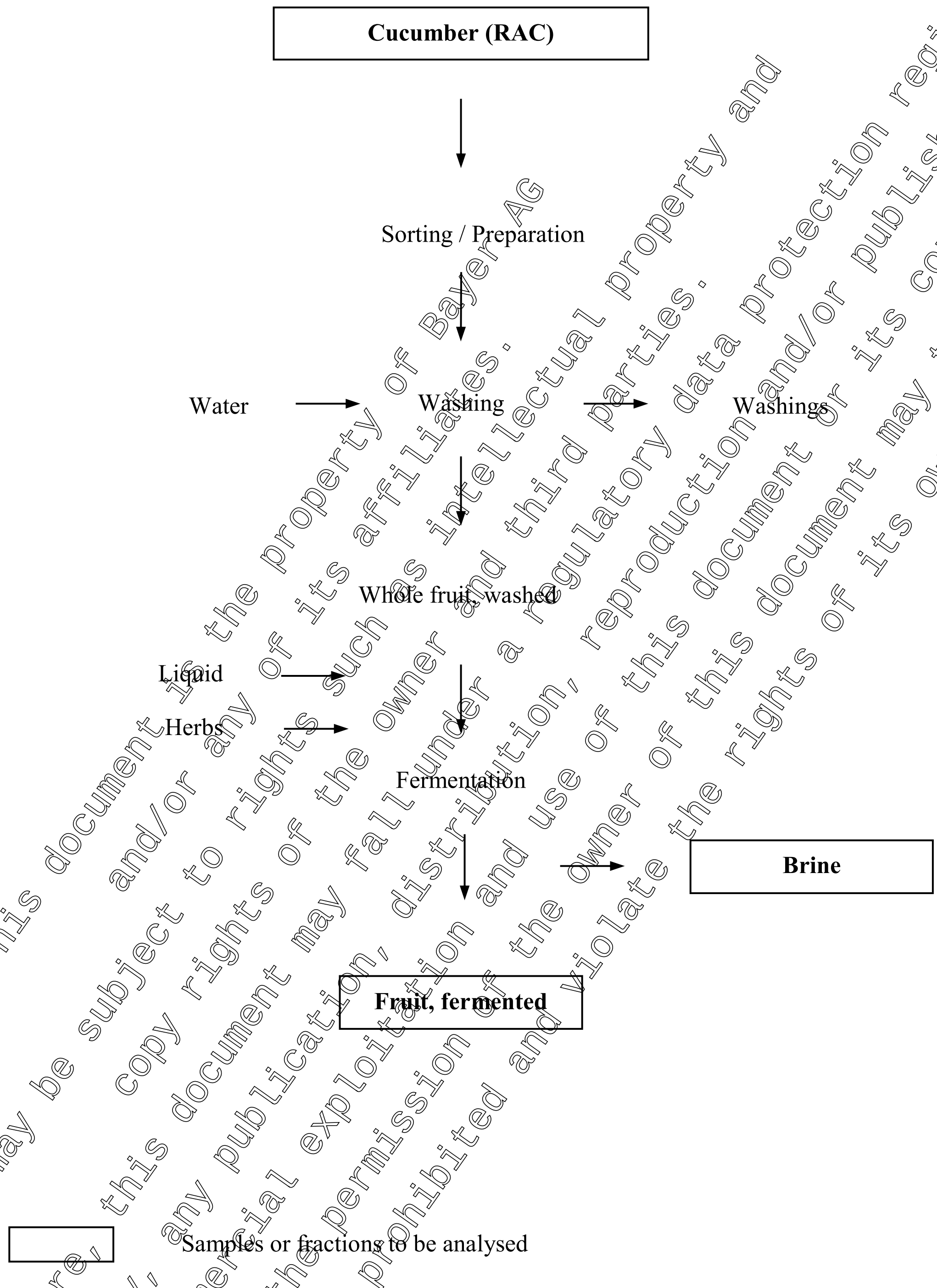

Table 6.5.4.9-2a: Application scenario in residue processing trials conducted in/on **cucumber** after spraying with BYI 02960 SL 200 in European fields*

Study No. **(Trial No.) Country Location Region Year**	**Crop Variety**	**FL**	**Application**			**GS**	**PHI (days)**
			No.	**kg/ha (a.s.)**	**kg/hl**		
10-3184 (10-3184-01) France [redacted] EU-S 2010	cucumber Marinda; Gherkin	200 SL	2	0.125	0.0250	88	3
10-3184 (10-3184-04) France [redacted] EU-S 2010	cucumber Vert petit de Paris	200 SL	2	0.125	0.0227	79	2

FL=formulation GS=growth stage (BBCH-code) at last treatment
EU-S=southern European residue region

* the field part was conducted in study 10-2184

Table 6.5.4.9-2b: Results of residue processing trials conducted in/on **cucumber** after spraying with BYI 02960 SL 200 in European fields

Study No. **(Trial No.) Country GLP**	**Portion analyzed**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
			BYI 02960	**DFA**	**BYI 02960-DFEAF**	**total residue of BYI 02960 calc.**
BYI 02960 SL 200						
10-3184 (10-3184-01) France GLP: yes	fruit (RAC)	3	0.06	0.09	<0.01	0.17
	preserve production					
	washings	3	<0.01	<0.02	<0.01	<0.04
	whole fruit, washed	3	0.09	0.14	<0.01	0.25
	preserve	3	0.03	0.07	<0.01	0.11
	fermented fruit production					
	fruit, fermented	3	0.02	0.05	<0.01	0.09
	brine	3	0.02	0.04	<0.01	0.07
10-3184 (10-3184-04) France GLP: yes	fruit (RAC)	2	0.03	0.06	<0.01	0.10
	preserve production					
	washings	2	<0.01	<0.02	<0.01	<0.04
	whole fruit, washed	2	0.02	0.09	<0.01	0.12
	preserve	2	0.02	0.06	<0.01	0.09
	fermented fruit production					
	fruit, fermented	2	0.01	0.04	<0.01	0.06
	brine	2	0.01	0.03	<0.01	0.06

DALT=days after last treatment; RAC = raw agricultural commodity

Table 6.5.4.9-3: Recovery data for BYI 02960 in **cucumber** and **cucumber matrices**

Study (Trial No.) GLP Year	Crop	Portion analyzed	a.s./ metabolite	n	Fortifi-cation level (mg/kg)	Recovery (%) Individual recoveries	Min	Max	Mean	RSD
10-3184 (10-3184-01) and (10-3184-04) GLP: yes 2010	cucumber	fruit	BYI 02960	6	0.01	98; 103; 102; 97; 97; 88	88	103	98	5.5
				1	0.02	96	96	96		
				4	0.1	105; 91; 101; 90	90	105	97	7.7
				2	1	92; 90	90	92		
				13	overall		88	105	96	5.8
			DFA	6	0.02	91; 110; 103; 103; 104; 88	88	110	100	8.5
				1	0.04	92	92	92		
				3	0.10	98; 97; 98	97	98	98	0.6
				1	0.20	95	95	95		
				2	1.0	86; 91	86	91	89	
				13	overall		86	110	97	7.3
			BYI 02960-DFEAF	6	0.01	90; 89; 96; 100; 91; 84	84	100	92	6.1
				1	0.02	97	97	97		
				4	0.10	97; 87; 92; 100	87	100	94	6.1
				2	1.0	95; 103	95	103	99	
				13	overall		84	103	94	6.0
	cucumber	washings	BYI 02960	5	0.01	112; 113; 113; 113; 115	112	115	113	1.0
				3	0.10	107; 108; 113	107	113	109	2.9
				8	overall		107	115	112	2.5
			DFA	5	0.02	106; 109; 111; 112; 113	106	113	110	2.5
				3	0.20	101; 101; 102	101	102	101	0.6
				8	overall		101	113	107	4.7
			BYI 02960-DFEAF	5	0.01	101; 102; 102; 104; 105	101	105	103	1.6
				3	0.10	97; 104; 110	97	110	104	6.3
				8	overall		97	110	103	3.6

Remark re. sample material *fruit*: also covers *whole fruit, washed*; *fruit, fermented*; and *preserve*

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Table 6.5.4.9-3 (cont'd): Recovery data for BYI 02960 in **cucumber** and **cucumber matrices**

Study (Trial No.) GLP Year	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortification level** (mg/kg)	**Recovery (%)**				
						Individual recoveries	**Min**	**Max**	**Mean**	**RSD**
10-3184 (10-3184-01) and (10-3184-04) GLP: yes 2010	cucumber	brine	BYI 02960	5	0.01	107; 107; 111; 113; 114	107	114	110	3.0
				3	0.10	109; 111; 112	109	112	111	1.4
				8	overall		107	114	111	2.4
			DFA	5	0.02	106; 107; 108; 110; 110	106	110	108	1.7
				3	0.20	98; 99; 105	98	105	101	3.8
				8	overall		98	110	105	4.4
			BYI 02960-DFEAF	5	0.01	92; 99; 103; 108; 110	92	110	102	7.1
				3	0.10	102; 103; 105	102	105	103	1.5
				8	overall		92	110	103	5.4

IIA 6.5.4.10 Barley

Report:	**KIIA 6.5.4.10/01, [redacted] & [redacted]; 2012**
Title:	Determination of the residues of BYI 02960 in/on spring barley and the processed fractions (malt sprouts; brewer's malt; brewer's grain, hops draff; brewer's yeast; beer; pearl barley; pearl barley rub off) after spraying of BYI 02960 SL 200 in the field in Germany
Report No. & Document No.:	10-3410 dated October 16, 2012 M-439853-01-1
Guidelines:	– EU Council Directive 91/414/EEC – EC Guidance working document 7029/VI/95 rev.5 – EU Guidance Working Document 7035/VI/95 rev. 5 – OECD Guideline for the Testing of Chemicals No. 508, Magnitude of the Pesticide Residues in Processed Commodities – EPA Ref. OPPTS 860.1520 SUPP
GLP:	yes (certified laboratory)

I. Materials and Methods

Due to the presence of measurable residues of BYI 02960 on harvested cereal crops determined in samples from field rotational crop residue trials (cf. section 6.6.3.1) as well as to the nature of cereal-crop preparation and consumption patterns, investigations on the effects of industrial processing have been conducted. Two trials were conducted in the northern European residue region, both in Germany, in order to determine the total residues of BYI 02960 in unprocessed spring barley grain and then in the primary processed products beer and pearl barley, as well as in intermediate fractions, including malt ([redacted] & [redacted]; 2012; KIIA 6.5.4.10/01).

In the field trials, BYI 02960 SL 200 was sprayed once at an application rate of approx. 460g a.s./ha and a water volume of 300 L/ha. The application scheme reflects an overdosing (approx. 3× higher than the envisaged EU worst case) in a spray application scheme, in order to ensure that detectable residues would be found in the relevant raw commodities at harvest, thus allowing elucidation of processing factors.

Spring barley (grain) samples to be processed were sampled 22 and 20 days after the treatment at commercial harvest (BBCH 89) in trials 10-3410-01 and 10-3410-02, respectively.

After processing (described below), residue analysis was performed according to method 01304 (for more information, cf. point IIA 4.3). The limits of quantitation were 0.01 mg/kg (BYI 02960 and DFEAF) and 0.02 mg/kg (DFA), expressed in parent compound equivalents, yielding a calculated total-residue LOQ of 0.04 mg/kg, in all matrices with the exception of hops draff. In hops draff, the limits of quantitation were 0.1 mg/kg (BYI 02960 and DFEAF) and 0.2 mg/kg (DFA), yielding a calculated total-residue LOQ of 0.4 mg/kg. Prior and parallel to the residue analysis, the method was validated by recovery experiments.

<u>Processing procedures:</u>
Barley grain "processing" was designed to simulate industrial procedures of grain into the processed

fractions (malt sprouts, brewer's malt, brewer's grain, hops draff, brewer's yeast, and beer, as well as in pearl barley and pearl barley rub-off).

Cleaning:
The field specimens for processing were cleaned. In order to obtain acceptable results, grain with a moisture content of approx. 14% was required. The optimal moisture content was already reached at the sampling date; therefore no drying of the field specimens was necessary before cleaning.

Malting:
Before malting was started, the grain was sieved (sieve mesh 2.5 mm). The steeping process was conducted as a combined wet and dry steeping. Sieved barley grain was transferred into a special steeping vessel. The final steeping degree was in the range of 44.2 to 44.4%.

For proper performance the duration of germination, the mean temperature of wet air and the relative humidity of the air around the kernels was controlled. During the intensive respiration, the steeped wares were turned over continuously. After germination, the life processes were terminated by kilning. Kiln-drying was conducted in a dry chamber. The max. temperature during the kiln-drying process was 80.0°C. After kiln-drying, the germ was removed mechanically by a trimmer. Brewer's malt and malt sprouts were sampled 2-4 days after malting. Until brewing, the malt was stored at room temperature.

Brewing:
Before mashing, the brewer's malt was dry milled in a special malt mill. The crushed malt was mixed with brew water. To produce Pilsener beer, mashing was started in a heatable tun.

After mash boiling, the wort was separated from the insoluble malt components (brewer's grain). The extract remaining in the brewer's grain was extracted by washing with hot water (first filter runnings). The wort separation was done using a refining vat. After separation, the brewer's grain was sampled.

Hop pellets were added and the separated wort was boiled (about 90 min at normal pressure). After boiling, the flocs (hops draff) were separated in a whirlpool, causing the sludge to deposit on the bottom in the shape of a cone. For cooling and ventilating the wort, an intra-plant circulation was used. By adding oxygen (intra-plant circulation), the conditions for the start of the fermentation were prepared. Hops draff was sampled.

In the pilot plant, the classical primary fermentation (low fermentation) was carried out in bottom-fermentation containers. Fermentation heat was dissipated by means of room ventilation. As soon as the extract content of the fermented young beer was 2% higher than the final attenuation, the storing time began. Before maturation, the young beer was cooled down. During the main fermentation, the yeast deposited on the tank bottom and was sampled as brewer's yeast.

At the beginning of maturation, the young beer was stored at room temperature (warm maturation to break down the diacetyl) in casks. Then the young beer was stored under pressure (approx. 0.8-1.8 bar) at approx. 0-2°C (cold maturation) for about 3-4 weeks. In this time, the remaining extract was fermented. Unwanted flavour and odorous substances were decomposed or expelled. Sludge particles and yeast settle at the bottom. The rack beer was filtered using a special filter combination. During filtration, all organisms harming the beer (bacteria and yeast) were removed and sludge particles were separated. The final product, beer, was sampled and the quality of the beer was analyzed.

Pearl barley production:
Before beginning pearl barley production, an optimal moisture content of barley grain of about 15% was achieved, therefore it was not necessary to dry or dampen the grain.

The specimens of spring barley were hulled using a vertical hulling machine. Each sample was hulled until the stipulated abrasion for pearl barley of 30-35% was reached. The degree of abrasion (pearling dust/bran and flour) was determined by the proportion of pearl barley with respect to the total portion of cleaned grain used for hulling process. Pearl barley and pearl barley rub off were sampled.

The processes are illustrated in flow diagrams 6.5.4.10-1 – 6.5.4.10-3.

II. Findings

The validation of the sample materials malt sprouts, brewer's yeast, and beer was conducted within the present study. Grain (represented by wheat grain) was validated in the main validation set for method 01304 (cf. point IIA 4.3). Hops draff was validated in study 10-3407 (cf. KIIA 6.3.2.1/01 and KIIA 6.5.4.2/01).

Concurrent recoveries were obtained from samples of grain, malt sprouts, brewer's yeast, and beer. The recoveries for the sample material *grain* are also representative for *brewer's malt*, *brewer's grain*, *pearl barley*, and *pearl barley rub-off*.

In all mentioned matrices, recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg and 0.10 mg/kg (expressed in BYI 02960 equivalents), with the exceptions of barley grain, where a level of 5.0 mg/kg was as well, and of hops draff, where the spiking levels were 0.10 mg/kg and 1.0 mg/kg. Mean recoveries for all matrices were 77-108%, with RSDs in the larger validations sets (n > 2) of 1.0-10.9%; n=1-5.

For DFA, concurrent recovery samples for spring barley grain and grain matrices (malt sprouts, brewer's yeast, and beer) were spiked at levels of 0.02 mg/kg and 0.20 mg/kg (expressed in BYI 02960 equivalents), with the exceptions of barley grain, where levels of 0.02 mg/kg, 0.50 mg/kg, and 5.0 mg/kg were spiked, and of hops draff, where the spiking levels were 0.20°mg/kg and 1.0°mg/kg. Mean recoveries in all matrices were 81-105%, with RSDs in the larger validations sets (n > 2) of 1.5-7.1%; n=1-5.

A tabular summary of the recovery values is presented below in table 6.5.4.10-4.

The total residues of BYI 02960 (parent compound plus DFA and DFEAF) in the harvested spring barley grain at BBCH growth stage 89 were found at 0.91 and 1.6 mg/kg in the first and second trials, respectively. These values were used for the calculation of "processing" factors.

● <u>Malting</u>:

<u>Malt sprouts</u>: The levels of the total residue of BYI 02960 in malt sprouts were from 0.97-1.2 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.91 (range: 0.75-1.07, n=2).

<u>Brewer's malt</u>: The levels of the total residue of BYI 02960 in brewer's malt were 0.44-0.88 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.52 (range: 0.48-0.55, n=2).

The transfer factors for malt sprouts and brewer's malt show a reduction in total residues of BYI 02960 for brewer's malt, which is used in the following process of beer brewing, while the residues remain in malt sprouts.

● <u>Brewing</u>:

<u>Brewer's grain</u>: In brewer's grain, the levels of the total residue of BYI 02960 were 0.07-0.10 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.075 (range: 0.04-0.11, n=2).

<u>Hops draff</u>: In hops draff, the levels of the total residue of BYI 02960 were 0.46-0.59 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.44 (range: 0.37-0.51, n=2).

<u>Brewer's yeast</u>: In brewer's yeast, the levels of the total residue of BYI 02960 were 0.09-0.20 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.12 (range: 0.10-0.13, n=2).

<u>Beer</u>: In beer, the levels of the total residue of BYI 02960 were 0.09-0.11 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.085 (range: 0.07-0.10, n=2).

The results of the transfer factors during the brewing process clearly indicate a reduction in total residues of BYI 02960 for the end product beer. A high amount of residues is removed from the process by the removal of hops draff.

● <u>Pearl barley production</u>:

<u>Pearl barley rub-off</u>: In pearl barley rub-off, the levels of the total residue of BYI 02960 were 2.9-4.1 mg/kg. The measured residue levels lead to a mean "processing" factor of 2.9 (range: 2.56-3.19, n=2).

<u>Pearl barley</u>: In pearl barley, the levels of the total residue of BYI 02960 were 0.13-0.17 mg/kg. The measured residue levels lead to a mean "processing" factor of 0.14 (range: 0.08-0.19, n=2).

These findings clearly indicate that total residues of BYI 02960 remain to a large extent in pearl barley rub-off and can be removed from barley grain by hulling, resulting in lower residues in the end product, pearl barley.

The transfer factors for the total residues of BYI 02960 are summarized below in tables 6.5.4.10-1 and 6.5.4.10-2. All trial data are summarised further below in table 6.5.4.10-3a & b and in greater detail in the Tier 1 summary forms.

Table 6.5.4.10-1: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in barley RACs and processed products (**processing into malt and beer)** following application of BYI 02960 SL 200

Trial number	grain	malt sprouts	brewer's malt	brewer's grain	hops draff	brewer's yeast	beer
10-3410-01	0.91	0.97 *(1.07)*	0.44 *(0.48)*	0.10 *(0.11)*	0.46 *(0.51)*	0.09 *(0.10)*	0.09 *(0.10)*
10-3410-02	1.6	1.2 *(0.75)*	0.88 *(0.55)*	0.07 *(0.04)*	0.59 *(0.37)*	0.20 *(0.13)*	0.11 *(0.07)*
Mean transfer factors:		*0.91*	*0.52*	*0.075*	*0.44*	*0.12*	*0.085*

Table 6.5.4.10-2: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in barley RACs and processed products (**processing into pearl barley**) following application of BYI 02960 SL 200

Trial number	grain	pearl barley rub-off	pearl barley
10-3410-01	0.91	2.9 *(3.19)*	0.17 *(0.19)*
10-3410-02	1.6	4.1 *(2.56)*	0.13 *(0.08)*
Mean transfer factors:		*2.9*	*0.14*

III. Conclusions

In order to determine "processing" factors for total residues of BYI 02960 from spring barley grain in malt and beer as well as in pearl barley, two processing studies have been conducted.

For malt sprouts and brewer's malt, mean processing factors of 0.91 and 0.52 were found, respectively. These transfer factors show a reduction in total residues of BYI 02960 for brewer's malt, which is used in the following process of beer brewing, while the residues remain in malt sprouts.

The mean processing factors for brewer's grain, hops draff, brewer's yeast, and beer were 0.075, 0.44, 0.12, and 0.085, respectively. These results clearly indicate a reduction in total residues of BYI 02960 for the end product beer during the brewing process. A high amount of residues is removed from the process by the removal of hops draff.

The mean value of total residue "processing" factors for pearl barley rub-off was 2.9, and 0.14 for pearl barley. These findings clearly indicate that total residues of BYI 02960 remain to a large extent in the pearl barley rub-off and can be removed from barley grain by hulling, resulting in lower residues in the end product, pearl barley.

Diagram 6.5.4.10-1: Industrial "processing" of grain to malt

Grain (RAC)

↓

Cleaning / Sieving

↓

Steeping
(steeping degree: 44.2–44.4%)

↓

Germination

↓

Malt Sprouts ← Trimmer ← Kiln-drying (max. temperature: 80°C) → **Brewer's Malt**

☐ Samples or fractions to be analysed

Diagram 6.5.4.10-2: Industrial "processing" of malt to beer

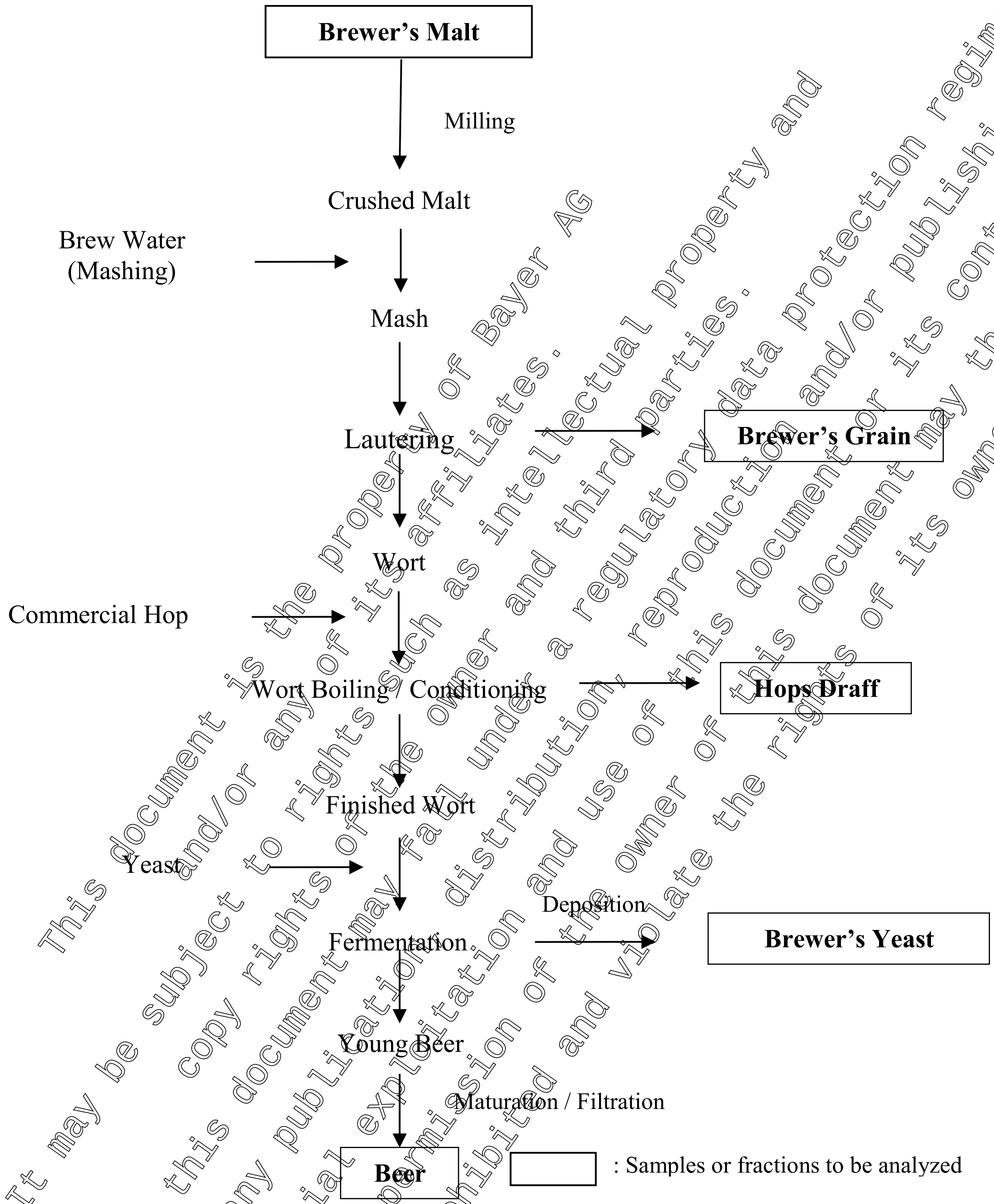

Diagram 6.5.4.10-3: Industrial "processing" of spring barley to pearl barley

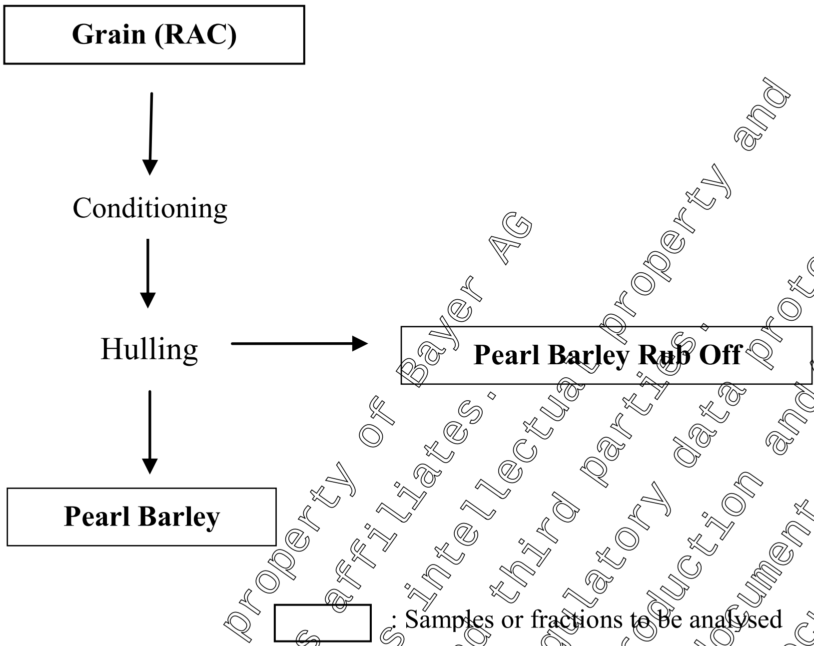

Table 6.5.4.10-3a: Application scenario in residue processing trials conducted in/on **barley** after spraying with BYI 02960 SL 200 in northern European fields

Study No. **(Trial No.) Country Location Region Year**	**Crop Variety**	**FL**	**Application**			
			No.	**kg/ha (a.s.)**	**kg/hl (a.s.)**	**GS**
10-3410 (10-3410-01) Germany [redacted] EU-N 2010	barley, spring Laverda	200 SL	1	0.46	0.15	83
10-3410 (10-3410-02) Germany [redacted] EU-N 2010	barley, spring Tocada	200 SL	1	0.46	0.153	87

FL=formulation
EU-N=northern European residue region
GS=growth stage (BBCH-code) at last treatment

Table 6.5.4.10-3b: Results of residue processing trials conducted in/on **barley** after spraying with BYI 02960 SL 200 in European fields

Study No. **(Trial No.) Country GLP**	**Portion analyzed**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
			BYI 02960	**DFA**	**BYI 02960-DFEAF**	**total residue of BYI 02960 calc.**
10-3410 (10-3410-01) Germany GLP: yes	grain (RAC)	22	0.84	0.04	0.03	0.91
	malt processing					
	malt sprouts	22	0.32	0.49/0.04**	0.16	0.97/0.06**
	brewer's malt	22	0.37	0.04	0.04	0.44
	beer production					
	brewer's grain	22	0.07	<0.02	<0.01	0.10
	hops draff	22	0.16	<0.2	<0.1	0.46
	brewer's yeast	22	0.06	<0.02	<0.01	0.09
	beer	22	0.06	<0.02	<0.01	0.09
	pearl barley production					
	pearl barley	22	0.12	0.03	0.03	0.17
	pearl barley rub-off	22	2.8	0.08	0.05	2.9
10-3410 (10-3410-02) Germany GLP: yes	grain (RAC)	20	1.6	0.03	0.02	1.6
	malt processing					
	malt sprouts	20	0.66	0.36	0.14	1.2
	brewer's malt	20	0.83	0.02	0.03	0.88
	beer production					
	brewer's grain	20	0.04	<0.02	<0.01	0.07
	hops draff	20	0.29	<0.2	<0.1	0.59
	brewer's yeast	20	0.17	<0.02	<0.01	0.20
	beer	20	0.08	<0.02	<0.01	0.11
	pearl barley production					
	pearl barley	20	0.10	<0.02	<0.01	0.13
	pearl barley rub-off	20	4.0	0.05	0.04	4.1

** residue in control sample; RAC = raw agricultural commodity

Table 6.5.4.10-4: Recovery data for BYI 02960 in **barley** and **barley matrices**

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortifi-cation level** (mg/kg)	**Recovery (%)** **Individual recoveries**	**Min**	**Max**	**Mean**	**RSD**
10-3410 (10-3410-01) and (10-3410-02) GLP: yes 2010	barley, spring	grain	BYI 02960	1	0.01	107	107	107		
				1	0.1	109	109	109		
				1	5	89	89	89		
				3	overall		89	109	102	10.8
			DFA	1	0.02	114	114	114		
				1	0.50	100	100	100		
				1	5.0	80	80	80		
				3	overall		80	114	98	17.4
			BYI 02960-DFEAF	1	0.01	97	97	97		
				1	0.10	97	97	97		
				1	5.0	96	96	96		
				3	overall		96	97	97	0.6
		malt sprouts*	BYI 02960	5	0.01	76; 66; 73; 82; 88	66	88	77	10.9
				3	0.1	84; 79; 85	79	85	83	3.9
				8	overall		66	88	79	9.1
			DFA	5	0.02	72; 78; 84; 85; 85	72	85	81	7.1
				3	0.20	83; 83; 87	83	87	84	2.7
				8	overall		72	87	82	5.9
			BYI 02960-DFEAF	5	0.01	96; 87; 90; 87; 94	87	96	91	4.5
				3	0.10	93; 88; 91	88	93	91	2.8
				8	overall		87	96	91	3.7

Remark re. sample material *grain*: also covers *brewer's malt*; *brewer's grain*; *pearl barley*; and *pearl barley rub-off*

* For recoveries of malt sprouts, the control sample used yielded residue levels of 0.0367 mg/kg of difluoroacetic acid. Therefore, the recoveries at the level of 0.02 mg/kg had to be background-corrected. The uncorrected values are given in brackets: 72 (258); 78 (262); 84 (268); 85 (268); 85 (268).

Continued on next page…

Table 6.5.4.10-4 (cont'd): Recovery data for BYI 02960 in **barley** and **barley matrices**

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortification level** (mg/kg)	**Recovery (%)** Individual recoveries	Min	Max	Mean	RSD
10-3410 (10-3410-01) and (10-3410-02) GLP: yes 2010	barley, spring	brewer's yeast	BYI 02960	5	0.01	102; 109; 106; 109; 99	99	109	105	4.2
				3	0.1	106; 108; 111	106	111	108	2.3
				8	overall		99	111	106	3.8
			DFA	5	0.02	92; 96; 97; 98; 101	92	101	97	3.4
				3	0.20	91; 90; 87	87	91	89	2.3
				8	overall		87	101	94	5.0
			BYI 02960-DFEAF	5	0.01	101; 102; 105; 102; 108	101	108	104	2.8
				3	0.10	103; 102; 104	102	104	103	1.0
				8	overall		101	108	103	2.2
		beer	BYI 02960	5	0.01	95; 103; 96; 94; 103	94	103	98	4.5
				3	0.1	97; 92; 94	92	97	94	2.7
				8	overall		92	103	97	4.3
			DFA	5	0.02	97; 99; 101; 99; 100	97	101	99	1.5
				3	0.20	92; 98; 95	92	98	95	3.2
				8	overall		92	101	98	3.0
			BYI 02960-DFEAF	5	0.01	94; 90; 101; 105; 100	90	105	98	6.1
				3	0.10	94; 105; 97	94	105	99	5.8
				8	overall		90	105	98	5.5
	barley, spring	hops draff**	BYI 02960	5	0.10	84; 94; 96; 105; 108	84	108	97	9.8
				3	1.0	101; 102; 105	101	105	103	2.0
				8	overall		84	108	99	7.8
			DFA	5	0.20	98; 99; 108; 109; 111	98	111	105	5.8
				3	1.0	97; 101; 102	97	102	100	2.6
				8	overall		97	111	103	5.3
			BYI 02960-DFEAF	5	0.10	103; 105; 105; 105; 109	103	109	105	2.1
				3	1.0	100; 104; 107	100	107	104	3.4
				8	overall		100	109	105	2.5

**recovery determinations for hops draff were performed in study 10-3407 (cf. KIIA 6.5.4.2/01)

IIA 6.5.4.11 Wheat

➢ **EU processing study**

Report:	**KIIA 6.5.4.11/01, [redacted] & [redacted]; 2012**
Title:	Determination of the residues of BYI 02960 in/on wheat and the processed fractions (semolina; semolina bran; whiteflour bran; white flour; white bread; whole meal; whole meal bread and wheat germ) after spraying of BYI 02960 SL 200 in the field in Germany
Report No. & Document No.:	10-3409, dated October 30, 2012 M-440307-01-1
Guidelines:	– EU Council Directive 91/414/EEC – EC Guidance working document 7029/VI/95 rev.5 – EU Guidance Working Document 7035/VI/95 rev. 5 – OECD Guideline for the Testing of Chemicals No. 508, Magnitude of the Pesticide Residues in Processed Commodities – EPA Ref. OPPTS 860.1520.SUPP
GLP:	yes (certified laboratory)

I. Materials and Methods

Due to the presence of measurable residues of BYI 02960 on harvested cereal crops determined in samples from field rotational crop residue trials (cf. section 6.6.3.1) as well as to the nature of cereal-crop preparation and consumption patterns, investigations on the effects of industrial processing have been conducted. In order to determine the magnitude of the relevant residues of BYI 02960 in/on processed fractions of wheat, two trials were conducted in the northern European residue region, in Germany, in order to determine the total residues of BYI 02960 in unprocessed wheat grains and then in the primary processing products flour and bread (white and whole wheat) and semolina, as well as in intermediate fractions, including wheat germ ([redacted] & [redacted], 2012; KIIA 6.5.4.11/01).

BYI 02960 SL 200 was sprayed once at an application rate of 460 g a.s./ha and a water volume of 300 L/ha. The application was conducted at a pre-harvest interval of 22 days and reflects an overdosing of approx. 3× the envisaged EU worst case, in order to ensure that detectable residues would be found in the relevant raw commodities at harvest, thus allowing elucidation of processing factors

After processing (described below), residue analysis was performed according to method 01304 (for more information, cf. IIA 4.3). The limits of quantitation were 0.01 mg/kg (BYI 02960 and DFEAF) and 0.02 mg/kg (DFA), expressed in parent compound equivalents, yielding a calculated total-residue LOQ of 0.04 mg/kg, in all matrices. Prior and parallel to the residue analysis, the method was validated by recovery experiments.

Wheat processing:
The processing of wheat samples into the processed fractions semolina, semolina bran, white-flour bran; white flour, white bread, whole meal, wholemeal bread, and wheat germ was performed to simulate industrial procedures at a laboratory scale

<u>Drying, cleaning, and conditioning of wheat grain</u>:
Frozen field samples for processing were defrosted, followed by drying for 12 hours at 30°C at the test site. The dried field samples were cleaned and then shipped at ambient temperature for further processing.

Weight and moisture content of grain specimens were determined on arrival. If the moisture content in the grain was above 15–16%, the specimens were dried at 30°C for approx. 9 hours. If the moisture content in the grain was below 15–16%, the specimens were moistened by addition of tap water. All grain samples were adjusted to a moisture content of 15.5-15.6%.

The process is illustrated in flow diagram 6.5.4.11-1.

<u>Milling of white flour (type 550) and baking of white bread</u>:
In a closed system with different pairs of smooth rollers and sifter passages, the grain was milled to straight flour, semolina, and semolina bran. Samples of semolina and semolina bran were collected.

In a further processing step, low grade meal (toppings) was separated from the semolina bran using a centrifuge/scouring machine. This process resulted in white flour bran and low grade meal (toppings). A sample of white-flour bran was collected.

The mineral contents of straight flour and low grade meal were determined. If the mineral content of straight flour exceeded 510-630 g/100 kg flour, both fractions were mixed until a mineral content of 510-630 g/100 kg flour was achieved, forming the processed fraction white flour (type 550). A sample of white flour (type 550) was taken.

For baking a 1.0 kg loaf of white bread, white flour (approx. 1.0 kg), yeast (approx. 40 g), salt (approx. 20 g), and water (approx. 0.7 L) were mixed. Subsequently, the dough was kneaded for 7 min and fermented for about 20 min. It was then moved for 10 min followed by a second fermentation period of 50 min. The baking process was conducted at 220°C for 30 min. Afterwards, a sample of white bread was taken (dependent on the wheat grain quality and the baking process/course, the processing parameters were adjusted and may vary in comparison to the above-mentioned values).

The process is illustrated in flow diagram 6.5.4.11-2.

<u>Milling of whole meal and baking of whole-meal bread</u>:
For the generation of whole meal and whole-meal bread, the same milling procedure was used as described for the production of white flour (type 550). After milling, the bran was cracked with an impact mill into smaller pieces. All milling products of the process were mixed homogeneously in a special flour mixer to generate the processed fraction whole meal. A sample of the whole meal was collected.

For baking a 1.0 kg loaf of whole-meal bread, whole meal (approx. 1.0 kg), yeast (approx. 40 g), salt (approx. 20 g), and water (approx. 0.7 L) were mixed. Subsequently, the resulting dough was kneaded for 7 min and fermented for about 20 min. It was then moved for 10 min followed by a second fermentation period of 40 min. The baking process was conducted at 220°C for 30 min. A sample of whole-meal bread was taken (dependent on the wheat grain quality and the baking process/course, the processing parameters were adjusted and may vary in comparison to the above-mentioned values).

The process is illustrated in flow diagram 6.5.4.11-3.

Production of wheat germ:
Wheat grain was broken to "bruised grain" in a special mill (roller mill with 0.5 mm roller distance). The fraction 400-1000 µm was collected, the fraction above 1000 µm was broken once more (0.3 mm roller distance). This milling/sieving process was performed a total of three times, with a final roller distance of 0.2 mm. The fractions obtained below 400 µm and the fraction above 1000 µm were completely excluded from further processing.

The fraction 400-1000 µm was put in a special separator ("Leichtgewichtsausleser"). Due to the different specific weights of the bran, semolina, and germ, the semolina/germ mixture was separated from most parts of the bran.

Subsequently, the semolina/germ mixture was milled to flour and small wheat germ discs (incl. parts of bran) in a mill with a pair of smooth rollers. The wheat germ with parts of bran was then sieved to separate the various fractions (germ with small parts of bran, and bran). From the separated germ discs, small parts of bran were removed manually. A sample of wheat germ was taken.

The process is illustrated in flow diagram 6.5.4.11-4.

II. Findings

The validation of the sample material wheat grain was done during the main validation work for method 01304 (cf. IIA 4.3). Validation of whole-meal bread was conducted in the present study (10-3409).

Concurrent recoveries were obtained from samples of wheat grain, meal, semolina bran, whole-meal bread. The recoveries for the sample material *grain* are also representative for *whole meal*, *white flour*, *semolina*, *semolina bran*, *white-flour bran*, and *wheat germ*; those for the sample material *whole-meal bread* are also representative for *white bread*.

In wheat grain and in whole-meal bread samples, concurrent recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg and 0.50 mg/kg (expressed in BYI 02960 equivalents); in wheat meal, spiking level was 0.50 mg/kg. In semolina samples, recovery samples for parent compound and DFEAF were spiked at 0.01 mg/kg. Mean recoveries for parent compound and DFEAF for all matrices were 84-110%, with RSDs in the larger validation sets (n>2) of 1.2-8.2%; n=3-5.

For DFA, concurrent recovery samples for wheat grain and for whole-meal bread were spiked at levels of 0.02 mg/kg and 0.50 mg/kg (expressed in BYI 02960 equivalents); the fortification level in wheat meal was 0.50 mg/kg. In semolina samples, recovery samples DFA were spiked at 0.02 mg/kg. Mean recoveries for DFA in all matrices were 72-89%, with RSDs in the larger validation sets (n>2) of 3.8-8.6%; n=3-5.

A tabular summary of the recovery values is presented below in table 6.5.4.11-3.

The total residues of BYI 02960 (parent compound plus DFA and DFEAF) in the harvested wheat grain (RAC) at day 22 ranged from 0.17-0.26 mg/kg. These values were used for the calculation of "processing" factors.

● Semolina, white flour and white bread:

Semolina and semolina bran: In semolina, total residues of BYI 02960 ranged from 0.09-0.37 mg/kg. In the semolina bran fraction, residues were considerably higher and ranged from 0.65-1.6 mg/kg. Resulting mean transfer factors were 0.95 and 5.0, respectively.

White flour, white-flour bran and white bread: In white flour, total residues of BYI 02960 ranged from 0.05-0.11 mg/kg; those in white-flour bran were considerably higher and ranged 0.85-2.0 mg/kg. In white bread, residues of total BYI 02960 ranged from 0.05-0.08 mg/kg. The resulting mean transfer factors were 0.35, 6.4, and 0.3, respectively.

Based on these values, it is evident that a large proportion of the residues concentrates in the bran fractions, while residues in white flour and white bread are clearly reduced.

● Whole meal and wholemeal bread:

In whole meal, total residues of BYI 02960 ranged from 0.24-0.40 mg/kg. In whole-meal bread, total residues BYI 02960 ranged from 0.15-0.25 mg/kg. The measured residue levels lead to mean "processing" factors of 1.5 for whole meal and 0.95 for whole-meal bread, respectively, showing a reduction of total residues of BYI 02960 during production of whole-meal bread in comparison to the concentration in the grain RAC.

● Wheat germ:

In wheat germ, total residues BYI 02960 ranged from 0.14-0.34 mg/kg. The measured residue levels lead to a mean "processing" factor of 1.1 for wheat germ, indicating that total residues of BYI 02960 are located in the wheat germ, in addition to the bran (as seen previously).

The transfer factors for the total residues of BYI 02960 for wheat processed fractions are summarised below in table 6.5.4.11-1. All trial data are summarised further below in table 6.5.4.11-2a & b and in greater detail in the Tier 1 summary forms.

Table 6.5.4.11-1: Summary of the total residues of BYI 02960 in mg/kg and transfer factors *(in italics and parentheses)* in wheat RACs and processed wheat commodities, following application of BYI 02960 SL 200

Trial number	wheat grain (RAC)	semolina bran	semolina	white-flour bran	white flour	white bread	whole-meal flour	whole-meal bread	wheat germ
10-3409-01 Germany	0.26	1.6 *(6.2)*	0.37 *(1.4)*	2.0 *(7.7)*	0.11 *(0.4)*	0.08 *(0.3)*	0.40 *(1.5)*	0.25 *(1.0)*	0.34 *(1.3)*
10-3409-02 Germany	0.17	0.65 *(3.8)*	0.09 *(0.5)*	0.85 *(5.0)*	0.05 *(0.3)*	0.05 *(0.3)*	0.24 *(1.4)*	0.15 *(0.9)*	0.14 *(0.8)*
Mean transfer factors:		*5.0*	*0.95*	*6.4*	*0.35*	*0.3*	*1.5*	*0.95*	*1.1*

III. Conclusions

In order to determine "processing" factors for total residues of BYI 02960 from wheat grain to semolina bran, semolina, white-flour bran, white flour, white bread, whole-meal flour, whole-meal bread, and wheat germ, processing studies have been conducted.

High total residues of BYI 02960 were found in semolina bran (0.65-1.6 mg/kg), resulting in a mean transfer factor of 5.0. In comparison, the residue levels for semolina were comparable to levels of the total residues of BYI 02960 in the RAC sample, resulting in a mean transfer factor of 0.95. Further separation resulted in white-flour bran, with residues of 0.85-2.0 mg/kg and a mean transfer factor of 6.4, indicating an accumulation of the residues in the bran fractions. In comparison, total residues of BYI 02960 in white flour were only between 0.05 and 0.11 mg/kg (mean transfer factor of 0.35), showing a clear reduction in residues in comparison to the RAC sample, grain. Preparation of white bread did not lead to an obvious additional reduction of the total residues of BYI 02960 (mean transfer factor of 0.3) in comparison to white flour.

The measured residues in whole meal and whole-meal bread lead to mean transfer factors of 1.5 for whole meal and 0.95 for whole-meal bread, showing a reduction of total residues of BYI 02960 during production of whole-meal bread compared to the RAC.

Total residues of BYI 02960 in wheat germ were found in the same range as for the RAC sample wheat grain, resulting in a mean transfer factor of 1.1, indicating that residues are not only located in bran, but also in wheat germ.

Diagram 6.5.4.11-1: Drying, cleaning, and conditioning of wheat grain

Wheat grain
(before processing)
↓
Defrosting
↓
Drying
↓
Cleaning
↓
Water (if necessary) → *Conditioning* → Water (in case of drying)
↓
Wheat grain
(with moisture content of 15-16%)

Diagram 6.5.4.11-2: Milling of white flour (type 550) and baking of white bread

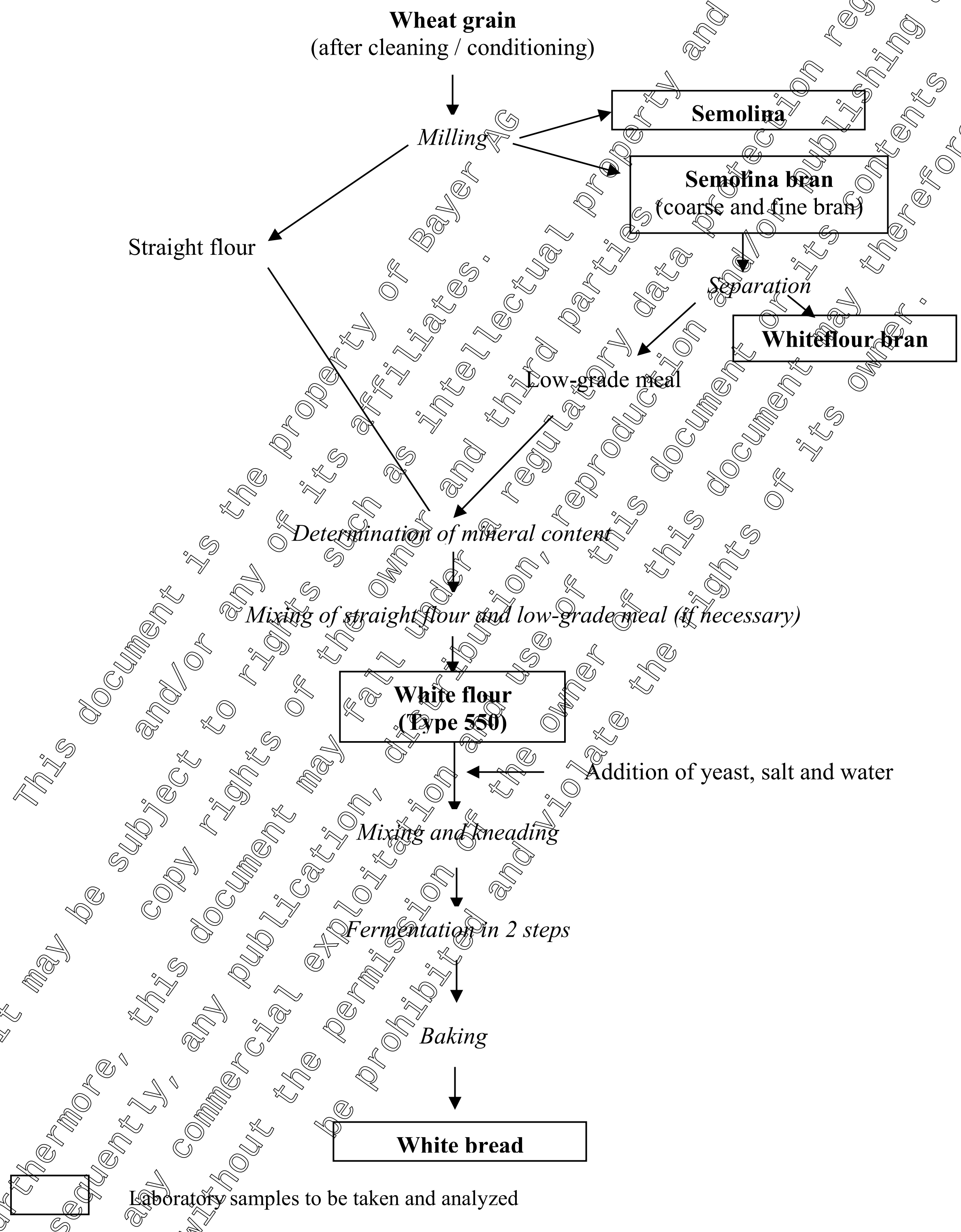

Diagram 6.5.4.11-3: Milling of whole-meal flour and baking of whole-meal bread

Diagram 6.5.4.11-4: Production of wheat germ

Wheat grain
(after cleaning / conditioning)

↓

Milling in 3 steps

↓

Bruised grain fraction of 400 – 1000 µm
(bran + semolina + germs)

↓

Separation → Bran

↓

Semolina and germ fraction

↓

Milling → Flour

↓

Wheat germ with parts of bran

↓

Sieving → Bran

↓

Wheat germ
(Germs with small parts of bran)

☐ Laboratory samples to be taken and analyzed

Table 6.5.4.11-2a: Application scenario in residue processing trials conducted in/on **wheat** after spraying with BYI 02960 SL 200 in European fields

Study No. **(Trial No.) Country Location Region Year**	**Crop Variety**	**FL**	**Application**			**GS**	**PHI (days)**
			No.	**kg/ha (a.s.)**	**kg/hl (a.s.)**		
10-3409 (10-3409-01) Germany [redacted] EU-N 2010	wheat Cubus (winter wheat)	200 SL	1	0.460	0.153	83	22
10-3409 (10-3409-02) Germany [redacted] EU-N 2010	wheat Toras (winter wheat)	200 SL	1	0.460	0.153	85	22

FL=formulation GS=growth stage (BBCH-code) at last treatment
EU-N=northern European residue region

Table 6.5.4.11-2b: Results of residue processing trials conducted in/on **wheat** after spraying with BYI 02960 SL 200 in European fields

Study No. (Trial No.) Country GLP	Portion analyzed	DALT (days)	Residues (mg/kg) expressed as BYI 02960 BYI 02960	DFA	BYI 02960-DFEAF	total residue of BYI 02960 calc.
BYI 02960 SL 200						
10-3409 (10-3409-01) Germany GLP: yes	grain (RAC)	22	0.23	0.02	<0.01	0.26
	milling of white flour and baking of white bread					
	semolina bran	22	1.1	0.50	<0.01	1.6
	semolina	22	0.32	0.03	<0.01	0.37
	white-flour bran	22	1.5	0.52	<0.01	2.0
	white flour	22	0.07	0.03	<0.01	0.11
	white bread	22	0.05	0.02	<0.01	0.08
	milling of wholemeal and baking of wholemeal bread					
	whole meal	22	0.36	0.03	<0.01	0.40
	whole-meal bread	22	0.22	<0.02	<0.01	0.25
	germ production					
	wheat germ	22	0.30	0.03	<0.01	0.34
10-3409 (10-3409-02) Germany GLP: yes	grain (RAC)	22	0.14	<0.02	<0.01	0.17
	milling of white flour and baking of white bread					
	semolina bran	22	0.61	0.02	<0.01	0.65
	semolina	22	0.06	<0.02	<0.01	0.09
	white-flour bran	22	0.81	0.03	<0.01	0.85
	white flour	22	0.02	<0.02	<0.01	0.05
	white bread	22	0.02	<0.02	<0.01	0.05
	milling of wholemeal and baking of wholemeal bread					
	whole meal	22	0.21	<0.02	<0.01	0.24
	whole-meal bread	22	0.12	<0.02	<0.01	0.15
	germ production					
	wheat germ	22	0.11	<0.02	<0.01	0.14

DALT=days after last treatment; RAC = raw agricultural commodity

Table 6.5.4.11-3: Recovery data for BYI 02960 in **wheat** and **wheat matrices**

Study **Trial No. Plot No. GLP Year**	**Crop**	**Portion analyzed**	**a.s./metabolite**	**n**	**Forti-fication level** (mg/kg)	**Recovery (%)** Individual recoveries	**Min**	**Max**	**Mean**	**RSD**
10-3409 (10-3409-01) and (10-3409-02) GLP: yes 2010	wheat	grain	BYI 02960	5	0.01	95; 96; 96; 99; 110	95	110	99	6.3
				3	0.50	87; 88; 91	87	91	89	2.3
				8	overall		87	110	95	7.6
			DFA	5	0.02	84; 89; 89; 91; 93	84	93	89	3.8
				3	0.50	71; 73; 81	71	81	75	7.1
				8	overall		71	93	84	9.9
			BYI 02960-DFEAF	5	0.01	85; 85; 90; 91; 96	85	96	89	5.2
				3	0.50	83; 85; 85	83	85	84	1.4
				8	overall		83	96	88	5.0
	wheat	meal	BYI 02960	3	0.50	88; 91; 93	88	93	91	2.8
			DFA	3	0.50	68; 73; 76	68	76	72	5.6
			BYI 02960-DFEAF	3	0.50	83; 83; 89	83	89	85	4.1
	wheat	semolina bran	BYI 02960	5	0.01	104; 107; 110; 110; 119	104	119	110	5.1
			DFA	5	0.02	80; 82; 86; 90; 99	80	99	87	8.6
			BYI 02960-DFEAF	5	0.01	79; 85; 88; 93; 98	79	98	89	8.2
	wheat	wholemeal bread	BYI 02960	5	0.01	98; 101; 102; 102; 106	98	106	102	2.8
				3	0.50	95; 97; 97	95	97	96	1.2
				8	overall		95	106	100	3.6
			DFA	5	0.02	80; 80; 84; 88; 89	80	89	84	5.1
				3	0.50	73; 76; 82	73	82	77	6.0
				8	overall		73	89	82	6.8
			BYI 02960-DFEAF	5	0.01	82; 85; 86; 86; 92	82	92	86	4.2
				3	0.50	84; 87; 88	84	88	86	2.4
				8	overall		82	92	86	3.4

Remark re. *grain*: also covers *whole meal*, *white flour*, *semolina*, *semolina bran*, *white-flour bran*, and *wheat germ*
Remark re. *whole-meal bread*: also covers *white bread*

➢ **US processing study**

Report:	**KIIA 6.5.4.11/02; [redacted]; 2012**
Title:	BYI 02960 200 SL – Magnitude of the Residue in/on Wheat Processed Commodities
Report No & Document No	RARVY031, dated March 13, 2012 M-427047-01-2
Guidelines:	US: EPA Residue Chemistry Test Guidelines OPPTS 860.1520, Processed Food/Feed Canada: PMRA DACO 7.4.5, Processed Food/Feed OECD: Guidelines for the Testing of Chemicals, 508, Magnitude of the Residues in Processed Commodities, Adopted Oct. 3, 2008. OECD Guidance Document on Magnitude of the Pesticide Residues in Processed Commodities.
GLP	Yes

Two field trials were conducted to measure the magnitude of BYI 02960 residues in/on wheat aspirated grain fractions and processed commodities following two broadcast foliar spray applications of BYI 02960 200 SL at 3X and 5X exaggerated application rates. BYI 02960 200 SL is a soluble concentrate formulation containing 200 g a.s./L.

Materials and Methods

BYI 02960 200 SL was applied to wheat plants at rates and timings as shown in Table 6.5.4.11-4.

Table 6.5.4.11-4: Study Use Pattern for BYI 02960 200 SL on Wheat

Trial Identification	Location (City, State, NAFTA Region, and Year)	End-use Product (Formulation)	Plot Name	Application: Method	Application: Method	Application: Timing/Growth Stage (BBCH)	Application: Actual Spray Volume GPA (L/ha)	Application: Rate lb a.s./A (kg a.s./ha)	Application: Method	Tank Mix Adjuvants
RV272-10PA	[redacted], IL Region 5 2010	BYI 02960 200 SL	TRT5X	Broad-cast Foliar	71 75	17 (160) 26 (240)	0.882 (0.989) 0.901 (1.01)	NA[a] 7	1.8 (1.9)	Dyne-Amic 0.25% v/v
RV273-10PA	Syracuse, NE Region 5 2010	BYI 02960 200 SL	TRT5X	Broad-cast Foliar	83 83	14 (130) 14 (130)	0.884 (0.991) 0.884 (0.991)	NA[a] 6	1.8 (1.9)	Dyne-Amic 0.25% v/v

[a] NA = Not applicable.

All applications were made using ground-based equipment. The additive, Dyne-Amic 0.25% v/v, was used in all applications.

Single composite wheat grain raw agricultural commodity (RAC) samples were collected at either a 19-day or 21-day PHI from the TRT5X plots. Single composite samples of grain were collected from the control plots on the same days the respective samples were collected from the treated plots.

Triplicate subsamples of wheat grain RAC were removed, and the remaining wheat grain was used to collect aspirated grain fractions and generate the processed commodities of bran, whole meal flour, white flour, middlings, shorts, germ, pasta (dried and cooked), white bread, whole meal bread, gluten, starch, pasta (cooked), pasta (fresh), pasta (dry), and cooking water.

The residue(s) of BYI 02960, DFA, and DFEAF were quantitated by LC/MS/MS using stable isotopically labeled internal standards standards. The individual analyte residues were summed to give a total BYI 02960 residue. Residue measurements below the analyte LOQ were summed into the total BYI 02960 residue value as the analyte LOQ value.

Findings

Concurrent recoveries of BYI 02960, DFA, and DFEAF were measured with each set of samples to verify method performance. All recoveries were corrected for any interferences in corresponding controls. The overall mean of the recoveries for each matrix ranged between 74 to 113%, and the standard deviation values were below 20% (Table 6.5.4.11-5).

Table 6.5.4.11-5: Summary of Recoveries of BYI 02960 Residues from Wheat RAC and Processed Commodities

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev (%)
Aspirated Grain Fractions	BYI 02960	0.200	3	103, 101, 93	99	5
		40.000	3	100, 104, 95	100	5
	DFA	0.200	3	100, 110, 109	106	5
		40.000	3	104, 99, 96	100	4
	DFEAF	0.200	3	89, 92, 94	92	3
		40.000	3	101, 97, 96	98	2
Bran	BYI 02960	0.010	3	89, 116, 84	96	17
		4.000	3	99, 102, 108	103	5
	DFA	0.050	3	97, 94, 85	92	6
		4.000	3	87, 85, 83	85	2
	DFEAF	0.010	3	84, 98, 98	93	8
		4.000	3	91, 92, 101	95	6
Cooking Water	BYI 02960	0.010	3	97, 98, 106	100	5
		0.200	3	93, 97, 91	93	3
	DFA	0.050	3	96, 98, 95	96	2
		0.200	3	99, 101, 96	99	3
	DFEAF	0.010	3	100, 76, 113	97	19
		0.200	3	103, 101, 94	99	5
Germ	BYI 02960	0.010	3	95, 114, 80	97	17
		4.000	3	98, 99, 114	104	9
	DFA	0.050	3	79, 77, 75	77	2
		4.000	3	71, 76, 77	75	3
	DFEAF	0.010	3	109, 112, 77	99	19
		4.000	3	89, 93, 90	91	2
Gluten	BYI 02960	0.010	3	115, 116, 106	113	5
		1.000	3	109, 92, 96	99	9
		4.000	3	99, 93, 96	96	3
	DFA	0.050	3	88, 91, 118	99	16
		1.000	3	88, 101, 104	98	9
		4.000	3	101, 102, 101	102	1
	DFEAF	0.010	3	100, 104, 102	102	2
		1.000	3	107, 102, 112	107	5
		4.000	3	107, 97, 88	98	9
Grain	BYI 02960	0.010	7	116, 74, 112, 90, 102, 77, 80	93	17
		2.500	3	90, 99, 105	98	8
	DFA	0.050	7	80, 78, 79, 89, 89, 92, 81	84	6
		2.500	3	79, 87, 87	84	5
	DFEAF	0.010	7	104, 100, 106, 107, 110, 107,115	107	5
		2.500	3	96, 95, 97	96	1

Table 6.5.4.11-5 (cont'd): Summary of Recoveries of BYI 02960 Residues from Wheat RAC and Processed Commodities

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev (%)
Pasta Fresh	BYI 02960	0.010	4	97, 71, 81, 106	89	16
		4.000	3	111, 106, 100	106	6
	DFA	0.050	4	94, 96, 94, 98	95	2
		4.000	3	95, 105, 100	100	5
	DFEAF	0.010	4	105, 94, 115, 116	107	10
		4.000	3	96, 116, 99	104	11
Shorts	BYI 02960	0.010	3	87, 91, 96	91	5
		4.000	3	98, 118, 106	107	10
	DFA	0.050	3	87, 83, 85	85	2
		4.000	3	85, 87, 89	87	2
	DFEAF	0.010	3	104, 110, 74	96	19
		4.000	3	113, 113,107	111	3
Starch	BYI 02960	0.010	3	101, 95, 101	99	4
		0.200	3	94, 81, 112	96	16
	DFA	0.050	3	90, 86, 88	88	2
		0.200	3	79, 82, 90	84	6
	DFEAF	0.010	3	110, 97, 101	102	7
		0.200	3	83, 101, 105	97	12
White Bread	BYI 02960	0.010	2	110, 105	108	NA[b]
	DFA	0.050	2	89, 92	90	NA[b]
	DFEAF	0.010	2	103, 105	104	NA[b]
White Flour	BYI 02960	0.010	3	102, 98, 111	103	7
		4.000	3	105, 118, 113	112	7
	DFA	0.050	3	88, 89, 99	92	6
		4.000	3	71, 76, 76	74	3
	DFEAF	0.010	3	98, 115, 115	109	10
		4.000	3	92, 120, 104	105	14
Whole meal flour	BYI 02960	0.010	2	103, 117	110	NA[b]
	DFA	0.050	2	73, 87	80	NA[b]
	DFEAF	0.010	2	85, 92	89	NA[b]
Whole meal Bread	BYI 02960	0.010	2	103, 106	104	NA[b]
		4.000	3	85, 88, 91	88	3
	DFA	0.050	2	88, 94	91	NA[b]
		4.000	3	83, 83, 82	83	1
	DFEAF	0.010	2	108, 113	111	NA[b]
		4.000	3	102, 85, 91	92	9

[a] Mean Recovery = mathematical average of all recoveries.

[b] NA = Not applicable. No standard deviation calculated when less than three recovery values are presented.

The freezer storage stability study indicates that BYI 02960 residues were stable in wheat grain as representative for the commodity group (high starch content) during frozen storage for at least 18 months (557 days) prior to analyses. The maximum storage period of frozen samples in this study for BYI 02960 was 430 days. A summary of the storage conditions are shown in the Table 6.5.4.11-6.

Table 6.5.4.11-6: Summary of Storage Conditions for all Soybean Commodities

Residue Component(s)	Matrix (RAC)	Average Storage Temperature (°C)[a]	Actual Storage Duration months (days)[b]	Interval of Demonstrated Storage Stability months (days)[c]
BYI 02960, DFA, DFEAF	Grain (RAC)	<0	13 (390)	18 (557)
BYI 02960, DFA, DFEAF	Aspirated Grain Fractions	<0	14 (430)	18 (557)
BYI 02960, DFA, DFEAF	Bran	<0	14 (408)	18 (557)
BYI 02960, DFA, DFEAF	Cooking Water	<0	14 (413)	18 (557)
BYI 02960, DFA, DFEAF	Cooking Water 2	<0	14 (414)	18 (557)
BYI 02960, DFA, DFEAF	Germ	<0	14 (415)	18 (557)
BYI 02960, DFA, DFEAF	Gluten	<0	14 (429)	18 (557)
BYI 02960, DFA, DFEAF	Middlings	<0	14 (408)	18 (557)
BYI 02960, DFA, DFEAF	Pasta, Cooked	<0	14 (419)	18 (557)
BYI 02960, DFA, DFEAF	Pasta, Dried and Cooked	<0	14 (411)	18 (557)
BYI 02960, DFA, DFEAF	Pasta, Dry	<0	14 (426)	18 (557)
BYI 02960, DFA, DFEAF	Pasta, Fresh	<0	14 (419)	18 (557)
BYI 02960, DFA, DFEAF	Shorts,	<0	14 (412)	18 (557)
BYI 02960, DFA, DFEAF	Starch	<0	14 (412)	18 (557)
BYI 02960, DFA, DFEAF	White Bread	<0	13 (387)	18 (557)
BYI 02960, DFA, DFEAF	White Flour	<0	14 (408)	18 (557)
BYI 02960, DFA, DFEAF	Whole meal Four	<0	14 (408)	18 (557)
BYI 02960, DFA, DFEAF	Whole meal Bread	<0	13 (387)	18 (557)

[a] The average storage temperature reported is from the time of sample collection at GLP Technologies through the last sample extraction. Samples were maintained in a laboratory freezer at all times except during preparation for sample analysis.

[b] The actual storage duration for the wheat grain RAC is the time from field sampling (harvest) through the last sample extraction. The actual storage duration for all commodities is from the time of commodity generation through the last sample extraction.

[c] [redacted], [redacted] [redacted]. 2012. Storage stability of BYI 02960, difluoroacetic acid, and difluoroethyl-amino-furanone in plant matrices. Bayer CropScience Report No. RARVP046, amended version including 18-month data (KIIA 6.1.1/01).

The BYI 02960, DFA, DFEAF, and total BYI 02960 residue data for wheat RAC and processed commodities are provided in Table 6.5.4.11-7.

Table 6.5.4.11-7: BYI 02960 Residue Data from Wheat RAC, Aspirated Grain Fractions, and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg a.s./ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV272-10PA	Wheat Grain	NA[c]	81	1.80 (2.02)	21	1.60 1.74 1.65	2.11 2.36 2.07	0.024 0.022 0.019	3.7 4.1 3.7 Avg. 3.9	NA[c]	NA[c]
RV273-10PA	Wheat Grain	NA[c]	87	1.82 (2.04)	19	1.13 1.28 1.45	2.58 3.07 3.13	0.032 0.031 0.039	3.7 4.4 4.6 Avg. 4.2	NA[c]	NA[c]
RV272-10PA	Wheat Grain	Aspirated Grain Fractions	90	NA[c]	NA[c]	21.6 20.8 26.3	16.5 18.9 21.9	0.215 0.194 0.235	38 40 48 Avg. 42	10.8X	10X
RV273-10PA	Wheat Grain	Aspirated Grain Fractions	90	NA[c]	NA[c]	27.7 30.0 25.4	15.5 13.8 14.7	0.209 0.189 0.185	43 44 40 Avg. 43	10.2X	
RV272-10PA	Wheat Grain	Bran	84	NA[c]	NA[c]	4.10 3.87 3.88	2.43 2.09 2.08	0.022 0.022 0.024	6.56 5.98 5.98 Avg. 6.18	1.6X	1.6X
RV273-10PA	Wheat Grain	Bran	84	NA[c]	NA[c]	2.99 2.89 3.09	3.20 3.09 3.34	0.029 0.021 0.035	6.23 6.01 6.47 Avg. 6.23	1.5X	
RV272-10PA	Wheat Grain	Cooking Water	NA[c]	NA[c]	NA[c]	0.011 0.013 <0.010	0.084 0.083 0.081	<0.010 <0.010 <0.010	0.10 0.11 0.10 Avg. 0.10	<1X	<1X
RV273-10PA	Wheat Grain	Cooking Water	NA[c]	NA[c]	NA[c]	0.012 0.012 0.012	0.142 0.142 0.147	<0.010 <0.010 <0.010	0.16 0.16 0.17 Avg. 0.17	<1X	

Continued on next page…

Table 6.5.4.11-7 (cont'd): BYI 02960 Residue Data from Wheat RAC, Aspirated Grain Fractions, and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg a.s./ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV272-10PA	Wheat Grain	Cooking Water 2	NA[c]	NA[c]	NA[c]	0.012 0.011 0.011	0.101 0.098 0.099	<0.010 <0.010 <0.010	0.12 0.12 0.12 Avg. 0.12	<1X	<1X
RV273-10PA	Wheat Grain	Cooking Water 2	NA[c]	NA[c]	NA[c]	0.010 0.012 0.012	0.119 0.107 0.121	<0.010 <0.010 <0.010	0.14 0.13 0.14 Avg. 0.14	<1X	
RV272-10PA	Wheat Grain	Germ	NA[c]	NA[c]	NA[c]	2.75 2.41 3.04	1.99 2.16 2.35	0.030 0.027 0.030	4.8 4.6 5.4 Avg. 5.3	1.4X	1.3X
RV273-10PA	Wheat Grain	Germ	NA[c]	NA[c]	NA[c]	2.11 2.10 2.19	2.92 2.97 2.70	0.035 0.039 0.043	5.1 5.1 4.9 Avg. 5.0	1.2X	
RV272-10PA	Wheat Grain	Gluten	NA[c]	NA[c]	NA[c]	0.341 0.327 0.384 0.387 0.336 0.372	0.608 0.642 0.679 0.147 0.159 0.165	<0.010 <0.010 <0.010 <0.010 <0.010 <0.010	0.96 0.98 1.1 0.54 0.51 0.55 Avg. 0.77	<1X	<1X
RV273-10PA	Wheat Grain	Gluten	NA[c]	NA[c]	NA[c]	0.619 0.667 0.680	2.23 1.76 1.85	0.016 0.015 0.017	2.9 2.4 2.5 Avg. 2.6	<1X	

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Table 6.5.4.11-7 (cont'd): BYI 02960 Residue Data from Wheat RAC, Aspirated Grain Fractions, and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg a.s./ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV272-10PA	Wheat Grain	Middlings	85	NA[c]	NA[c]	1.34 1.27 1.34	1.86 1.91 1.95	0.020 0.022 0.020	3.2 3.2 3.3 Avg. 3.2	<1X	<1X
RV273-10PA	Wheat Grain	Middlings	84	NA[c]	NA[c]	0.780 0.766 0.794	2.79 2.64 2.77	0.022 0.024 0.024	3.6 3.4 3.6 Avg. 3.5	<1X	
RV272-10PA	Wheat Grain	Pasta, Cooked	NA[c]	NA[c]	NA[c]	0.120 0.103 0.085	0.398 0.387 0.317	<0.010 <0.010 <0.010	0.53 0.50 0.41 Avg. 0.48	<1X	<1X
RV273-10PA	Wheat Grain	Pasta, Cooked	NA[c]	NA[c]	NA[c]	0.108 0.118 0.114	0.606 0.503 0.573	<0.010 <0.010 <0.010	0.72 0.63 0.70 Avg. 0.68	<1X	
RV272-10PA	Wheat Grain	Pasta, Dried and Cooked	NA[c]	NA[c]	NA[c]	0.138 0.146 0.148	0.484 0.549 0.553	<0.010 <0.010 <0.010	0.63 0.70 0.71 Avg. 0.68	<1X	<1X
RV273-10PA	Wheat Grain	Pasta, Dried and Cooked	NA[c]	NA[c]	NA[c]	0.139 0.107 0.116	0.707 0.620 0.651	<0.010 <0.010 <0.010	0.86 0.74 0.78 Avg. 0.79	<1X	
RV272-10PA	Wheat Grain	Pasta, Dry	NA[c]	NA[c]	NA[c]	0.383 0.394 0.417	1.87 1.82 1.82	0.015 0.015 0.016	2.3 2.2 2.3 Avg. 2.3	<1X	<1X
RV273-10PA	Wheat Grain	Pasta, Dry	NA[c]	NA[c]	NA[c]	0.478 0.382 0.409	2.98 2.56 2.54	0.025 0.025 0.024	3.5 3.0 3.0 Avg. 3.1	<1X	

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Table 6.5.4.11-7 (cont'd): BYI 02960 Residue Data from Wheat RAC, Aspirated Grain Fractions, and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg a.s./ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV272-10PA	Wheat Grain	Pasta, Fresh	NA[c]	NA[c]	NA[c]	0.303 0.283 0.332	1.46 1.39 1.44	0.010 <0.010 0.011	1.8 1.7 1.8 Avg. 1.7	<1X	<1X
RV273-10PA	Wheat Grain	Pasta, Fresh	NA[c]	NA[c]	NA[c]	0.325 0.283 0.293	2.27 2.24 2.17	0.016 0.018 0.016	2.6 2.5 2.5 Avg. 2.5	<1X	
RV272-10PA	Wheat Grain	Shorts	85	NA[c]	NA[c]	1.93 2.08 2.15	1.99 2.07 2.18	0.018 0.022 0.012	3.9 4.2 4.3 Avg. 4.2	1.1X	<1X
RV273-10PA	Wheat Grain	Shorts	84	NA[c]	NA[c]	0.764 0.799 0.809	2.54 2.72 2.63	0.030 0.026 0.010	3.3 3.5 3.4 Avg. 3.4	<1X	
RV272-10PA	Wheat Grain	Starch	NA[c]	NA[c]	NA[c]	0.018 0.020 0.019	0.109 0.098 0.111	<0.010 <0.010 <0.010	0.14 0.13 0.14 Avg. 0.14	<1X	<1X
RV273-10PA	Wheat Grain	Starch	NA[c]	NA[c]	NA[c]	<0.010 0.011 0.011	0.067 0.070 0.069	<0.010 <0.010 <0.010	0.087 0.091 0.090 Avg. 0.089	<1X	
RV272-10PA	Wheat Grain	White Bread	NA[c]	NA[c]	NA[c]	0.239 0.233 0.237	1.22 1.13 1.11	<0.010 <0.010 <0.010	1.5 1.4 1.4 Avg. 1.4	<1X	<1X
RV273-10PA	Wheat Grain	White Bread	NA[c]	NA[c]	NA[c]	0.285 0.290 0.305	1.83 2.01 1.99	0.014 0.014 0.017	2.1 2.3 2.3 Avg. 2.2	<1X	

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Table 6.5.4.11-7 (cont'd): BYI 02960 Residue Data from Wheat RAC, Aspirated Grain Fractions, and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg a.s./ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV272-10PA	Wheat Grain	White Flour	NA[c]	NA[c]	NA[c]	0.364 0.338 0.367	1.58 1.56 1.61	0.014 0.012 0.014	2.0 1.9 2.0 Avg. 2.0	<1X	<1X
RV273-10PA	Wheat Grain	White Flour	NA[c]	NA[c]	NA[c]	0.390 0.433 0.436	2.22 2.45 2.72	0.019 0.016 0.021	2.6 2.9 3.2 Avg. 2.9	<1X	
RV272-10PA	Wheat Grain	Whole meal Flour	NA[c]	NA[c]	NA[c]	2.04 2.01 2.24	2.08 2.09 1.96	0.024 0.023 0.020	4.1 4.1 4.2 Avg. 4.2	1.1X	1X
RV273-10PA	Wheat Grain	Whole meal Flour	NA[c]	NA[c]	NA[c]	1.51 1.41 1.44	3.29 3.07 3.43	0.023 0.024 0.034	4.8 4.5 4.9 Avg. 4.7	1.1X	
RV272-10PA	Wheat Grain	Whole meal Bread	NA[c]	NA[c]	NA[c]	1.21 1.26 1.29	1.46 1.48 1.42	0.016 0.016 0.019	2.7 2.8 2.7 Avg. 2.7	<1X	<1X
RV273-10PA	Wheat Grain	Whole meal Bread	NA[c]	NA[c]	NA[c]	0.849 0.818 0.855	2.01 1.93 1.97	0.019 0.018 0.020	2.9 2.8 2.8 Avg. 2.8	<1X	

[a] Total BYI 02960 residue is the sum of BYI 02960, DFA, and DFEAF residue in parent equivalents. Residue measurements below the analyte LOQ were summed into the Total BYI 02960 residue value as the analyte LOQ value. These totals represent the upper limit of what the residue levels might be.

[b] Total BYI 02960 Processing Factor = Average Total residue in processed sample/average total residue in unprocessed sample. Processing factors calculated to be less than 1X were reported as <1X.

[c] NA = Not applicable.

Conclusion

A summary of the calculated processing factors for wheat aspirated grain fractions and processed commodities are shown in Table 6.5.4.11-8.

Following a five-fold (5X) exaggerated application of BYI 02960 to two separate trials of wheat, the average total BYI 02960 residue did not concentrate (processing factor ≤1X) in cooking water, cooking water 2, gluten, middlings, pasta (cooked), pasta (dried and cooked), pasta (dry), pasta (fresh), shorts, starch, white bread, white flour, whole meal bread, and whole meal flour. However, the total BYI 02960 residue did concentrate in aspirated grain fractions (10X), bran (1.6X), and germ (1.3X).

The processing factors determined for total BYI 02960 residue in this study are less than the theoretical concentration factors based on Separation into Components cited in the EPA Residue Chemistry Test Guideline OPPTS 860.1520 which are 7.7X for wheat bran, 1.4X for wheat flour, and 8.3X for wheat shorts.

The residue data and subsequent calculated processing factors provided in this report are suitable for regulatory purposes.

Table 6.5.4.11-8: Summary of Total BYI 02960 Processing Factors Calculated Wheat Aspirated Grain Fractions and Processed Commodities

RAC	Processed Commodity	Average Total BYI 02960 Residue Processing Factor
Wheat Grain	Aspirated Grain Fractions	10X
Wheat Grain	Bran	1.6X
Wheat Grain	Germ	1.3X
Wheat Grain	Cooking water, cooking water 2, gluten, middlings, pasta (cooked), pasta (dried and cooked), pasta (dry), pasta (fresh), shorts, starch, white bread, white flour, whole meal bread, whole meal flour	≤1X

IIA 6.5.4.12 Coffee

Report:	**KIIA 6.5.4.12/01, [redacted]; 2012**
Title:	BYI 02960 200 SL – Magnitude of the Residue in/on Processed Commodities for Coffee; U.S., Canada and E.U. Import Tolerances
Report No & Document No	RARVP075, dated June 27, 2012. M-433200-01-1
Guidelines:	US: EPA Residue Chemistry Test Guidelines OPPTS 860.1520, Processed Food/Feed Canada: PMRA DACO 7.4.5, Processed Food/Feed OECD: Guidelines for the Testing of Chemicals, 508. Magnitude of the Residues in Processed Commodities, Adopted Oct. 3, 2008. OECD Guidance Document on Magnitude of the Pesticide Residues in Processed Commodities.
GLP	Yes

Two field trials located in Brazil and Mexico were conducted to measure the magnitude of BYI 02960 residues in/on processed commodities following a single soil drench application followed by three broadcast foliar spray applications of BYI 02960 200 SL at 2X exaggerated application rates. BYI 02960 200 SL is a soluble concentrate formulation containing 200 g a.s./L.

Materials and Methods

BYI 02960 200 SL was applied to coffee plants at rates and timings as shown in Table 6.5.4.12-1. All foliar applications were made using ground-based equipment. Methylated seed oil (MSO) or Dyne-Amic were used in all of the applications at a rate of 0.25% (v/v).

Single composite samples of coffee cherries were collected from the treated plots at a target pre-harvest interval (PHIs) of 14 days.

Single composite samples of coffee cherries were collected from the untreated control plot (UTC) on the same day that the target 14-day PHI samples were collected from the treated plots.

According to normal commercial practice in Brazil (trial RV235-11PA) and in various regions in Mexico (trial RV247-11PA) coffee cherries were allowed to air-dry before removing the outer hull and parchment using a machine that simulates large-scale commercial production of coffee beans, green. For trial RV235-11PA (Brazil) the cherries were allowed to air-dry for 10-days before removing the outer hull and parchment. For trial RV247-11PA (Mexico), coffee cherries were placed into forced-air drying ovens at a temperature of 122ºF (50ºC) for four days, followed by air-drying for eight days to yield the required sample size of coffee bean, green after removing the outer hull and parchment.

The dried coffee beans were placed into properly labelled residue sample bags for shipment to the Bayer Research Park (BRP). Each sample was divided into two parts that were shipped on two different days, ensuring that the first part arrived safely at BRP before shipping the second part.

Table 6.5.4.12-1: Study Use Pattern for BYI 02960 200 SL on Coffee

Trial Identification	Location (City, State, NAFTA Region, and Year)	End-use Product (Formulation)	Application							Tank Mix Adjuvants
			Plot Name	Method	Timing/Growth Stage (BBCH)	Actual Spray Volume GPA (L/ha)	Rate lb a.s./A (kg a.s./ha)	Retreatment Interval (days)	Total Rate lb a.s./A (kg a.s./ha)	
RV235-11PA	[redacted], São Paulo, Brazil 2011	BYI 02960 SL 200	TRT2X	Soil drench	BBCH 77	16 (149)	1.093 (1.225)	NA[a]	2.169 (2.431)	NA[b]
				Foliar broadcast	BBCH 79	44 (411)	0.362 (0.409)	91		MSO 0.25% v/v
					BBCH 80	40 (374)	0.353 (0.396)	14		MSO 0.25% v/v
					BBCH 85	43 (398)	0.358 (0.401)	14		MSO 0.25% v/v
RV247-11PA	[redacted] 2011	BYI 02960 SL 200	TRT2X	Soil drench	BBCH 72	21 (201)	1.076 (1.206)	NA[a]	2.145 (2.404)	NA[b]
				Foliar broadcast	BBCH 81	43 (402)	0.358 (0.401)	85		Dyne-Amic 0.25% v/v
					BBCH 81	43 (403)	0.356 (0.399)	12		Dyne-Amic 0999.25 % v/v
					BBCH85	43 (402)	0.355 (0.398)	13		Dyne-Amic 0.25% v/v

[a] NA = Not applicable.

After receipt at BRP, one part of each sample was shipped to GLP Technologies, Navasota, Texas, and the other part was shipped to the University of [redacted] Food Technology Center, Caldwell, [redacted] for processing into coffee bean, roasted; and coffee, instant.

At each processing laboratory, triplicate subsamples of coffee RAC (coffee bean, green) were removed from the bulk samples for analysis of BYI 02960 residues. The remainder of each bulk sample was used to generate the processed commodities, coffee bean, roasted, and coffee, instant.

The residue(s) of BYI 02960, DFA, and DFEAF were quantitated by HPLC-MS/MS using stable isotopically labelled internal standards. The individual analyte residues were summed to give a total BYI 02960 residue. Residue measurements below the analyte LOQ were summed into the total BYI 02960 residue value as the analyte LOQ value.

Findings

Concurrent recoveries of BYI 02960, DFA, and DFEAF were measured with each set of samples to verify method performance. All recoveries were corrected for any interferences in corresponding controls. The overall mean of the recoveries for each matrix at each fortification level was within the acceptable range of 70 to 110%, and the standard deviation (SD) values were less than 20% (Table 6.5.4.12-2).

Table 6.5.4.12-2: Summary of Recoveries of BYI 02960 Residues from Coffee RAC and Processed Commodities

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev. (%)
Coffee Green Bean	BYI 02960	1.000	4	106, 96, 94, 87	96	8
		2.000	3	87, 90, 92	90	2
	DFA	1.000	4	83, 84, 86, 87	85	2
		2.000	3	82, 80, 81	81	1
	DFEAF	1.000	4	92, 93, 86, 92	91	3
		2.000	3	93, 95, 92	93	2
Coffee Roasted Bean	BYI 02960	0.010	3	89, 82, 86	86	4
		2.000	3	97, 101, 102	100	3
	DFA	0.050	3	85, 87, 98	90	7
		2.000	3	81, 85, 87	84	3
	DFEAF	0.010	3	106, 92, 107	102	9
		2.000	3	92, 103, 98	98	6
Instant Coffee	BYI 02960	0.050	3	110, 103, 103	106	4
		0.100	3	97, 105, 92	98	7
		5.000	3	100, 103, 93	99	5
	DFA	0.050	3	103, 100, 108	104	4
		0.100	3	106, 99, 96	100	5
		5.000	3	104, 101, 103	103	2
	DFEAF	0.050	3	110, 97, 76	94	17
		0.100	3	108, 87, 111	102	13
		5.000	3	98, 100, 103	100	2

[a] Mean Recovery = mathematical average of all recoveries

The freezer storage stability study indicates that BYI 02960 residues were stable in coffee beans during frozen storage for at least 18 months (560 days) prior to analyses. The maximum storage period of frozen samples in this study for BYI 02960 was 121 days. A summary of the storage conditions are shown in the Table 6.5.4.12-3.

Table 6.5.4.12-3: Summary of Storage Conditions for Coffee RAC and Processed Commodities

Residue Component(s)	Matrix (RAC)	Maximum Average Storage Temperature (°C) [a]	Actual Storage Duration months (days) [b]	Interval of Demonstrated Storage Stability months (days)[c]
BYI 02960	Coffee bean, green	<0	4 (115)	18 (560)
BYI 02960	Coffee bean, roasted	<0	4 (121)	18 (560)
BYI 02960	Coffee, instant	<0	4 (119)	18 (560)

[a] The maximum average storage temperature is from the time of sample receipt at BRP (coffee bean, green) or from the time that processed fractions were generated and stored frozen (coffee bean, roasted, coffee, instant) until sample extraction and is the maximum of all average freezer temperatures at BRP and the processing facilities. While preparing for sample analysis, the samples were maintained in a laboratory freezer.

[b] The actual storage duration for the wheat grain RAC is the time from field sampling (harvest) through the last sample extraction. The actual storage duration for all commodities is from the time of commodity generation through the last sample extraction.

[c] [redacted], [redacted], [redacted]. 2012. Storage stability of BYI 02960, difluoroacetic acid, and difluoroethyl-amino-furanone in plant matrices. Bayer CropScience Report No. RARVP046, amended version including 18-month data (KIIA 6.1.1/01).

The BYI 02960, DFA, DFEAF, and total BYI 02960 residue data for coffee RAC and processed commodities are provided in Table 6.5.4.12-4.

Table 6.5.4.12-4: BYI 02960 Residue Data from Coffee RAC and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg a.s./ha)	Preharvest Interval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)	Processing Factor[b]	Average Processing Factor
Coffee Bean, Green					LODs:	0.0031	0.0079	0.0036	0.0079		
RV235-11PA	GLP Technologies	Coffee bean, green	NA[d]	2.169 (2.431)	14	0.4186	0.1355	0.0265	0.5806	NA[d]	NA[d]
						0.3308	0.0996	0.0196	0.4500		
						0.3619	0.1178	0.0204	0.5001		
								Average:	0.5103		
	University of [redacted]	Coffee bean, green	NA[d]	2.169 (2.431)	14	0.3176	0.1035	0.0196	0.4407		
						0.2984	0.1019	0.0213	0.4216		
						0.3958	0.1093	0.0156	0.5207		
								Average:	0.4610		

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Table 6.5.4.12-4 (cont'd): BYI 02960 Residue Data from Coffee RAC and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg a.s./ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)	Processing Factor[a]	Average Processing Factor
RV247-11PA	GLP Technologies	Coffee bean, green	NA[d]	2.145 (2.404)	14	1.1632	0.4874	0.0972	1.7477	NA[d]	
						0.9291	0.5092	0.1209	1.5591		
						0.8544	0.5080	0.0957	1.4581		
								Average:	1.5883		
	University of [redacted]	Coffee bean, green	NA[d]	2.145 (2.404)	14	0.9520	0.4564	0.1003	1.5086		
						1.0110	0.5146	0.1035	1.6291		
						1.3346	0.5973	0.1280	2.0598		
								Average:	1.8445		
Coffee Bean, Roasted					LODs:	0.0031	0.0079	0.0036	0.0079		
RV235-11PA	GLP Technologies	Coffee bean, green	Coffee bean, roasted	2.169 (2.431)	14	0.1884	0.0917	0.0126	0.2927	<1X	<1
						0.2066	0.0961	0.0148	0.3175		
						0.2031	0.0882	0.0140	0.3053		
								Average:	0.3052		
	University of [redacted]	Coffee bean, green	Coffee bean, roasted	2.169 (2.431)	14	0.1870	0.0794	0.0068	0.2732		
						0.1960	0.0834	0.0054	0.2848		
						0.1964	0.0791	0.0092	0.2846		
								Average:	0.2809		
RV247-11PA	GLP Technologies	Coffee bean, green	Coffee bean, roasted	2.145 (2.404)	14	0.6724	0.5303	0.0570	1.2597	<1X	
						0.7470	0.5575	0.0629	1.3674		
						0.7595	0.5621	0.0710	1.3926		
								Average:	1.3399		
	University of [redacted]	Coffee bean, green	Coffee bean, roasted	2.145 (2.404)	14	0.5714	0.5627	0.0486	1.1827		
						0.5803	0.5902	0.0476	1.2180		
						0.5656	0.6401	0.0505	1.2563		
								Average:	1.2190		

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Table 6.5.4.12-4 (cont'd): BYI 02960 Residue Data from Coffee RAC and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg a.s./ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)	Processing Factor	Average Processing Factor
Coffee, Instant					LODs:	0.0031	0.0079	0.0036	0.0079		
RV235-11PA	GLP Technologies	Coffee bean, green	Coffee, Instant	2.169 (2.431)	14	0.4070	0.3690	0.0280	0.8040	2.3	2.8
						0.3200	0.3850	0.0370	0.7420		
						0.3600	0.3900	0.0191	0.7691		
								Average:	0.7717		
	University of [redacted]	Coffee bean, green	Coffee, Instant	2.169 (2.431)	14	1.0000	0.6440	0.0399	1.6839		
						0.6220	0.4530	0.0186	1.0936		
						0.9840	0.6230	0.0287	1.6357		
								Average:	1.4711		
RV247-11PA	GLP Technologies	Coffee bean, green	Coffee, Instant	2.145 (2.404)	14	2.5300	2.3300	0.2690	5.1290	3.0	
						2.4100	2.3200	0.2560	4.9860		
						2.2000	2.3700	0.2730	4.8430		
								Average:	4.9860		
	University of [redacted]	Coffee bean, green	Coffee, Instant	2.145 (2.404)	14	1.8800	3.1200	0.2040	5.2040		
						1.7400	3.2700	0.1810	5.1910		
						1.7900	3.2500	0.2110	5.2510		
								Average:	5.2153		

[a] Pre-Harvest Interval (PHI) is the interval between last application and Sample Cut Date.
[b] Total BYI 02960 residue is the sum of BYI 02960, DFA, and DFEAF residue in parent equivalents.
[c] Total BYI 02960 Processing Factor = Average Total residue in processed sample/average total residue in unprocessed RAC. Processing factors calculated to be less than 1X were reported as <1X. For risk assessment purposes any processing factor reported as <1X can be calculated from the refined residue data presented in Appendix 5a.
[d] NA = Not applicable.

Conclusion

A summary of the calculated processing factors for coffee processed commodities are shown in Table 6.5.4.12-5.

Following a two-fold (2X) exaggerated application of BYI 02960 to two separate trials of coffee, the average total BYI 02960 residue values did not concentrate (processing factor ≤1) in coffee bean, roasted. The residues did, however, concentrate in coffee, instant (3X).

The processing factors determined for total BYI 02960 residue in this study are less than the theoretical concentration factors based on Separation into Components cited in the EPA Residue Chemistry Test Guideline OPPTS 860.1520 which is 4.5 for coffee.

The processing factors determined for each of the trials for each processed commodity were sufficiently close together that no additional field trials are needed.

Table 6.5.4.12-5: Summary of Total BYI 02960 Processing Factors Calculated Coffee Processed Commodities

RAC	Processed Commodity	Average Total BYI 02960 Residue Processing Factor
Coffee bean, green	Coffee bean, roasted	<1X
Coffee bean, green	Coffee, instant	3X

IIA 6.5.4.13 Corn

Report:	**KIIA 6.5.4.13/01, [redacted]; 2012**
Title:	BYI 02960 200 SL – Magnitude of the Residue in/on Field Corn Processed Commodities
Report No & Document No	RARVY030, dated February 9, 2012 M-424774-01-1
Guidelines:	US: EPA Residue Chemistry Test Guidelines OPPTS 860.1520, Processed Food/Feed Canada: PMRA DACO 7.4.5, Processed Food/Feed OECD: Guidelines for the Testing of Chemicals, 508, Magnitude of the Residues in Processed Commodities, Adopted Oct. 3, 2008. OECD Guidance Document on Magnitude of the Pesticide Residues in Processed Commodities.
GLP	Yes

Two field trials were conducted to measure the magnitude of BYI 02960 residues in/on field corn aspirated grain fractions and processed commodities following two broadcast foliar spray applications of BYI 02960 200 SL at 3X and 5X exaggerated application rates. BYI 02960 200 SL is a soluble concentrate formulation containing 200 g a.s./L.

Materials and Methods

BYI 02960 200 SL was applied to field corn at target rates and timings as shown in Table 6.5.4.13-1.

Table 6.5.4.13-1: Study Use Pattern for BYI 02960 200 SL on Field Corn.

Trial Identification	Location (City, State, NAFTA Region, and Year)	End-use Product (Formulation)	Plot Name	Application						Tank Mix Adjuvants
				Method	Timing/Growth Stage (BBCH)	Actual Spray Volume GPA (L/ha)	Rate lb a.s./A (kg a.s./ha)	Retreatment Interval (days)	Total Rate lb a.s./A (kg a.s./ha)	
RV270-10PA	[redacted], IL Region 5 2010	BYI 02960 200 SL	TRT3F	Foliar Broad-cast	79 83	17 (159) 26 (243)	0.539 (0.605) 0.539 (0.605)	NA[a] 5	1.1 (1.2)	Dyne-Amic 0.25% v/v
RV270-10PA	[redacted], IL Region 5 2010	BYI 02960 200 SL	TRT5G	Foliar Broad-cast	87 87	30 (280) 39 (365)	0.902 (1.01) 0.899 (1.01)	NA[a] 7	1.8 (2.0)	Dyne-Amic 0.25% v/v

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Table 6.5.4.13-1 (cont'd): Study Use Pattern for BYI 02960 200 SL on Field Corn.

Trial Identification	Location (City, State, NAFTA Region, and Year)	End-use Product (Formulation)	Plot Name	Application							Tank Mix Adjuvants
				Method	Timing/Growth Stage (BBCH)	Actual Spray Volume GPA (L/ha)	Rate lb a.s./A (kg a.s./ha)	Retreatment Interval (days)	Total Rate lb a.s./A (kg a.s./ha)		
RV271-10PA	[redacted], IA Region 5 2010	BYI 02960 200 SL	TRT3F	Foliar Broad-cast	85 85	33 (309) 33 (309)	0.553 (0.620) 0.551 (0.617)	NA 5	1.1 (1.2)		Dyne-Amic 0.25% v/v
RV271-10PA	[redacted] IA Region 5 2010	BYI 02960 200 SL	TRT5G	Foliar Broad-cast	89 89	32 (299) 31 (290)	0.917 (1.03) 0.902 (1.01)	NA 8	1.8 (2.0)		Dyne-Amic 0.25% v/v

[a] NA = Not applicable.

All applications were made using ground-based equipment. The additive, Dyne-Amic 0.25% v/v, was used in all applications.

Single composite field corn forage RAC (raw agricultural commodity) samples were collected at a 6-day or 7-day pre-harvest interval (PHI) from plot TRT3F. Single composite field corn grain RAC samples were collected at a 21-day PHI from plot TRT5G. Single composite samples of forage and grain were collected from the control plots on the same day the respective samples were collected from the treated plots.

Triplicate subsamples of field corn forage RAC were removed, and the remaining fresh forage was ensiled and collected as silage. Triplicate subsamples of field corn grain RAC were removed, and the remaining field corn grain was used to collect aspirated grain fractions and generate the processed commodities of starch, refined oil, steep water, and germ from wet milling and grits, flour, meal, refined oil, bran and germ from dry milling.

The residue(s) of BYI 02960, DFA, and DFEAF were quantitated by LC/MS/MS using stable isotopically labelled internal standards. The individual analyte residues were summed to give a total BYI 02960 residue. Residue measurements below the analyte LOQ were summed into the total BYI 02960 residue value as the analyte LOQ value.

Findings

Concurrent recoveries of BYI 02960, DFA, and DFEAF were measured with each set of samples to verify method performance. All recoveries were corrected for any interferences in corresponding controls. The overall mean of the recoveries for all matrices ranged between 72 to 117%, and the standard deviation values were below 20% (Table 6.5.4.13-2).

Table 6.5.4.13-2: Summary of Recoveries of BYI 02960 Residues from Field Corn

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev (%)
Aspirated Grain Fractions	BYI 02960	0.010	4	83, 98, 101, 89	93	9
		1.000	3	101, 118, 102	107	10
	DFA	0.050	4	80, 90, 95, 82	87	7
		1.000	3	91, 104, 101	99	7
	DFEAF	0.010	4	113, 103, 116, 100	108	8
		1.000	3	100, 117, 109	109	9
Bran	BYI 02960	0.010	3	94, 107, 108	103	8
		1.000	3	83, 84, 94	87	6
	DFA	0.050	3	86, 84, 86	86	1
		1.000	3	85, 79, 86	83	4
	DFEAF	0.010	3	109, 98, 119	108	11
		1.000	3	101, 82, 90	91	10
Flour	BYI 02960	0.010	3	105, 81, 89	92	12
	DFA	0.050	3	78, 76, 74	76	2
	DFEAF	0.010	3	119, 98, 102	106	11
Forage	BYI 02960	0.010	3	99, 100, 90	96	6
		2.000	3	87, 95, 85	89	5
		15.000	3	89, 91, 85	88	3
	DFA	0.050	3	94, 113, 108	105	10
		2.000	3	88, 96, 94	92	4
		15.000	3	89, 90, 86	88	2
	DFEAF	0.010	3	118, 116, 117	117	1
		2.000	3	85, 94, 94	91	5
		15.000	3	84, 85, 79	83	3
Germ Dry Milling	BYI 02960	0.010	3	90, 97, 99	95	5
	DFA	0.050	3	74, 86, 86	82	7
	DFEAF	0.010	3	79, 94, 103	92	12
Germ Wet Milling	BYI 02960	0.010	3	93, 84, 93	90	5
		1.000	3	83, 80, 91	85	5
	DFA	0.050	3	76, 70, 71	72	3
		1.000	3	71, 74, 70	72	2
	DFEAF	0.010	3	110, 85, 101	99	13
		1.000	3	87, 80, 89	85	5

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Table 6.5.4.13-2 (cont'd): Summary of Recoveries of BYI 02960 Residues from Field Corn

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev (%)
Grain	BYI 02960	0.010	7	91, 104, 93, 94, 112, 89, 96	97	8
		1.000	3	96, 90, 86	91	5
	DFA	0.050	7	81, 82, 80, 85, 103, 103, 94	90	10
		1.000	3	89, 80, 84	85	5
	DFEAF	0.010	7	99, 105, 81, 115, 116, 116, 118	107	14
		1.000	3	106, 82, 91	93	12
Grits	BYI 02960	0.010	3	74, 98, 95	89	13
	DFA	0.050	3	80, 82, 80	81	1
	DFEAF	0.010	3	89, 119, 103	104	15
Meal Dry Milled	BYI 02960	0.010	3	76, 75, 97	82	13
		1.000	3	97, 97, 93	96	2
	DFA	0.050	3	72, 72, 78	74	3
		1.000	3	84, 85, 91	87	4
	DFEAF	0.010	3	111, 117, 94	108	12
		1.000	3	91, 91, 104	95	8
Oil Dry Milled	BYI 02960	0.010	3	100, 76, 112	96	19
		1.000	3	104, 102, 103	103	1
	DFA	0.050	3	97, 79, 108	95	15
		1.000	3	105, 104, 105	105	1
	DFEAF	0.010	3	103, 88, 107	99	10
		1.000	3	104, 101, 94	99	5
Oil Wet Milled	BYI 02960	0.010	3	85, 80, 95	87	8
		1.000	3	110, 106, 103	107	4
	DFA	0.050	3	83, 82, 89	84	4
		1.000	3	95, 105, 103	102	3
	DFEAF	0.010	3	92, 83, 91	89	5
		1.000	3	85, 101, 96	94	8
Silage	BYI 02960	0.010	3	109, 89, 110	103	12
		2.000	3	93, 100, 99	97	4
		10.000	3	94, 92, 103	96	6
	DFA	0.050	3	82, 98, 82	87	10
		2.000	3	100, 99, 99	99	1
		10.000	3	87, 89, 90	89	1
	DFEAF	0.010	3	103, 115, 103	107	7
		2.000	3	103, 97, 96	98	4
		10.000	3	85, 83, 90	86	4
Starch	BYI 02960	0.010	3	90, 90, 105	95	9
		1.000	3	92, 95, 99	95	4
	DFA	0.050	3	105, 79, 81	89	15
		1.000	3	82, 85, 79	82	3
	DFEAF	0.010	3	104, 99, 118	107	10
		1.000	3	97, 96, 87	93	5

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Table 6.5.4.13-2 (cont'd): Summary of Recoveries of BYI 02960 Residues from Field Corn

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev (%)
Steep Water	BYI 02960	0.010	3	89, 98, 100	96	6
		1.000	3	103, 101, 106	103	3
	DFA	0.050	3	105, 96, 89	97	8
		1.000	3	105, 103, 105	105	1
	DFEAF	0.010	3	108, 99, 99	102	6
		1.000	3	105, 99, 95	100	5

[a] Mean Recovery = mathematical average of all recoveries.

The freezer storage stability study indicates that BYI 02960 residues were stable in field corn commodities during frozen storage for at least 18 months (557 days) prior to analyses. The maximum storage period of frozen samples in this study for BYI 02960 was 305 days. A summary of the storage conditions are shown in the Table 6.5.4.13-3.

Table 6.5.4.13-3: Summary of Storage Conditions for all Field Corn Commodities

Residue Component(s)	Matrix (RAC)	Average Storage Temperature (°C)[a]	Actual Storage Duration months (days)[b,c]
BYI 02960, DFA, DFEAF	Forage (RAC)	<0	10 (305)
BYI 02960, DFA, DFEAF	Silage	<0	8 (247)
BYI 02960, DFA, DFEAF	Grain (RAC)	<0	6 (189)
BYI 02960, DFA, DFEAF	Aspirated Grain Fractions	<0	7 (202)
BYI 02960, DFA, DFEAF	Bran	<0	7 (205)
BYI 02960, DFA, DFEAF	Flour	<0	6 (189)
BYI 02960, DFA, DFEAF	Germ Dry Milling	<0	7 (197)
BYI 02960, DFA, DFEAF	Germ Wet Milling	<0	7 (197)
BYI 02960, DFA, DFEAF	Grits	<0	7 (195)
BYI 02960, DFA, DFEAF	Meal Dry Milled	<0	7 (205)
BYI 02960, DFA, DFEAF	Oil Dry Milled	<0	7 (210)
BYI 02960, DFA, DFEAF	Oil Wet Milled	<0	7 (213)

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Table 6.5.4.13-3 (cont'd): Summary of Storage Conditions for all Field Corn Commodities

Residue Component(s)	Matrix (RAC)	Average Storage Temperature (°C)[a]	Actual Storage Duration months (days)[b,c]
BYI 02960, DFA, DFEAF	Starch	<0	7 (204)
BYI 02960, DFA, DFEAF	Steep Water	<0	7 (209)

a The average storage temperature reported is from the time of sample collection at GLP Technologies through the last sample extraction. Samples were maintained in a laboratory freezer at all times except during preparation for sample analysis.

b The actual storage duration for the field corn forage and grain RACs is the time from field sampling (harvest) through the last sample extraction for these matrices. The actual storage duration for all commodities is from the time of commodity generation through the last sample extraction.

c [redacted], [redacted]. [redacted] 2012. Storage stability of BYI 02960, difluoroacetic acid, and difluoroethyl-amino-furanone in plant matrices. Bayer CropScience Report No. RARVP046, amended version including 18-month data (KIIA 6.1.1/01).

The BYI 02960, DFA, DFEAF, and total BYI 02960 residue data for field corn forage, silage, corn grain, aspirated grain fractions, and corn processed commodities are provided in Tables 6.5.4.13-4 and 6.5.4.13-5.

Table 6.5.4.13-4: BYI 02960 Residue Data from Field Corn Forage RAC and Silage

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Preharvest Interval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV270-10PA	Corn Forage	NA[c]	24,28[d]	1.08 (1.21)	7	4.43 12.4 3.10	0.131 0.397 0.207	0.041 0.108 0.020	4.6 13 3.3 Avg: 7.0	NA[c]	NA[c]
RV271-10PA	Corn Forage	NA[c]	38,46[d]	1.10 (1.24)	6	9.01 8.37 11.2	0.249 0.263 0.300	0.070 0.067 0.104	9.3 8.7 12 Avg: 9.9	NA[c]	NA[c]

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Table 6.5.4.13-4 (cont'd): BYI 02960 Residue Data from Field Corn Forage RAC and Silage

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV270-10PA	Corn Forage	Silage	34	NA	NA	6.82 6.41 7.27	0.310 0.303 0.298	0.032 0.032 0.034	7.2 6.8 7.6 Avg. 7.2	1X	1X
RV271-10PA	Corn Forage	Silage	34	NA	NA	7.35 6.82 7.58	0.185 0.204 0.171	0.017 0.019 0.015	7.6 7.0 7.8 Avg. 7.5	<1X	

[a] Total BYI 02960 residue is the sum of BYI 02960, DFA, and DFEAF residue in parent equivalents.

[b] Total BYI 02960 Processing Factor = Average Total residue in processed sample/average total residue in unprocessed sample. Processing factors calculated to be less than 1X were reported as <1X.

[c] NA = Not applicable.

[d] Two of the three triplicate sub-samples were analyzed for percent dry matter. Both values are reported and not averaged.

Table 6.5.4.13-5: BYI 02960 Residue Data from Field Corn Grain RAC, Aspirated Grain Fractions and Field Corn Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV270-10PA	Corn Grain	NA[c]	86	1.80 (2.02)	21	0.012 0.012 0.011	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.072 0.072 0.071 Avg. 0.072	NA[c]	NA[c]
RV271-10PA	Corn Grain	NA[c]	83	1.82 (2.04)	21	0.026 0.020 0.026	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.086 0.080 0.087 Avg. 0.084	NA[c]	NA[c]

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Table 6.5.4.13-5 (cont'd): BYI 02960 Residue Data from Field Corn Grain RAC, Aspirated Grain Fractions and Field Corn Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV270-10PA	Corn Grain	Aspirated Grain Fractions	90	NA[c]	NA[c]	0.308 0.385 0.286 0.297 0.252 0.299	<0.050 <0.050 <0.050 <0.050 <0.050 <0.050	<0.010 <0.010 <0.010 <0.010 <0.010 <0.010	0.37 0.45 0.35 0.36 0.31 0.36 Avg. 0.37	5.1X	
RV271-10PA	Corn Grain	Aspirated Grain Fractions	89	NA[c]	NA[c]	0.488 0.471 0.597 0.427 0.485 0.522	<0.050 <0.050 <0.050 <0.050 <0.050 <0.050	<0.010 <0.010 <0.010 <0.010 <0.010 <0.010	0.55 0.53 0.66 0.49 0.55 0.58 Avg. 0.56	6.6X	6X
RV270-10PA	Corn Grain	Bran	NA[c]	NA[c]	NA[c]	0.023 0.022 0.020	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.083 0.082 0.081 Avg. 0.082	1.1X	
RV271-10PA	Corn Grain	Bran	NA[c]	NA[c]	NA[c]	0.090 0.089 0.094	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.15 0.15 0.15 Avg. 0.15	1.8X	1.5X
RV270-10PA	Corn Grain	Flour	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV271-10PA	Corn Grain	Flour	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	

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Table 6.5.4.13-5 (cont'd): BYI 02960 Residue Data from Field Corn Grain RAC, Aspirated Grain Fractions and Field Corn Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV270-10PA	Corn Grain	Germ Dry Milling	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	1.X
RV271-10PA	Corn Grain	Germ Dry Milling	NA[c]	NA[c]	NA[c]	0.029 0.028 0.030	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.089 0.088 0.090 Avg. 0.089	1.1X	
RV270-10PA	Corn Grain	Germ Wet Milling	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV271-10PA	Corn Grain	Germ Wet Milling	NA[c]	NA[c]	NA[c]	0.014 0.013 0.013	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.074 0.073 0.073 Avg. 0.073	<1X	
RV270-10PA	Corn Grain	Grits	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV271-10PA	Corn Grain	Grits	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	
RV270-10PA	Corn Grain	Meal Dry Milled	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV271-10PA	Corn Grain	Meal Dry Milled	NA[c]	NA[c]	NA[c]	<0.010 0.011 0.011	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 0.071 0.071 Avg. 0.071	<1X	

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Table 6.5.4.13-5 (cont'd): BYI 02960 Residue Data from Field Corn Grain RAC, Aspirated Grain Fractions and Field Corn Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV270-10PA	Corn Grain	Oil Dry Milled	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV271-10PA	Corn Grain	Oil Dry Milled	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	
RV270-10PA	Corn Grain	Oil Wet Milled	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV271-10PA	Corn Grain	Oil Wet Milled	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	
RV270-10PA	Corn Grain	Starch	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV271-10PA	Corn Grain	Starch	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	
RV270-10PA	Corn Grain	Steep Water	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	1X
RV271-10PA	Corn Grain	Steep Water	NA[c]	NA[c]	NA[c]	0.013 0.011 0.012	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.073 0.071 0.072 Avg. 0.072	1X	

[a] Total BYI 02960 residue is the sum of BYI 02960, DFA, and DFEAF residue in parent equivalents. Residue measurements below the analyte LOQ were summed into the Total BYI 02960 residue value as the analyte LOQ value. These totals represent the upper limit of what the residue levels might be.
[b] Total BYI 02960 Processing Factor = Average Total residue in processed sample/average total residue in unprocessed sample. Processing factors calculated to be less than 1X were reported as <1X.
[c] NA = Not applicable.

Conclusion

A summary of the calculated processing factors for corn commodities are shown in the table below:

Table 6.5.4.13-6: Summary of Total BYI 02960 Processing Factors Calculated for Corn Silage, Aspirated Grain Fractions and Corn Processed Commodities

RAC	Processed Commodity	Average Total BYI 02960 Residue Processing Factor
Field Corn Forage	Silage	1X
Field Corn Grain	Aspirated Grain Fractions	6X
Field Corn Grain	Bran	1.5X
Field Corn Grain	Germ (Dry Milling) and Steep Water	1X
Field Corn Grain	Flour, Germ (Wet Milling), Grits, Meal (Dry Milled), Oil (Wet and Dry Milled), and Starch	<1X

The average total BYI 02960 residue did not concentrate (processing factor ≤1X) in silage, and the processed commodities of flour, germ (dry milling), germ (wet milling), grits, meal (dry milled), oil (dry milled), oil (wet milled), starch and steep water. However, the residue did concentrate in aspirated grain fractions (6X) and bran (1.5X).

The processing factors determined for total BYI 02960 residue in this study are less than the maximum theoretical concentration factors by crop cited in Table 1 of the EPA Residue Chemistry Test Guideline OPPTS 860.1520 which is 25X for corn grain oil.

IIA 6.5.4.14 Cotton

Report:	**KIIA 6.5.4.14/01, [redacted]; 2012**
Title:	BYI 02960 200 SL – Magnitude of the Residue in Cotton Processed Commodities (Crop Subgroup 20C)
Report No & Document No	RARVY033, dated June 22, 2012. M-433122-01-1
Guidelines:	US: EPA Residue Chemistry Test Guidelines OPPTS 860.1520, Processed Food/Feed Canada: PMRA DACO 7.4.5, Processed Food/Feed OECD: Guidelines for the Testing of Chemicals, 508, Magnitude of the Residues in Processed Commodities, Adopted Oct. 3, 2008. OECD Guidance Document on Magnitude of the Pesticide Residues in Processed Commodities.
GLP	Yes

Two field trials were conducted to measure the magnitude of BYI 02960 residues in/on cotton processed commodities following two broadcast foliar spray applications of BYI 02960 200 SL at 3X and 5X exaggerated application rates. BYI 02960 200 SL is a soluble concentrate formulation containing 200 g a.s./L. The 3X treatment plot was a reserve plot which was not harvested.

Materials and Methods

BYI 02960 200 SL was applied to cotton plants at 5x exaggerated rate and timings as shown in Table 6.5.4.14-1. All applications were made using ground-based equipment. The additive, Dyne-Amic 0.25% v/v, was used in all applications

Single composite seed cotton samples were harvested at a 13 to 14-day pre-harvest interval (PHI) from TRT5X plots (plots receiving 5X exaggerated application rates). Single composite samples of seed cotton samples were harvested from the control plots on the same day the respective samples were collected from the treated plots.

After ginning, triplicate subsamples of undelinted seed, the raw agricultural commodity (RAC), were removed, and the remaining undelined seed was used to generate the processed commodities of meal, hulls, refined oil (bleached and deodorized (RBD oil), solvent extracted crude oil, pre-clarified crude oil, and neutralized crude oil.

Table 6.5.4.14-1: Study Use Pattern for BYI 02960 200 SL on Cotton

Trial Identification	Location (City, State, NAFTA Region, and Year)	End-use Product (Formulation)	Plot Name	Application						Tank Mix Adjuvants
				Method	Timing/Growth Stage (BBCH)	Actual Spray Volume GPA (L/ha)	Rate lb a.s./A (kg a.s./ha)	Retreatment Interval (days)	Total Rate lb a.s./A (kg a.s./ha)	
RV276-10PA	[redacted] AR Region 4 2010	BYI 02960 200 SL	TRT5X	Foliar Broad-cast	88 89	10 (93) 10 (93)	0.893 (1.00) 0.892 (1.00)	NA[a] 10	1.8 (2.0)	Dyne-Amic 0.25% v/v
RV277-10PA	[redacted], TX Region 8 2010	BYI 02960 200 SL	TRT5X	Foliar Broad-cast	87 88	20 (187) 18 (168)	0.881 (0.988) 0.882 (0.989)	NA[a] 9	1.8 (2.0)	Dyne-Amic 0.25% v/v

[a] NA = Not applicable.

The residue(s) of BYI 02960, DFA, and DFEAF were quantitated by LC/MS/MS using stable isotopically labeled internal standards standards. The individual analyte residues were summed to give a total BYI 02960 residue. Residue measurements below the analyte LOQ were summed into the total BYI 02960 residue value as the analyte LOQ value.

Findings

Concurrent recoveries of BYI 02960, DFA, and DFEAF were measured with each set of samples to verify method performance. All recoveries were corrected for any interferences in corresponding controls. The overall mean of the recoveries for each matrix at each fortification level was within the acceptable range of 70 to 110%, and the standard deviation (SD) values were less than 20% (Table 6.5.4.14-2).

Table 6.5.4.14-2: Summary of Recoveries of BYI 02960 Residues from Cotton RAC and Processed Commodities

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev (%)
Undelinted Cottonseed RAC	BYI 02960	0.010	3	117, 97, 101	105	11
		3.000	3	100, 98, 99	99	1
	DFA	0.050	3	68, 93, 77	79	13
		3.000	3	88, 92, 91	90	2
	DFEAF	0.010	3	76, 82, 79	79	3
		3.000	3	103, 94, 101	99	5
Meal	BYI 02960	0.010	3	103, 97, 115	105	9
		1.000	3	102, 108, 106	105	3
	DFA	0.050	3	73, 79, 79	77	4
		1.000	3	83, 83, 83	83	0
	DFEAF	0.010	3	106, 104, 76	95	17
		1.000	3	102, 100, 95	99	4
Hulls	BYI 02960	0.010	3	97, 87, 93	92	5
		1.000	3	102, 105, 89	99	9
	DFA	0.050	3	75, 72, 69	72	3
		1.000	3	87, 90, 92	90	3
	DFEAF	0.010	3	99, 110, 59	89	27
		1.000	3	99, 93, 95	96	3
Cotton Oil	BYI 02960	0.010	4	121, 90, 103, 83	99	17
	DFA	0.050	4	74, 84, 103, 101	91	14
	DFEAF	0.010	4	86, 97, 95, 83	90	7

[a] Mean Recovery = mathematical average of all recoveries.

Storage stability of BYI 02960, DFA, and DFEAF are being tested in orange fruit (high acid content representative), spinach leaves and tomato fruit (high water content representatives), wheat grain (high starch content representative), navy bean seed (high protein content representative), coffee and soybean seed (high oil content representatives), sugar cane and tobacco.

The freezer storage stability study indicates that BYI 02960 residues were stable in coffee and soybean seed (representative for high oil content) for at least 18 months (558 days). The maximum storage period of frozen samples in this study for BYI 02960 was 449 days. A summary of the storage conditions are shown in the Table 6.5.4.14-3.

Table 6.5.4.14-3: Summary of Storage Conditions for Cotton RAC and Processed Commodities

Residue Component(s)	Matrix (RAC)	Average Storage Temperature (°C)[a]	Actual Storage Duration months (days)[b]	Interval of Demonstrated Storage Stability months (days)[c]
BYI 02960; DFA; DFEAF	Undelinted Cottonseed RAC	<0	14 (449)	18 (558)
BYI 02960; DFA; DFEAF	Meal	<0	6 (190)	18 (558)

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Table 6.5.4.14-3 (cont'd): Summary of Storage Conditions for Cotton RAC and Processed Commodities

Residue Component(s)	Matrix (RAC)	Average Storage Temperature (°C)[a]	Actual Storage Duration months (days)[b]	Interval of Demonstrated Storage Stability months (days)[c]
BYI 02960; DFA; DFEAF	Hulls	<0	6 (185)	18 (558)
BYI 02960; DFA; DFEAF	Refined Oil (Bleached and Deodorized)	<0	5 (176)	18 (558)
BYI 02960; DFA; DFEAF	Solvent Extracted Crude Oil	<0	6 (187)	18 (558)
BYI 02960; DFA; DFEAF	Pre-Clarified Crude Oil	<0	6 (189)	18 (558)
BYI 02960; DFA; DFEAF	Neutralized Crude Oil	<0	6 (189)	18 (558)

a The average storage temperature reported is from the time of sample collection at GLP Technologies through the last sample extraction. Samples were maintained in a laboratory freezer at all times except during preparation for sample analysis.

b The actual storage duration for the undelinted cottonseed RACs is the time from date harvested (picked) through the last sample extraction for these matrices. The actual storage duration for all commodities is from the time of commodity generation through the last sample extraction.

c [redacted], [redacted]. 2012. Storage stability of BYI 02960, difluoroacetic acid, and difluoroethyl-amino-furanone in plant matrices. Bayer CropScience Report No. RARVP046, amended version including 18-month data (KIIA 6.1.1/01).

The BYI 02960, DFA, DFEAF, and total BYI 02960 residue data for cotton RAC and processed commodities are provided in Table 6.5.4.14-4.

Table 6.5.4.14-4: BYI 02960 Residue Data from Cotton RAC and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Interval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV276-10PA	Undelinted Cottonseed	NA[c]	94	1.8 (2.0)	14	2.40 1.35 0.494	<0.050 <0.050 <0.050	0.083 0.021 0.011	2.5 1.4 0.51 Avg. 1.5	NA[c]	NA[c]
RV277-10PA	Undelinted Cottonseed	NA[c]	91	1.8 (2.0)	14	0.302 0.271 0.167	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.32 0.28 0.20 Avg. 0.26	NA[c]	

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Table 6.5.4.14-4 (cont'd): BYI 02960 Residue Data from Cotton RAC and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV276-10PA	Undelinted Cottonseed	Meal	94	NA[c]	NA[c]	0.046 0.056 0.054	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.053 0.064 0.062 Avg. 0.059	<1X	<1X
RV277-10PA	Undelinted Cottonseed	Meal	94	NA[c]	NA[c]	0.077 0.042 0.066	0.079 0.055 0.062	<0.010 <0.010 <0.010	0.16 0.10 0.13 Avg. 0.13	<1X	
RV276-10PA	Undelinted Cottonseed	Hullls	91	NA[c]	NA[c]	0.184 0.127 0.094	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.19 0.13 0.10 Avg. 0.14	<1X	<1X
RV277-10PA	Undelinted Cottonseed	Hullls	84	NA[c]	NA[c]	0.205 0.201 0.291	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.21 0.21 0.30 Avg. 0.24	<1X	
RV276-10PA	Undelinted Cottonseed	Refined Oil (RBD)	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV277-10PA	Undelinted Cottonseed	Refined Oil (RBD)	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	
RV276-10PA	Undelinted Cottonseed	Solvent Exrtracted Crude Oil	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV277-10PA	Undelinted Cottonseed	Solvent Exrtracted Crude Oil	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	

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Table 6.5.4.14-4 (cont'd): BYI 02960 Residue Data from Cotton RAC and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV276-10PA	Undelinted Cottonseed	Pre-Clarified Crude Oil	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV277-10PA	Undelinted Cottonseed	Pre-Clarified Crude Oil	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	
RV276-10PA	Undelinted Cottonseed	Neutralised Crude Oil	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV277-10PA	Undelinted Cottonseed	Neutralised Crude Oil	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	

a Total BYI 02960 residue is the sum of BYI 02960, DFA, and DFEAF residue in parent equivalents. Residue measurements below the analyte LOQ were summed into the Total BYI 02960 residue value as the analyte LOQ value. These totals represent the upper limit of what the residue levels might be.

b Total BYI 02960 Processing Factor = Average total BYI 02960 residue in processed sample/average total BYI 02960 residue in unprocessed sample. Processing factors calculated to be less than 1X were reported as <1X.

c NA = Not applicable.

Conclusion

A summary of the calculated processing factors for cotton processed commodities are shown in Table 6.5.4.14-5.

Following a two-fold (2X) exaggerated application of BYI 02960 to two separate trials of coffee, the average total BYI 02960 residue values did not concentrate (processing factor ≤1) in meal, hulls, refined oil (bleached and deodorized), solvent extracted crude oil, pre-clarified crude oil, and neutralized crude oil.

The processing factors determined for total BYI 02960 residue in this study are less than the theoretical concentration factors cited in the EPA Residue Chemistry Test Guideline OPPTS 860.1520.

Table 6.5.4.14-5: Summary of Total BYI 02960 Processing Factors Calculated Coffee Processed Commodities

RAC	Processed Commodity	Average Total BYI 02960 Residue Processing Factor
Undelinted cottonseed	Meal, hulls, all oils	<1X

IIA 6.5.4.15 Peanut

Report:	**KIIA 6.5.4.15/01, [redacted]; 2012**
Title:	BYI 02960 200 SL – Magnitude of the Residue in/on Peanut Processed Commodities
Report No & Document No	RARVY032, dated May 4, 2012. M-430523-01-2
Guidelines:	US: EPA Residue Chemistry Test Guidelines OPPTS 860.1520, Processed Food/Feed Canada: PMRA DACO 7.4.5, Processed Food/Feed OECD: Guidelines for the Testing of Chemicals, 508, Magnitude of the Residues in Processed Commodities, Adopted Oct. 3, 2008. OECD Guidance Document on Magnitude of the Pesticide Residues in Processed Commodities.
GLP	Yes

Two field trials were conducted to measure the magnitude of BYI 02960 residues in/on peanut processed commodities following two broadcast foliar spray applications of BYI 02960 200 SL at 3X and 5X exaggerated application rates. BYI 02960 200 SL is a soluble concentrate formulation containing 200 g a.s./L.

Materials and Methods

BYI 02960 200 SL was applied to peanut plants at rates and timings as shown in Table 6.5.4.15-1.

Table 6.5.4.15-1: Study Use Pattern for BYI 02960 200 SL on Peanut

Trial Identification	Location (City, State, NAFTA Region, and Year)	End-use Product (Formulation)	Plot Name	Application						Tank Mix Adjuvants
				Method	Timing/Growth Stage (BBCH)	Actual Spray Volume GPA (L/ha)	Rate lb a.s./A (kg a.s./ha)	Retreatment Interval (days)	Total Rate lb a.s./A (kg a.s./ha)	
RV274-10PA	[redacted], VA Region 2 2010	BYI 02960 200 SL	TRT5X	Foliar Broad-cast	87 88	12 (112) 12 (112)	0.896 (1.00) 0.907 (1.02)	NA[a] 10	1.8 (2.0)	Dyne-Amic 0.25% v/v
RV275-10PA	[redacted], TX Region 6 2010	BYI 02960 200 SL	TRT5X	Foliar Broad-cast	88 89	18 (168) 18 (168)	0.884 (0.991) 0.899 (1.00)	NA[a] 8	1.8 (2.0)	Dyne-Amic 0.25% v/v

[a] NA = Not applicable.

All applications were made using ground-based equipment. The additive, Dyne-Amic 0.25% v/v, was used in all applications.

Single composite unshelled peanut samples were dug at a 7-day pre-harvest interval (PHI) from TRT5X plots (plots receiving 5X exaggerated application rates). Single composite samples of unshelled peanuts were dug from the control plots on the same day the respective samples were collected from the treated plots.

Triplicate subsamples of nut without shell (nutmeat), the raw agricultural commodity (RAC) were removed, and the remaining peanut nutmeats were used to generate the processed commodities of meal, refined oil, peanut butter and dry roasted peanuts.

The residue(s) of BYI 02960, DFA, and DFEAF were quantitated by LC/MS/MS using stable isotopically labeled internal standards standards. The individual analyte residues were summed to give a total BYI 02960 residue. Residue measurements below the analyte LOQ were summed into the total BYI 02960 residue value as the analyte LOQ value.

Findings

Concurrent recoveries of BYI 02960, DFA, and DFEAF were measured with each set of samples to verify method performance. All recoveries were corrected for any interferences in corresponding controls. The overall mean of the recoveries for each matrix was within the acceptable range of 70 to 110%, and the standard deviation values were below 20% (Table 6.5.4.15-2).

Table 6.5.4.15-2: Summary of Recoveries of BYI 02960 Residues from Peanut

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev (%)
Peanut Nutmeat (Nut without shell)	BYI 02960	0.010	3	107, 103, 79	96	15
		0.500	3	100, 84, 101	95	10
	DFA	0.050	3	82, 68, 75	75	7
		0.500	3	86, 84, 91	87	4
	DFEAF	0.010	3	77, 81, 87	82	5
		0.500	3	102, 93, 102	99	5
Meal	BYI 02960	0.010	3	77, 83, 78	79	3
		0.500	6	93, 88, 91, 91, 96, 91	92	3
	DFA	0.050	3	79, 71, 73	74	4
		0.500	6	78, 74, 73, 73, 73,75	74	2
	DFEAF	0.010	3	101, 90, 89	94	7
		0.500	6	99, 95, 91, 100, 92, 87	94	5
Refined Oil	BYI 02960	0.010	3	95, 90, 114	100	13
		0.500	3	107, 99, 104	103	4
	DFA	0.050	3	106, 89, 82	92	12
		0.500	3	102, 100, 99	100	2
	DFEAF	0.010	3	106, 103, 97	102	4
		0.500	3	103, 99, 105	102	3

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Table 6.5.4.15-2 (cont'd): Summary of Recoveries of BYI 02960 Residues from Peanut

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev (%)
Peanut Butter	BYI 02960	0.010	3	101, 102, 94	99	4
		0.500	3	72, 99, 83	85	14
	DFA	0.050	3	87, 95, 81	88	7
		0.500	3	71, 91, 81	81	10
	DFEAF	0.010	3	74, 89, 92	85	9
		0.500	3	87, 98, 91	92	6
Dry Roasted Peanut	BYI 02960	0.010	3	84, 81, 91	85	5
		0.500	3	81, 75, 74	77	4
	DFA	0.050	3	96, 88, 73	86	12
		0.500	3	89, 93, 84	89	5
	DFEAF	0.010	3	92, 80, 77	83	8
		0.500	3	95, 91, 91	92	2

[a] Mean Recovery = mathematical average of all recoveries

The freezer storage stability study indicates that BYI 02960 residues were stable in coffee beans and soybean seeds as representative crops of the respective crop commodity (high oil content) during frozen storage for at least 18 months (558 days) prior to analyses. The maximum storage period of frozen samples in this study for BYI 02960 was 465 days. A summary of the storage conditions are shown in the Table 6.5.4.15-3.

Table 6.5.4.15-3: Summary of Storage Conditions for Peanut Commodities

Residue Component(s)	Matrix (RAC)	Average Storage Temperature (°C)[a]	Actual Storage Duration months (days)[b]	Interval of Demonstrated Storage Stability months (days)[c]
BYI 02960 DFA DFEAF	Nut without Shell (nutmeat) RAC	<0	13 (390)	18 (558)
BYI 02960 DFA DFEAF	Meal	<0	13 (390)	18 (558)
BYI 02960 DFA DFEAF	Refined Oil	<0	13 (389)	18 (558)
BYI 02960 DFA DFEAF	Peanut Butter	<0	13 (391)	18 (558)
BYI 02960 DFA DFEAF	Dry Roasted Peanut	<0	16 (465)	18 (558)

[a] The average storage temperature reported is from the time of sample collection at GLP Technologies through the last sample extraction. Samples were maintained in a laboratory freezer at all times except during preparation for sample analysis.

[b] The actual storage duration for the peanut RACs is the time from date dug through the last sample extraction for these matrices. The actual storage duration for all commodities is from the time of commodity generation through the last sample extraction.

c [redacted], [redacted]. [redacted]. 2012. Storage stability of BYI 02960, difluoroacetic acid, and difluoroethyl-amino-furanone in plant matrices. Bayer CropScience Report No. RARVP046, amended version including 18-month data (KIIA 6.1.1/01).

The BYI 02960, DFA, DFEAF, and total BYI 02960 residue data for peanut RAC and peanut processed commodities are provided in Table 6.5.4.15-4.

Table 6.5.4.15-4: BYI 02960 Residue Data from Peanut RAC and Peanut Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV274-10PA	Nut meat	NA[c]	NA[c]	1.8 (2.0)	7	0.107 0.114 0.147	0.302 0.316 0.310	<0.010 <0.010 <0.010	0.419 0.440 0.467 Avg. 0.442	NA[c]	NA[c]
RV275-10PA	Nut meat	NA[c]	NA[c]	1.8 (2.0)	7	0.012 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.072 <0.070 <0.070 Avg. 0.071	NA[c]	NA[c]
RV274-10PA	Nut meat	Meal	93	NA[c]	NA[c]	0.172 0.190 0.181	0.361 0.421 0.401	<0.010 <0.010 <0.010	0.543 0.621 0.592 Avg. 0.585	1.3	1.2X
RV275-10PA	Nut meat	Meal	93	NA[c]	NA[c]	0.026 0.016 0.018	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.086 0.076 0.078 Avg. 0.080	1.1	
RV274-10PA	Nut meat	Refined oil	NA[d]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV275-10PA	Nut meat	Refined oil	NA[d]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	

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Table 6.5.4.15-4 (cont'd): BYI 02960 Residue Data from Peanut RAC and Peanut Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV274-10PA	Nut meat	Peanut Butter	NA[c]	NA[c]	NA[c]	0.026 0.026 0.025	0.210 0.170 0.163	<0.010 <0.010 <0.010	0.246 0.206 0.198 Avg. 0.217	<1X	<1X
RV275-10PA	Nut meat	Peanut Butter	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	
RV274-10PA	Nut meat	Dry Roasted Peanut	NA[c]	NA[c]	NA[c]	0.024 0.028 0.020	0.204 0.201 0.169	<0.010 <0.010 <0.010	0.238 0.239 0.199 Avg. 0.225	<1X	<1X
RV275-10PA	Nut meat	Dry Roasted Peanut	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	

[a] Total BYI 02960 residue is the sum of BYI 02960, DFA, and DFEAF residue in parent equivalents. Residue measurements below the analyte LOQ were summed into the Total BYI 02960 residue value as the analyte LOQ value. These totals represent the upper limit of what the residue levels might be.

[b] Total BYI 02960 Processing Factor = Average Total residue in processed sample/average total residue in unprocessed sample. Processing factors calculated to be less than 1X were reported as <1X.

[c] NA = Not applicable.

Conclusion

A summary of the calculated processing factors for peanut processed commodities are shown in Table 6.5.4.15-5.

Following a five-fold (5X) exaggerated application of BYI 02960 to two separate trials of peanut plants, the average total BYI 02960 residue did not concentrate (processing factor <1X) in refined oil, peanut butter, and dry roasted peanuts. However, the total BYI 02960 residue did concentrate slightly in peanut meal (1.2X).

The processing factors determined for BYI 02960 total residue in this study are less than the theoretical concentration factors cited in the EPA Residue Chemistry Test Guideline OPPTS 860.1520 which lists factors of 3.0X for peanuts, 2.2X for meal and 2.8X for oil.

The residue data and subsequent calculated processing factors provided in this report are suitable for regulatory purposes.

Table 6.5.4.15-5: Summary of Total BYI 02960 Processing Factors Calculated for Peanut Processed Commodities

RAC	Processed Commodity	Average Total BYI 02960 Residue Processing Factor
Peanut Nutmeat (Nut without shell)	Meal	1.2X
	Refined oil, Peanut Butter, Dry Roasted Peanuts	<1X

IIA 6.5.4.16 Potato

Report:	**KIIA 6.5.4.16/01, [redacted]; 2012**
Title:	BYI 02960 200 SL – Magnitude of the Residue in/on Potato Processed Commodities
Report No & Document No	RARVY038, dated May 7, 2012. M-430542-01-2
Guidelines:	US: EPA Residue Chemistry Test Guidelines OPPTS 860.1520, Processed Food/Feed Canada: PMRA DACO 7.4.5, Processed Food/Feed OECD: Guidelines for the Testing of Chemicals, 508, Magnitude of the Residues in Processed Commodities, Adopted Oct. 3, 2008. OECD Guidance Document on Magnitude of the Pesticide Residues in Processed Commodities.
GLP	Yes

Two field trials were conducted to measure the magnitude of BYI 02960 residues in/on potato processed commodities following two broadcast foliar spray applications of BYI 02960 200 SL at 3X and 5X exaggerated application rates. BYI 02960 200 SL is a soluble concentrate formulation containing 200 g **a.s.**/L.

Materials and Methods

BYI 02960 200 SL was applied to potato plants at rates and timings as shown in Table 6.5.4.16-1.

Table 6.5.4.16-1: Study Use Pattern for BYI 02960 200 SL on Potato

Trial Identification	Location (City, State, NAFTA Region, and Year)	End-use Product (Formulation)	Plot Name	Application						Tank Mix Adjuvants
				Method	Timing/Growth Stage (BBCH)	Actual Spray Volume GPA (L/ha)	Rate lb a.s./A (kg a.s./ha)	Retreatment Interval (days)	Total Rate lb a.s./A (kg a.s./ha)	
RV202-11PA	[redacted], KS Region 5 2011	BYI 02960 200 SL	TRT5X	Foliar Broad-cast	47 48	33 (309) 35 (327)	0.853 (0.957) 0.890 (0.997)	NA[a] 6	1.7 (1.9)	Dyne-Amic 0.25% v/v
RV203-11PA	[redacted], WA Region11 2011	BYI 02960 200 SL	TRT5X	Foliar Broad-cast	47 48	40 (374) 40 (374)	0.903 (1.01) 0.904 (1.01)	NA[a] 7	1.8 (2.0)	Dyne-Amic 0.25% v/v

[a] NA = Not applicable.

All applications were made using ground-based equipment. The additive, Dyne-Amic 0.25% v/v, was used in all applications.

Single composite potato tuber samples were dug at a 6 or 7-day pre-harvest interval (PHI) from TRT5X plots (plots receiving 5X exaggerated application rates). Single composite samples of potato tubers were dug from the control plots on the same day the respective samples were dug from the treated plots.

Triplicate subsamples of potato tubers, unwashed, the raw agricultural commodity (RAC) were removed. The remaining potato tubers were washed (triplicate subsamples removed), washings collected (wash water) and the potato processed commodities of crisps, flakes, wet peel, starch, tuber with peel cooked, peeled tuber, tuber cooked, (steamed, peeled, and mashed), and cooking (boiling) water generated.

The residue(s) of BYI 02960, DFA, and DFEAF were quantitated by LC/MS/MS using stable isotopically labeled internal standards standards. The individual analyte residues were summed to give a total BYI 02960 residue. Residue measurements below the analyte LOQ were summed into the total BYI 02960 residue value as the analyte LOQ value.

Findings

Concurrent recoveries of BYI 02960, DFA, and DFEAF were measured with each set of samples to verify method performance. All recoveries were corrected for any interferences in corresponding controls. The overall mean of the recoveries for each matrix was within the acceptable range of 70 to 110%, and the standard deviation values were below 20% (Table 6.5.4.16-2).

Table 6.5.4.16-2: Summary of Recoveries of BYI 02960 Residues from Potato RAC and Processed Commodities

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev (%)
Potato Tuber (RAC)	BYI 02960	0.010	7	98, 90, 88, 79, 76, 77, 115	89	14
	DFA	0.050	7	106, 106, 98, 115, 93, 91, 108	102	9
	DFEAF	0.010	7	89, 87, 93, 89, 92, 98, 89	91	4
Potato Tuber Washed	BYI 02960	0.100	3	87, 83, 83	84	2
	DFA	0.100	3	89, 92, 111	97	12
	DFEAF	0.100	3	91, 102, 89	94	7
Potato Washings (Wash Water)	BYI 02960	0.010	3	87, 93, 113	98	14
		0.100	3	92, 94, 79	88	8
	DFA	0.050	3	89, 90, 98	92	5
		0.100	3	84, 84, 84	84	1
	DFEAF	0.010	3	97, 97, 100	98	2
		0.100	3	94, 95, 91	93	2

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Table 6.5.4.16-2 (cont'd): Summary of Recoveries of BYI 02960 Residues from Potato RAC and Processed Commodities

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev (%)
Potato Crisps	BYI 02960	0.010	3	117, 78, 75	90	23
		0.100	3	76, 81, 78	78	2
	DFA	0.050	3	78, 83, 79	80	3
		0.100	3	84, 74, 74	77	6
	DFEAF	0.010	3	81, 83, 81	82	1
		0.100	3	85, 79, 86	84	4
Potato Flakes	BYI 02960	0.010	3	78, 81, 104	88	15
		0.500	3	94, 85, 110	96	12
	DFA	0.050	3	83, 99, 74	86	13
		0.500	3	79, 78, 77	78	1
	DFEAF	0.010	3	94, 77, 76	83	10
		0.500	3	90, 87, 87	88	2
Potato Wet Peel	BYI 02960	0.010	3	89, 95, 84	89	6
		0.100	3	95, 92, 82	90	7
	DFA	0.050	3	90, 90, 91	90	1
		0.100	3	83, 86, 83	84	2
	DFEAF	0.010	3	104, 100, 85	96	10
		0.100	3	92, 96, 94	94	2
Potato Starch	BYI 02960	0.010	3	90, 106, 78	91	14
		0.500	3	86, 100, 106	97	10
	DFA	0.050	3	107, 101, 94	101	6
		0.500	3	89, 96, 94	93	4
	DFEAF	0.010	3	90, 84, 102	92	9
		0.500	3	86, 97, 96	93	6
Potato Tuber with Peel, Cooked (boiled)	BYI 02960	0.010	3	81, 110, 74	88	19
		0.100	3	78, 81, 87	82	5
	DFA	0.050	3	86, 84, 76	82	5
		0.100	3	83, 74, 77	78	4
	DFEAF	0.010	3	80, 84, 87	84	3
		0.100	3	91, 87, 85	88	4
Potato Tuber Peeled	BYI 02960	0.100	2	106, 90	98	NA[b]
	DFA	0.100	2	108, 104	106	NA[b]
	DFEAF	0.100	2	97, 101	99	NA[b]
Potato Cooked, (steamed), Peeled, Mashed	BYI 02960	0.010	3	88, 98, 85	91	7
		0.100	3	83, 82, 90	85	5
	DFA	0.050	3	88, 92, 90	90	2
		0.100	3	80, 82, 83	82	2
	DFEAF	0.010	3	91, 82, 102	92	10
		0.100	3	92, 88, 91	90	2

Table 6.5.4.16-2 (cont'd): Summary of Recoveries of BYI 02960 Residues from Potato RAC and Processed Commodities

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev (%)
Potato Cooking (boiling) Water	BYI 02960	0.010	3	87, 103, 81	90	11
		0.100	3	86, 92, 92	90	4
	DFA	0.050	3	104, 101, 101	102	2
		0.100	3	93, 98, 96	96	2
	DFEAF	0.010	3	107, 100, 94	100	7
		0.100	3	97, 94, 97	96	2

a Mean Recovery = mathematical average of all recoveries.
b NA = Not applicable. Standard deviation cannot be calculated when less than three values are presented.

The freezer storage stability study indicates that BYI 02960 residues were stable in a representative crop of the respective crop commodity (high starch content) during frozen storage for at least 18 months (557 days) prior to analysis. The maximum storage period of frozen samples in this study for BYI 02960 was 216 days. A summary of the storage conditions are shown in the Table 6.5.4.16-3.

Table 6.5.4.16-3: Summary of Storage Conditions for all Potato Commodities

Residue Component(s)	Matrix (RAC)	Average Storage Temperature (°C)[a]	Actual Storage Duration months (days)[b]	Interval of Demonstrated Storage Stability months (days)[c]
BYI 02960 DFA DFEAF	Potato Tuber (RAC)	<0	6 (204)	18 (557)
BYI 02960 DFA DFEAF	Potato Tuber Washed	<0	6 (199)	18 (557)
BYI 02960 DFA DFEAF	Potato Washings	<0	7 (211)	18 (557)
BYI 02960 DFA DFEAF	Potato Crisps	<0	7 (216)	18 (557)
BYI 02960 DFA DFEAF	Potato Flakes	<0	6 (203)	18 (557)
BYI 02960 DFA DFEAF	Potato Wet Peel	<0	7 (214)	18 (557)
BYI 02960 DFA DFEAF	Potato Starch	<0	6 (203)	18 (557)
BYI 02960 DFA DFEAF	Potato Tuber with Peel, Cooked	<0	6 (212)	18 (557)

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Table 6.5.4.16-3 (cont'd): Summary of Storage Conditions for all Potato Commodities

Residue Component(s)	Matrix (RAC)	Average Storage Temperature (°C)[a]	Actual Storage Duration months (days)[b]	Interval of Demonstrated Storage Stability months (days)[c]
BYI 02960 DFA DFEAF	Potato Tuber Peeled	<0	6 (202)	18 (557)
BYI 02960 DFA DFEAF	Potato Tuber Steamed, Mashed	<0	6 (210)	18 (557)
BYI 02960 DFA DFEAF	Potato Cooking Water	<0	7 (212)	18 (557)

[a] The average storage temperature reported is from the time of sample generation at the University of [redacted] Food Technology Center through the last sample extraction. Samples were maintained in a laboratory freezer at all times except during preparation for sample analysis.

[b] The actual storage duration for the potato RACs is the time from date dug through the last sample extraction for these matrices. The actual storage duration for all commodities is from the time of commodity generation through the last sample extraction.

[c] [redacted], [redacted]. [redacted]. 2012. Storage stability of BYI 02960, difluoroacetic acid, and difluoroethyl-amino-furanone in plant matrices. Bayer CropScience Report No. RARVP046, amended version including 18-month data (KIIA 6.1.1/01).

The BYI 02960, DFA, DFEAF, and total BYI 02960 residue data for potato RAC and processed commodities are provided in Table 6.5.4.16-4.

Table 6.5.4.16-4: BYI 02960 Residue Data from Potato RAC and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Interval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV202-11PA	Tuber	NA[c]	16	1.7 (1.9)	7	<0.010 0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 0.070 <0.070 Avg. <0.070	NA[c]	NA[c]
RV203-11PA	Tuber	NA[c]	23	1.8 (2.0)	7	<0.010 0.015 <0.010	<0.050 0.058 0.054	<0.010 <0.010 <0.010	<0.070 0.083 0.074 Avg. 0.075	NA[c]	

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Table 6.5.4.16-4 (cont'd): BYI 02960 Residue Data from Potato RAC and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV202-11PA	Tuber	Tuber, Washed	NA[c]	NA[c]	NA[c]	0.015 0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.075 0.070 <0.070 Avg. 0.072	1X	1X
RV203-11PA	Tuber	Tuber, Washed	NA[c]	NA[c]	NA[c]	0.018 0.010 0.013	0.053 0.054 <0.050	<0.010 <0.010 <0.010	0.081 0.074 0.073 Avg. 0.076	1X	
RV202-11PA	Tuber	Potato Washings (Wash Water)	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV203-11PA	Tuber	Potato Washings (Wash Water)	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	
RV202-11PA	Tuber	Potato Crisps	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	1X
RV203-11PA	Tuber	Potato Crisps	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	0.073 0.075 0.074	<0.010 <0.010 <0.010	0.093 0.095 0.093 Avg. 0.094	1.3X	
RV202-11PA	Tuber	Potato Flakes	NA[c]	NA[c]	NA[c]	0.014 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.074 <0.070 <0.070 Avg. 0.071	1X	1.3X
RV203-11PA	Tuber	Potato Flakes	NA[c]	NA[c]	NA[c]	0.017 <0.010 0.012	0.105 0.090 0.103	<0.010 <0.010 <0.010	0.13 0.11 0.12 Avg. 0.12	1.6X	

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Table 6.5.4.16-4 (cont'd): BYI 02960 Residue Data from Potato RAC and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV202-11PA	Tuber	Potato Wet Peel	10	NA[c]	NA[c]	0.014 0.014 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.074 0.075 <0.070 Avg. 0.073	1X	<1X
RV203-11PA	Tuber	Potato Wet Peel	14	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	
RV202-11PA	Tuber	Potato Starch	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV203-11PA	Tuber	Potato Starch	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	
RV202-11PA	Tuber	Potato Tuber with Peel Cooked (boiled)	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV203-11PA	Tuber	Potato Tuber with Peel Cooked (boiled)	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 0.049	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	
RV202-11PA	Tuber	Potato Tuber Peeled	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	1X
RV203-11PA	Tuber	Potato Tuber Peeled	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	0.052 0.057 0.061	<0.010 <0.010 <0.010	0.072 0.077 0.081 Avg. 0.077	1X	

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Table 6.5.4.16-4 (cont'd): BYI 02960 Residue Data from Potato RAC and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV202-11PA	Tuber	Potato Tuber Cooked ,Peeled, Mashed	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV203-11PA	Tuber	Potato Tuber Cooked ,Peeled, Mashed	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	
RV202-11PA	Tuber	Potato Cooking (boiling) Water	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV203-11PA	Tuber	Potato Cooking (boiling) Water	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	

[a] Total BYI 02960 residue is the sum of BYI 02960, DFA, and DFEAF residue in parent equivalents. Residue measurements below the analyte LOQ were summed into the Total BYI 02960 residue value as the analyte LOQ value. These totals represent the upper limit of what the residue levels might be.

[b] Total BYI 02960 Processing Factor = Average Total residue in processed sample/average total residue in unprocessed (RAC) sample. Processing factors calculated to be less than 1X were reported as <1X

[c] NA = Not applicable.

Conclusion

A summary of the calculated processing factors for potato processed commodities are shown in Table 6.5.4.16-5.

Following a five-fold (5X) exaggerated application of BYI 02960 to two separate trials of potato plants, the average total BYI 02960 residue did not concentrate (processing factor ≤1X) in potato tuber washed, washings (wash water from tubers), potato crisps, tuber peeled, cooking (boiling) water, wet peel, starch, tuber with peel (cooked), and tuber cooked (steamed, peeled, and mashed). However, the residue did concentrate slightly in potato flakes (1.3X).

The processing factors determined for BYI 02960 total residue in this study are less than the theoretical concentration factors cited in the EPA Residue Chemistry Test Guideline OPPTS 860.1520 which lists factors of 5.0X for potatoes, 4.7X for potato flakes and 4.0X for potato processed waste (wet peel).

The residue data and subsequent calculated processing factors provided in this report are suitable for regulatory purposes.

Table 6.5.4.16-5: Summary of Total BYI 02960 Processing Factors Calculated for Potato Processed Commodities

RAC	Processed Commodity	Average Total BYI 02960 Residue Processing Factor
Potato Tuber (Unwashed)	Potato Flakes	1.3X
	Potato tuber washed, Washings (wash water from tubers), Potato Crisps, Tuber peeled, Cooking (boiling) water, Wet Peel, Starch, Tuber with peel (cooked), Tuber, (cooked, steamed, peeled, and mashed).	<1X

IIA 6.5.4.17 Soybean

Report:	**KIIA 6.5.4.17/01; [redacted]; 2012**
Title:	BYI 02960 200 SL – Magnitude of the Residue in/on Soybean Processed Commodities
Report No & Document No	RARVY029, dated April 4, 2012 M-428939-01-2
Guidelines:	US: EPA Residue Chemistry Test Guidelines OPPTS 860.1520, Processed Food/Feed Canada: PMRA DACO 7.4.5, Processed Food/Feed OECD: Guidelines for the Testing of Chemicals, 508, Magnitude of the Residues in Processed Commodities, Adopted Oct. 3, 2008. OECD Guidance Document on Magnitude of the Pesticide Residues in Processed Commodities.
GLP	Yes

Two field trials were conducted to measure the magnitude of BYI 02960 residues in/on soybean aspirated grain fractions and processed commodities following two broadcast foliar spray applications of BYI 02960 200 SL at 3X and 5X exaggerated application rates. BYI 02960 200 SL is a soluble concentrate formulation containing 200 g a.s./L.

Materials and Methods

BYI 02960 200 SL was applied to soybean plants at rates and timings as shown in Table 6.5.4.17-1.

Table 6.5.4.17-1: Study Use Pattern for BYI 02960 200 SL on Soybean

Trial Identification	Location (City, State, NAFTA Region, and Year)	End-use Product (Formulation)	Plot Name	Application						Tank Mix Adjuvants
				Method	Timing/Growth Stage (BBCH)	Actual Spray Volume GPA (L/ha)	Rate lb a.s./A (kg a.s./ha)	Retreatment Interval (days)	Total Rate lb a.s./A (kg a.s./ha)	
RV268-10PA	[redacted], NE Region 5 2010	BYI 02960 200 SL	TRT5X	Broad-cast foliar	79 89	20 (187) 20 (187)	0.898 (1.00) 0.890 (0.998)	NA[a] 9	1.8 (2.0)	Dyne-Amic 0.25% v/v
RV269-10PA	[redacted], NE Region 5 2010	BYI 02960 200 SL	TRT5X	Broad-cast foliar	79 79	16 (150) 16 (150)	0.890 (0.997) 0.889 (0.997)	NA[a] 8	1.8 (1.9)	Dyne-Amic 0.25% v/v

[a] NA = Not applicable.

All applications were made using ground-based equipment. The additive, Dyne-Amic 0.25% v/v, was used in all applications.

Single composite soybean seed RAC (raw agricultural commodity) samples were collected at 19-day or 21-day pre-harvest interval (PHI) from the TRT5X plots (plots receiving 5X exaggerated application rates). Single composite samples of seed were collected from the control plots on the same day the respective samples were collected from the treated plots.

Triplicate subsamples of soybean seed RAC were removed and the remaining soybean seed was used to collect aspirated grain fractions and generate the processed commodities of meal, hulls, refined oil, soymilk and defatted flour.

The residue(s) of BYI 02960, DFA, and DFEAF were quantitated by HPLC-MS/MS using stable isotopically labelled internal standards. The individual analyte residues were summed to give a total BYI 02960 residue. Residue measurements below the analyte LOQ were summed into the total BYI 02960 residue value as the analyte LOQ value.

Findings

Concurrent recoveries of BYI 02960, DFA, and DFEAF were measured with each set of samples to verify method performance. All recoveries were corrected for any interferences in corresponding controls. The overall mean of the recoveries for each matrix ranged between 72 to 111%, and the standard deviation values were below 20% (Table 6.5.4.17-2).

Table 6.5.4.17-2: Summary of Recoveries of BYI 02960 Residues from Soybean RAC and Processed Commodities

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev (%)
Soybean Seed Dry RAC	BYI 02960	0.010	7	97, 97, 92, 102, 90, 102, 96	97	5
		1.000	3	95, 87, 96	93	5
	DFA	0.050	7	75, 74, 91, 75, 81, 76, 77	78	6
		1.000	3	77, 79, 87	81	6
	DFEAF	0.010	7	95, 90, 94, 92, 98, 83, 95	92	5
		1.000	3	95, 93, 96	95	2
Aspirated Grain Fractions	BYI 02960	0.250	3	79, 93, 87	86	7
		15.000	3	98, 91, 86	92	6
	DFA	0.050	3	98, 100, 104	101	3
		0.250	3	85, 91, 95	90	5
		15.000	3	86, 84, 86	85	1
	DFEAF	0.050	3	81, 97, 105	94	12
		0.250	3	86, 85, 97	89	7
		15.000	3	93, 90, 90	91	2

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Table 6.5.4.17-2 (cont'd): Summary of Recoveries of BYI 02960 Residues from Soybean RAC and Processed Commodities

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)[a]	Std. Dev (%)
Hulls	BYI 02960	0.010	3	103, 76, 101	93	15
		1.000	3	91, 90, 87	89	2
	DFA	0.050	3	84, 84, 83	83	1
		1.000	3	81, 76, 78	78	2
	DFEAF	0.010	3	108, 84, 109	100	14
		1.000	3	98, 80, 82	87	10
Meal	BYI 02960	0.010	3	83, 111, 78	91	18
		1.000	3	85, 93, 104	94	10
	DFA	0.050	3	75, 71, 74	73	2
		1.000	3	71, 70, 92	78	13
	DFEAF	0.010	3	105, 93, 86	94	10
		1.000	3	91, 86, 110	96	12
Refined Oil	BYI 02960	0.010	3	97, 99, 80	92	10
		1.000	3	104, 109, 92	101	9
	DFA	0.050	3	101, 109, 101	103	5
		1.000	3	108, 114, 97	106	9
	DFEAF	0.010	3	101, 108, 98	102	5
		1.000	3	105, 115, 95	105	10
Soymilk	BYI 02960	0.010	3	100, 99, 95	98	3
		1.000	3	99, 97, 98	98	1
	DFA	0.050	3	96, 98, 92	95	3
		1.000	3	107, 97, 102	102	5
	DFEAF	0.010	3	94, 107, 92	98	8
		1.000	3	109, 100, 101	104	5
Defatted Flour	BYI 02960	0.010	3	116, 104, 114	111	7
		1.000	3	100, 87, 91	93	7
	DFA	0.050	3	88, 78, 81	83	5
		1.000	3	76, 72, 69	72	4
	DFEAF	0.010	3	107, 89, 92	96	10
		1.000	3	85, 92, 82	86	5

[a] Mean Recovery = mathematical average of all recoveries.

The freezer storage stability study indicates that BYI 02960 residues were stable in soybean matrices during frozen storage for at least 18 months prior to analysis. The maximum storage period of frozen samples in this study for BYI 02960 was 336 days. A summary of the storage conditions are shown in the Table 6.5.4.17-3.

Table 6.5.4.17-3: Summary of Storage Conditions for all Soybean Commodities

Residue Component(s)	Matrix (RAC)	Average Storage Temperature (°C)[a]	Actual Storage Duration months (days)[b]	Interval of Demonstrated Storage Stability months[c]
BYI 02960, DFA, DFEAF	Soybean Seed RAC	<0	9 (266)	18 (558)
BYI 02960, DFA, DFEAF	Aspirated Grain Fractions	<0	7 (221)	18 (558)
BYI 02960, DFA, DFEAF	Meal	<0	11 (336)	18 (558)
BYI 02960, DFA, DFEAF	Hulls	<0	5 (169)	18 (558)
BYI 02960, DFA, DFEAF	Refined Oil	<0	9 (262)	18 (558)
BYI 02960, DFA, DFEAF	Soymilk	<0	9 (262)	18 (558)
BYI 02960, DFA, DFEAF	Defatted Flour	<0	9 (266)	18 (558)

a The average storage temperature reported is from the time of sample collection at GLP Technologies through the last sample extraction. Samples were maintained in a laboratory freezer at all times except during preparation for sample analysis.

b The actual storage duration for the soybean seed RAC is the time from field sampling (harvest) through the last sample extraction for this matrix. The actual storage duration for all commodities is from the time of commodity generation through the last sample extraction.

c [redacted], [redacted]. [redacted] 2012. Storage stability of BYI 02960, difluoroacetic acid, and difluoroethyl-amino-furanone in plant matrices. Bayer CropScience Report No. RARVP046, amended version including 18-month data (KIIA 6.1.1/01).

The BYI 02960, DFA, DFEAF, and total BYI 02960 residue data for soybean RAC and processed commodities are provided in Table 6.5.4.17-4.

Table 6.5.4.17-4: BYI 02960 Residue Data from Soybean RAC, Aspirated Grain Fractions, and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Interval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV268-10PA	Seed	NA[c]	90	1.80 (2.00)	21	0.748 0.657 0.680	0.051 0.052 0.054	0.059 0.056 0.059	0.86 0.76 0.79 Avg. 0.81	NA[c]	NA[c]
RV269-10PA	Seed	NA[c]	86	1.8 (1.99)	19	0.452 0.396 0.394	0.318 0.288 0.312	0.350 0.333 0.310	1.1 1.0 1.0 Avg. 1.1	NA[c]	NA[c]

Table 6.5.4.17-4 (cont'd): BYI 02960 Residue Data from Soybean RAC, Aspirated Grain Fractions, and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV268-10PA	Seed	Aspirated Grain Fractions	91	NA[c]	NA[c]	10.2 10.3 12.6	0.509 0.375 0.401	0.243 0.221 0.231	11 11 13 Avg. 12	14.8X	11X
RV269-10PA	Seed	Aspirated Grain Fractions	91	NA[c]	NA[c]	4.78 4.71 5.03	1.52 1.43 1.47	0.599 0.570 0.512	6.9 6.7 7.0 Avg. 6.9	6.3X	
RV268-10PA	Seed	Meal	89	NA[c]	NA[c]	0.561 0.597 0.622	0.062 0.063 0.062	0.076 0.069 0.072	0.70 0.73 0.76 Avg. 0.73	<1X	1X
RV269-10PA	Seed	Meal	89	NA[c]	NA[c]	0.488 0.521 0.549	0.413 0.421 0.492	0.409 0.417 0.446	1.3 1.4 1.5 Avg. 1.4	1.3X	
RV268-10PA	Seed	Hulls	89	NA[c]	NA[c]	0.619 0.346 0.668	0.053 <0.050 0.060	0.063 0.036 0.068	0.74 0.41 0.80 Avg. 0.65	<1X	<1X
RV269-10PA	Seed	Hulls	87	NA[c]	NA[c]	0.476 0.463 0.515	0.239 0.235 0.245	0.269 0.313 0.310	0.98 1.0 1.1 Avg. 1.0	<1X	
RV268-10PA	Seed	Refined Oil	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	<1X
RV269-10PA	Seed	Refined Oil	NA[c]	NA[c]	NA[c]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.070 <0.070 <0.070 Avg. <0.070	<1X	

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Table 6.5.4.17-4 (cont'd): BYI 02960 Residue Data from Soybean RAC, Aspirated Grain Fractions, and Processed Commodities

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Inerval (days)	BYI 02960 Residue (mg/kg)	DFA (mg a.s. equiv./kg)	DFEAF (mg a.s. equiv./kg)	Total BYI 02960 Residue (mg a.s. equiv./kg)[a]	Total BYI 02960 Residue Processing Factor[b]	Average Total BYI 02960 Processing Factor
RV268-10PA	Seed	Milk	NA[c]	NA[c]	NA[c]	0.030 0.029 0.028	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	0.090 0.089 0.088 Avg. 0.089	<1X	<1X
RV269-10PA	Seed	Milk	NA[c]	NA[c]	NA[c]	0.035 0.040 0.036	<0.050 <0.050 <0.050	0.020 0.024 0.021	0.11 0.11 0.11 Avg. 0.11	<1X	
RV268-10PA	Seed	Defatted Flour	NA[c]	NA[c]	NA[c]	0.719 0.756 0.709	0.071 0.083 0.072	0.081 0.085 0.087	0.87 0.92 0.87 Avg. 0.89	1.1X	1X
RV269-10PA	Seed	Defatted Flour	NA[c]	NA[c]	NA[c]	0.561 0.486 0.435	0.435 0.393 0.341	0.438 0.378 0.328	1.4 1.3 1.1 Avg. 1.3	1.2X	

[a] Total BYI 02960 residue is the sum of BYI 02960, DFA, and DFEAF residue in parent equivalents. Residue measurements below the analyte LOQ were summed into the Total BYI 02960 residue value as the analyte LOQ value. These totals represent the upper limit of what the residue levels might be.

[b] Total BYI 02960 Processing Factor = Average Total residue in processed sample/average total residue in unprocessed sample. Processing factors calculated to be less than 1X were reported as <1X.

[c] NA = Not applicable.

Conclusion

A summary of the calculated processing factors for soybean aspirated grain fractions and processed commodities are shown in Table 6.5.4.17-5.

Following a five-fold (5X) exaggerated application of BYI 02960 to two separate trials of soybeans, mature seed was collected. Aspirated grain fractions were then generated and the remaining soybean seed was processed into meal, hulls, refined oil, soymilk, and defatted flour. The average total BYI 02960 residue did not concentrate (processing factor ≤1X) in all soybean processed commodities. However, the total BYI 02960 residue did concentrate in aspirated grain fractions (11X).

The processing factors determined for BYI 02960 total residue in this study are less than the theoretical concentration factors based on separation into components cited in the EPA Residue Chemistry Test Guideline OPPTS 860.1520 which are 11.3X for soybean hulls, 2.2X for soybean meal, and 12X for soybean oil.

The residue data and subsequent calculated processing factors provided in this report are suitable for regulatory purposes.

Table 6.5.4.17-5: Summary of Total BYI 02960 Processing Factors Calculated Soybean Aspirated Grain Fractions and Soybean Processed Commodities

RAC	Processed Commodity	Average Total BYI 02960 Residue Processing Factor
Soybean Seed	Aspirated Grain Fractions	11X
Soybean Seed	Meal, Hulls, Refined Oil, Soymilk, and Defatted Flour	≤1X

IIA 6.5.4.18 Sugar cane

Report:	**KIIA 6.5.4-18/01; [redacted]; 2012**
Title:	BYI 02960 200 SL – BYI 02960 200 SL - Request for Waiver of the Requirements for the BYI 02960 Magnitude of the Residue in Sugarcane Processed Commodities in Florida (Rotational Crop Regional Tolerance).
Report No & Document No	RARVX001, dated June 18, 2012 M-432700-01-1
Guidelines:	US: EPA Residue Chemistry Test Guidelines OPPTS 860.1520, Processed Food/Feed Canada: PMRA DACO 7.4.5, Processed Food/Feed OECD: Guidelines for the Testing of Chemicals, 508, Magnitude of the Residues in Processed Commodities, Adopted Oct. 3, 2008. OECD Guidance Document on Magnitude of the Pesticide Residues in Processed Commodities.
GLP	Yes

The purpose of this study was to determine if the total residues of BYI 02960, fenamidone, fluopyram, and spiromesifen concentrate in sugarcane and sugarcane processed commodities. In this report, the effect of commercial processing on the total BYI 02960 residues in sugarcane processed commodities is addressed. The effects of commercial processing on fenamidone, fluopyram, and spiromesifen residues will be reported separately.

A single field trial was conducted to measure the magnitude of BYI 02960 residues in/on sugarcane processed commodities following one application of BYI 02960 200 SL (applied as a tank mix with Fenamidone SC 500, Fluopyram 500 SC, and Spiromesifen 240 SC) to bare soil followed by planting of sugarcane 14 days later as a rotational crop. BYI 02960 200 SL is a soluble concentrate formulation containing 200 g a.s./L.

Materials and Methods

BYI 02960 200 SL was applied to sugar cane plants at rates and timings as shown in Table 6.5.4.18-1.

Table 6.5.4.18-1: Study Use Pattern for BYI 02960 200 SL on Sugarcane

Trial Identification	Location (City, State, NAFTA Region, and Year)	End-use Product (Formulation)	Application								Tank Mix Adjuvants
			Plot Name	Method	Timing/Growth Stage (BBCH)	Actual Spray Volume GPA (L/ha)	Rate lb a.s./A (kg a.s./ha)	Retreatment Interval (days)	Total Rate lb a.s./A (kg a.s./ha)		
RV288-10PA	[redacted], FL Region 3 2010	BYI 02960 200 SL	TRT5X	Foliar Spray	14-Day Pre-plant	29 (270)	1.87 (2.10)	NA[b]	1.87 (2.10)		None

[a] NA = Not applicable
TRT5X = plot receiving 5X exaggerated application rates

A single application of BYI 02960 200 SL was made to the TRT3X and TRT5X plots. The TRT3X treated plot was initially established as a reserve plot for sugarcane collection and later was not needed and so was not harvested. The application of BYI 02960 200 SL to the TRT5X plot was made at a rate of 1.87 lb BYI 02960/A (2.10 kg BYI 02960/ha) 14 days prior to planting sugarcane as a rotational crop. The spray volume was 29 GPA (270 L/ha). The application was made using ground-based equipment. There were no adjuvants added to the spray mixture.

The application method and timing reflect the proposed label specifications for the rotation of sugarcane following use of BYI 02960 200 SL on target crops. The application rate of BYI 02960 200 SL to the TRT5X plot is equivalent to five times (5X) the total maximum proposed label rate for a single growing season (seasonal application). This application rate was selected to increase the likelihood of BYI 02960 residues in the sugarcane stalk (cane) so that concentration factors in processed commodities could be adequately determined.

A single composite sugarcane stalk (cane) sample was cut at earliest commercial harvest (ECH) from the TRT5X plot. A single composite sample of sugarcane stalk (cane) sample was cut from the control plot on the same day the respective sample was collected from the treated plot.

Triplicate subsamples of sugarcane stalk (cane), the raw agricultural commodity (RAC), were removed and the remaining sugarcane stalk (cane) was used to generate the processed commodities of molasses, refined sugar, and bagasse.

The residue(s) of BYI 02960, DFA, and DFEAF were quantitated by LC/MS/MS using stable isotopically labeled internal standards standards. The individual analyte residues were summed to give a total BYI 02960 residue. Residue measurements below the analyte LOQ were summed into the total BYI 02960 residue value as the analyte LOQ value.

Findings

Concurrent recoveries of BYI 02960, DFA, and DFEAF were measured with each set of samples to verify method performance. All recoveries were corrected for any interferences in corresponding controls. All recoveries for the sugarcane stalk (cane) RAC matrix were within the acceptable range of 70 to 110% (Table 6.5.4.18-2).

Table 6.5.4.18-2: Summary of Recoveries of BYI 02960 Residues from Sugarcane

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%)	Standard Deviation (%)
Sugarcane Stalk (Cane)	BYI 02960	0.10	1	88	88	NA[a]
	DFA	0.10	1	81	81	NA[a]
	DFEAF	0.10	1	92	92	NA[a]

[a] NA = Not applicable. No standard deviation calculated when less than three recovery values are presented.

The freezer storage stability study indicates that BYI 02960 residues were stable in sugarcane commodities during frozen storage for at least 18 months (559 days) prior to analysis. The maximum storage period of frozen samples in this study for BYI 02960 was 178 days (6 months). A summary of the storage conditions are shown in Table 6.5.4.18-3.

Table 6.5.4.18-3: Summary of Storage Conditions for Sugarcane Commodities

Residue Component(s)	Matrix (RAC)	Maximum Average Storage Temperature (°C) [a]	Actual Storage Duration Months (Days) [b]	Interval of Demonstrated Storage Stability Months (Days) [c]
BYI 02960; DFEAF; DFA	Sugarcane Stalk (Cane)	<5	6 (178)	18 (559)

[a] The average storage temperature reported is from the time of sample collection at GLP Technologies through the last sample extraction. Samples were maintained in a laboratory freezer at all times except during preparation for sample analysis.

[b] The actual storage duration for the wheat grain RAC is the time from field sampling (harvest) through the last sample extraction. The actual storage duration for all commodities is from the time of commodity generation through the last sample extraction.

[c] [redacted], [redacted]. [redacted]. 2012. Storage stability of BYI 02960, difluoroacetic acid, and difluoroethyl-amino-furanone in plant matrices. Bayer CropScience Report No. RARVP046, amended version including 18-month data (KIIA 6.1.1/01).

The BYI 02960, DFA, DFEAF, and total BYI 02960 residue data for sugarcane RAC are provided in Table 6.5.4.18-4.

Table 6.5.4.18-4: BYI 02960 Residue Data from Sugarcane RAC Commodity

Trial Identification	RAC	Processed Commodity	% Dry Matter	Total Rate Lb ai/A (kg ai/ha)	Pre-harvest Interval (days)	BYI 02960 Residue (mg/kg)	DFA Residue (mg a.s.equiv.(kg)	DFEAF Residue (mg a.s.equiv.(kg)	Total BYI 02960 Residue (mg a.s.equiv.(kg)[a]	Total BYI 02960 Residue Processing Factor
RV288-10PA	Sugarcane	NA[b]	NA[b]	BYI 02960 200 SL 1.87 (2.10)	NA[b]	<0.010 <0.010 <0.010	<0.050 <0.050 <0.050	<0.010 <0.010 <0.010	<0.07 <0.07 <0.07 Avg. <0.07	NA[b]

[a] Total BYI 02960 residue is the sum of BYI 02960, DFA, and DFEAF residue in parent equivalents. Residue measurements below the analyte LOQ were summed into the Total BYI 02960 residue value as the analyte LOQ value. These totals represent the upper limit of what the residue levels might be.

[b] NA = Not applicable.

Conclusion

Following a five-fold (5X) exaggerated application of BYI 02960 to bare soil followed by planting of sugarcane 14 days later as a rotational crop, the average total BYI 02960 residue in sugarcane stalk (cane) was less than the Total BYI 02960 LOQ of 0.07 ppm (<0.07 ppm). In addition, no Total BYI 02960 residue above the Total BYI 02960 LOQ of 0.07 ppm was observed in sugarcane stalk (cane) collected from a sugarcane rotational crop tolerance setting study [Bayer CropScience Report No. RARVP030; KIIA 6.6.3.2/01]. Therefore, the sugarcane processed commodities were not analyzed for residues of BYI 02960 and no processing factors were determined according to US regulations. A waiver of the requirement to conduct analyses of the sugarcane processed commodities should be granted in the US and therefore no processing factors for sugar cane will be available.

IIA 6.6 Residues in succeeding crops

The nature and level of residues in succeeding crops (confined rotational crops, field rotational crops) is influenced by the amount of active ingredient applied to the soil, by the degradation behaviour in soil, and by the uptake of parent compound and soil metabolites by the roots. Additionally, parent compound and soil metabolites can be metabolized by the plants, where hydroxylation reactions and formation of conjugates are often observed.

The aerobic degradation of BYI 02960 in soil was investigated in laboratory studies (see KIIA 7.1.1/01-06). The primary metabolic pathway of BYI 02960 in soil is molecular cleavage resulting in the metabolites difluoroacetic acid (DFA) and 6-chloronicotinic acid (6-CNA). DFA has been identified in all soils tested with a maximum percentage of 34%. 6-CNA was identified in several soils tested with a maximum percentage of 17%. Additionally, the minor metabolites BYI 02960-desdifluoroethyl (maximum level 0.4%) and BYI 02960-chloro (maximum level 1.8%) have been identified. Further microbial breakdown led to the formation of significant amounts of carbon dioxide and soil bound residues.

Since the exposure of following crops to BYI 02960 soil residues cannot be excluded, the metabolism of BYI 02960 was investigated in representative rotational crops (wheat, Swiss chard and turnips) following soil application of either [pyridinylmethyl-UL-^{14}C] or [furanone-4-^{14}C] radiolabelled active substance. The application rates were slightly above the anticipated maximum field rate of 400 g a.s./ha (for US uses). [Ethyl-1-^{14}C]BYI 02960 was not available for a confined rotational crop study when the studies were started. Therefore, no detection of ^{14}C-difluoroacetic acid was possible. To estimate the residue levels of difluoroacetic acid in the crop samples, non-radiolabelled difluoroacetic acid was analysed in the samples originating from the CRC studies with the other radiolabels by LC-MS/MS according to the conditions of residue analytical method 01304 (see KIIA 6.2.1/12).

IIA 6.6.1 Theoretical consideration of the nature and level of the residue

Confined rotational crop studies were planned as part of standard procedure. The results of the studies strongly indicated that residues are also to be expected under true field conditions.

IIA 6.6.2 Metabolism and distribution studies on representative crops

Report:	**KIIA 6.6.2/01, [redacted], A.; 2011**
Title:	Metabolism of [furanone-4-^{14}C]BYI 02960 in confined rotational crops
Report No & Edition No	MEF-11/365 M-438180-01-1
Guidelines:	OECD 502 Metabolism in Rotational Crops US EPA Residue Chemistry Test Guideline OPPTS 860.1850: Confined Accumulation in Rotational Crops European Parliament and Council Regulation (EC) No 1107/2009
GLP	yes

Executive Summary

The metabolism of the insecticide BYI 02960 was investigated in the representative rotational crops wheat, Swiss chard and turnips from three consecutive rotations. [Furanone-4-^{14}C]BYI 02960 was formulated as an SL 300 and sprayed onto the soil of a planting container (approx. 1 m^2). The actual application rate corresponded to 436 g a.s./ha, slightly above the anticipated maximum seasonal field rate of 400 g a.s./ha. The crops were each sown at 29, 135 and 296 days after the soil application, representing the first, second and third rotation.

Intermediate raw agricultural commodities (RACs) investigated were Swiss chard immature, wheat forage and wheat hay. All other RACs (wheat straw, wheat grain, Swiss chard, turnip leaves and turnip roots) were harvested at maturity.

The TRR values for all RACs are given in the following table.

Table 6.6.2-1 TRR values in the different RACs of the three rotations after soil application of [furanone-4-^{14}C]BYI 02960

TRR [mg/kg]	**Wheat**				**Swiss chard**		**Turnips**	
	forage	**hay**	**straw**	**grain**	**imm.**	**mature**	**leaves**	**roots**
1st rotation	0.783	2.003	6.290	0.478	0.848	0.871	0.679	0.074
2nd rotation	0.193	1.081	1.519	0.103	0.311	0.263	0.158	0.014
3rd rotation	0.111	0.254	0.462	0.047	0.180	0.152	0.090	0.008

Except for wheat grain, extraction efficiencies ranged from 70% to 97% for all commodities of all rotations after conventional extraction with acetonitrile/water mixtures. Subsequent exhaustive extraction steps (microwave and/or digestive extraction steps), applied to the post extraction solids in wheat grain and wheat straw, released additional significant amounts of radioactivity and increased the extraction efficiencies to a range of 83% to 98% of the TRR. Thus overall, it was shown that the exhaustive extraction steps applied were able to release high amounts of radioactivity if conventional extraction was not sufficient.

Parent compound and metabolites in the extracts were analysed by reversed phase HPLC. Identification was achieved by spectroscopic evidence (LC-MS/MS) after isolation and purification of the respective compounds from the conventional extracts of wheat straw or Swiss chard of the 1st rotation. HPLC co-chromatography with the isolated and identified radiolabelled metabolites allowed

the assignment of the compounds in other extracts. Additionally, HPLC comparison of the metabolite profiles of the different extracts among each other and with the ones of the confined rotational crop study performed with [pyridinylmethyl-^{14}C]BYI 02960, completed the picture. The polar fraction detected in wheat grains was identified by TLC co-chromatography using the natural compound (glucose/carbohydrates) identified in the tomato metabolism study conducted with [furanone-4-^{14}C]BYI 02960, as reference compound. Other polar metabolites/fractions were also analysed by normal phase TLC

Parent compound was the most prominent compound in all RACs of all rotations, except in wheat grains, where it was detected as a minor compound only. The main compound detected in grains accounted for approx. 70% of the TRR in the sample of the 1st rotation and was identified as a natural compound (glucose/carbohydrates). Major metabolites in other wheat RACs, Swiss chard and turnips were BYI 02960-OH-glyc, -glyoxylic acid, -difluoroethyl-amino-furanone, -difluorethyl-amino-furanone-OH-glyc and BYI 02960-bromo-amino-furanone which were detected in a range of approx. 10% - 22% of the TRR in numerous samples. All other identified metabolites were detected at minor or trace levels. In total, fourteen metabolites were identified; six of them were specific to the radiolabel tested.

[Furanone-4-^{14}C]BYI 02960 was rather extensively metabolised in confined rotational crops. The following metabolic routes were observed:

- cleavage of the pyridinylmethylamine bond and formation of metabolites based on difluoroethyl-amino-furanone and amino-furanone structures,
- BYI 02960-difluorethyl-amino-furanone conjugation with either mercapto-lactic acid or conjugation with carbohydrates after hydroxylation,
- hydroxylation of the methylene group of the furanone moiety followed by conjugation with carbohydrates and sulphate,
- oxidative degradation of the furanone moiety to BYI 02960-acetic acid, which was either subjected to conjugation with glucose or to a further oxidation step
- complete degradation of the furanone moiety and incorporation of carbon atoms into the natural compound pool, i.e. into glucose/carbohydrates, and
- halogenation of the furanone ring with bromine or chlorine.

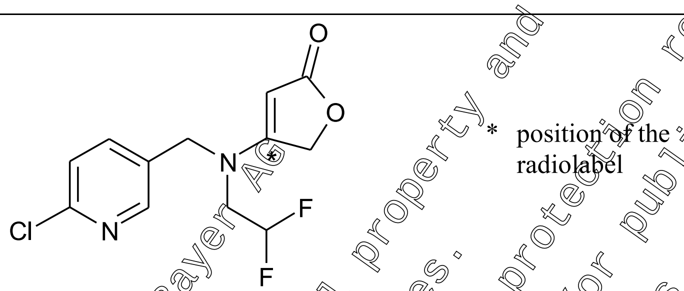
Halogenation of the furanone moiety of the active substance probably occurred in the soil which is supported by the fact that small amounts of halogenated parent compound have been identified in the aerobic soil degradation studies. Metabolite BYI 02960-glyoxylic acid, the oxidation product of BYI 02960-acetic acid, was probably a transient soil metabolite that was taken up by the plants, since it was only prominent in the samples of the 1st rotation.

On the basis of these results, a metabolic pathway of [furanone-4-^{14}C]BYI 02960 in confined rotational crops can be proposed.

I. Materials and Methods

A. Materials

1. Test Material:

Chemical structure	
Radiolabelled test material	[furanone-4-^{14}C]BYI 02960
Specific radioactivity	3.97 MBq/mg (106.46 µCi/mg)
Chemical Purity	> 99% (HPLC)
Radiochemical purity	> 99% (HPLC and TLC)

The supplied radiolabelled test compound [furanone-4-^{14}C]BYI 02960 was dissolved in acetonitrile. Formulation of the test compound was performed prior to the application: An appropriate amount of this stock solution was evaporated to dryness. The respective amount of blank formulation SL 300 was added and the mixture was homogenised using an ultrasonic bath (radioactive formulation). The sample was adjusted to a final volume of approx. 100 mL with water and homogenised by stirring to get the ready-to-use spray dilution.

2. Soil: "[redacted]4" (sandy loam soil from Germany), pH ($CaCl_2$) = 6.9, 58% sand, 28% silt and 14% clay, 2.1% organic carbon, cation exchange capacity (CEC) of 8.1 meq/100 g

3. Plants:

rotational crop	variety	representative for crop group
spring wheat	Thasos	small grain
Swiss chard	Lukullus	leafy vegetable
turnips	Rondo	root crop

B. Study Design

Experimental conditions:

BYI 02960 was applied as an SL formulation with a computer controlled track sprayer onto the bare soil of a planting container (surface area of approx. 1 m^2). The application rate was 436 g a.s./ha and was slightly above the anticipated maximum seasonal rate of BYI 02960. The treated soil remained undisturbed for an aging period of 29 days. After this period, the upper layer of the soil (approx. 15 cm) was intensively mixed and wheat, Swiss chard and turnips of the first rotation were sown. Wheat was sown on approx. 50% (0.5 m^2) of the soil area of the planting container. Swiss chard and turnips were each sown on 25% (0.25 m^2) of the soil area of the container. At day 135 and 296 after the application (after harvest of the mature wheat - the crop with the longest vegetation period) the soil was cultivated again and the crops of the second and third rotation were sown, respectively. With each rotation the plots of the crops in the container were changed. Wheat was sown on the plot where Swiss chard and turnips had been sown in the preceding rotation and Swiss chard and turnips were sown on the plot where wheat was sown before.

Sampling:
Raw agricultural commodities (RAC) sampled for this study included the immature samples forage and hay from wheat, and an immature sample of Swiss chard. All other samples (wheat straw and wheat grain, mature Swiss chard, turnip leaves and turnip roots) were harvested at maturity of each rotation.

About 20% of the wheat plants were cut shortly above the ground as forage sample at BBCH growth stage 29-31 (stem elongation). At BBCH 79-83 (late milk to early dough stage) again 20% of the wheat plants were cut as hay sample and dried at room temperature for three to five 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. A part of the Swiss chard plants were sampled at an immature stage (BBCH 44-46) and the remaining plants at maturity (BBCH 49). The Swiss chard plants were cut above the roots. The mature turnips plants were removed from soil, separated into leaves and roots. The plant materials were cut in pieces before homogenization with liquid nitrogen using a Polytron homogenizer.

Aliquots of the homogenized samples were used to estimate the TRR in the sample material by combustion and were used for extraction. Remaining homogenized sample material was stored in a freezer at approx. -18 °C.

C. Analytical Procedures

Extraction:
An aliquot of each homogenized RAC was extracted conventionally three to four times with ACN/water (8:2, v/v). The extracts were combined, purified using a pre-conditioned SPE RP 18 cartridge, concentrated and analysed by HPLC. The radioactivity in the extracts was determined by LSC, in the solids by combustion followed by LSC. The actual TRR values of the samples were determined by summing up the radioactivity measured in the extracts and in the remaining solids. If needed, solids were further extracted exhaustively using microwave conditions. Post-extraction solids of wheat straw (1st and 2nd rotation) were subjected to a sequential extraction procedure after one exhaustive extraction step with ACN/water (8:2, v/v) at increased temperature (60 °C) under microwave conditions. The solids of the microwave extraction step were subjected to a treatment with sodium chloride solution (2 h at 100 °C under microwave assistance), a diastase incubation (approx. 20 h at 26 °C), a treatment with EDTA solution (3 h at 100 °C under microwave assistance) and a cellulase treatment (approx. 20 h at 40 °C) at adjusted temperatures to break down the plant cell walls and liberate residues bound to cell walls or in the cells. The remaining solids of the sequential extraction were extracted finally in two steps with a 5N HCl and a 5N NaOH solution (each 2 h at 100 °C). Extracts of the first three exhaustive extraction steps were concentrated and analysed separately by HPLC. Extracts of the EDTA, the cellulase and the HCl treatment were combined and adjusted to pH 7. The combined extract was concentrated, centrifuged and analysed by HPLC. The NaOH extract was not submitted to HPLC due to its high viscosity.

Post-extraction solids of grains from the 1st and the 2nd rotation were subjected to three subsequent exhaustive extraction steps: Microwave extraction with ACN/water at 100 °C followed by a digestion step with diastase (20 h at 26 °C) and subsequent microwave extraction with a sodium chloride solution (2 h at 100 °C). Only the first exhaustive extract was analysed by HPLC, the two following extracts were highly viscous due to a high matrix load and could not injected in the HPLC system. Therefore a further aliquot of the post extraction solids of grains from the 1st rotation was subjected to digestion with diastase over 14 days at ambient temperature. The residues in the diastase digestion solution were further characterized by partitioning againt dichloromethane.

Quantification:
Parent compound and metabolites in the extracts were analysed by reversed phase HPLC coupled to a radioactivity detector with a glass scintillator cell. The HPLC chromatograms (= metabolite profiles) were integrated for quantification of compounds.

Identification and characterisation:
Identification of parent compound and metabolites was based on the metabolite profiles of the conventional extracts of Swiss chard and wheat straw of the first rotation. These extracts showed all major and minor metabolites also detected in the other extracts. Therefore, parent compound, all major and most minor metabolites were isolated from these extracts, purified and identified by HPLC-MS/MS. Two metabolites were co-eluting in the extract of wheat straw when analysed with the profiling method. To ensure the right assignment in other extracts, the respective peak was isolated by semi-preparative HPLC and re-analysed with an acidic method which was able to separate the two compounds, if present. Based on these assignments, the compounds in all conventional and exhaustive extracts of all rotations were identified by comparison with the metabolite patterns of wheat straw and Swiss chard. The presence of several metabolites was additionally confirmed by HPLC co-chromatography using the isolated compounds as reference compounds. Confirmation of assignments by HPLC co-chromatography became important since variations in retention times of some metabolites and distortion of peaks was observed when analysing extracts of wheat forage (1st rotation) and Swiss chard (2nd rotation) at different time points. The retention shift was most probabaly caused by an interaction between matrix components and metabolites. Natural label-specific compounds detected in wheat grains were identified by TLC co-chromatography subsequent to a diastase digestion step using a metabolite isolated and identified in the tomato metabolism study performed with [furanone-4-^{14}C]BYI 02960. The same natural compound was identified in turnip roots by TLC comparison of the isolated and purified metabolites.

Storage stability:
All samples were conventionally extracted and analysed by HPLC within a few days after sampling. Quantitative ^{14}C-HPLC analysis of the extracts was performed with the profiling method BYI02960_NEUTR within one week after harvest. Only for wheat forage and hay, Swiss chard and turnips from the 1st rotation, the metabolic profile was measured with the preliminary profiling method BYI02960_CRC directly after extraction. The preliminary method was based on the same type of column and the same eluents but had a slightly shorter gradient. The metabolite profiles obtained from the two methods were comparable, however profiling method BYI02960_NEUTR showed an improved separation for some metabolites. For better comparison of metabolic pattern over all RACs of all rotations, the profiles of wheat forage and hay, Swiss chard and turnips of the 1st rotation were

re-analysed with method BYI02960_NEUTR about 1 – 2 months after extract preparation. These new metabolic profiles were then considered as basis for quantification. Extract stability has been demonstrated for this time period.

Exhaustive extractions were started for wheat straw and wheat grain within approx. two to seven months after harvest. Since the compounds identified in the exhaustive extracts were comparable with the compounds of the conventional extracts, it was concluded that the residues in the solids were stable and reflected the released residues at the time of exhaustive extraction.

Thus it can be concluded that the residues in all matrices were sufficiently stable during the experimental period of the study and that the first quantified profiles represented the metabolic pattern in the samples at harvest. Nevertheless, storage stability of BYI 02960 residues in frozen sample material was additionally demonstrated in wheat straw (1st and 2nd rotation) and in Swiss chard (1st rotation) for a storage period of about 18 to 24 months. The stored sample material was subjected to a second extraction. Analysis of the new extracts showed the same metabolite patterns as the first extracts and confirmed the storage stability of the residues in the stored RACs.

Extract stability has been demonstrated for the time of the sample preparation and the identification process of metabolites, as well. The metabolite patterns of stored extracts remained stable when re-analysing extracts, e.g. for isolation of metabolites or identification purposes. Neither significant degradation nor transformation of metabolites in extracts was observed.

Hence, 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 [furanone-4-^{14}C]BYI 02960 was investigated in the rotational crops spring wheat, Swiss chard and turnips following application on the soil. The active substance was applied as an SL formulation on the bare soil at a rate of 436 g/ha at 29 days before sowing of the crops representing the first rotation. Crops of the 2nd and 3rd rotation were sown 135 and 296 days after application. Immature Swiss chard, wheat forage and wheat hay were harvested as intermediate raw agricultural commodities (RACs). All other RACs (wheat straw, wheat grain, Swiss chard, turnip leaves and turnip roots) were harvested at maturity.

The TRR values of all RACs declined significantly (by a factor of 5 to 13) from the first to the third rotation. Highest residues were detected in the non-edible commodities wheat straw and wheat hay, as shown above in Table 6.6.2-1.

Radioactive residues were efficiently extracted from all commodities of all rotations with acetonitrile/water mixtures, except for wheat grain and wheat straw (only 14.6% to 20.4% and 70.3% to 77.6% of the TRR and was detected after conventional extraction, respectively). For wheat grain and wheat straw additional exhaustive extraction steps were applied for the samples of the 1st and 2nd rotation. Exhaustive extraction comprised one extraction step with acetonitrile/water (8:2; v/v) at increased temperature (60 °C) under microwave assistance and additional sequential extraction steps including enzymatic digestion steps. Exhaustive extraction steps released an additional portion of 68% – 73% of the TRR from the solids of grains and about 21% – 27% of the TRR from the solids of straw resulting in total extraction efficiencies ranging between 83% and 98% of the TRR.

Parent compound BYI 02960 and about 30 metabolites were detected in the conventional and exhaustive extracts of the various samples of the three rotations. Of these the active substance and 14 metabolites were identified by LC-MS/MS. The other metabolites, none of them exceeding 5% of the TRR or 0.05 mg/kg., were characterised by their extraction behaviour and their retention in radio-HPLC or TLC. The amounts of active substance and metabolites in all RACs are summarized in Table 6.6.2-2 to Table 6.6.2-7 for the three rotations.

Parent compound was by far the main component detected in all matrices of all rotations, except for wheat grain. Parent accounted for 34% to 64% of the TRR in the commodities of the 1st rotation, for 28% to 68% in the 2nd rotation and covered 18% to 72% in the 3rd rotation, not considering grains. In wheat grains, only trace amounts of parent compound were detected (<1% and 2% of the TRR). The highest proportion of parent compound was always detected in turnip leaves.

Six of the identified metabolites were specific to the radiolabel used: BYI 02960-difluoroethyl-amino-furanone, its conjugate BYI 02960-mercapto-lactic acid, BYI 02960-difluoroethyl-amino-furanone-OH-glyc, BYI 02960-amino-furanone, BYI 02960-bromo-amino-furanone, and the natural compound glucose (or probably an isomeric carbohydrate). The natural compound was identified as the main component in wheat grain after subjecting the post extraction solids of the conventional extraction (1st rotation) to a diastase digestion step. The released radioactivity in the aqueous digestion solution was partitioned against dichloromethane. The majority of the radioactivity remained in the aqueous phase indicating that the metabolite was probably a polar natural compound. Isolation of the polar fraction by semi-preparative HPLC and following analysis by normal phase TLC showed one spot indicating that the fraction is represented most probably by one compound. TLC co-chromatography with the natural compound isolated and identified in the tomato metabolism study with [furanone-4-^{14}C]BYI 02960 confirmed the correspondance of the metabolites. TLC analysis of the isolated polar fractions detected in the conventional and exhaustive extracts of wheat straw and in the conventional extracts of Swiss chard and turnip roots revealed that these fractions were represented by several compound (up to eight). Only minor percentages of the fractions appear identical with glucose. Based upon TLC, for turnip roots, a trace amount was assigned to the natural compound.

Label unspecific metabolites (= metabolites common to both radiolabels tested) were BYI 02960-OH and its conjugates, BYI 02960-acetic acid, its conjugate BYI 02960-acetic acid-glyc and its successor molecule BYI 02960-glyoxylic acid and the chlorinated/brominated parent compound. These metabolites were also detected in the CRC study conducted with [pyridinylmethyl-^{14}C]BYI 02960. The metabolites BYI 02960-acetic acid and BYI 02960-OH-glyc were not separated by the HPLC profiling method and co-eluted in one peak or one peak zone. Separation and sub-quantification of the metabolites was shown for wheat straw (1st rotation), Swiss chard (1st rotation) and turnip leaves (1st rotation) as representative crops. Therefore the corresponding peak zones were isolated by semi-preparative HPLC, concentrated and re-analysed with an acidic HPLC method which separated the two metabolites. The ratios of BYI 02960-acetic acid and BYI 02960-OH-glyc obtained for wheat straw were assigned to all wheat samples, the ratio of Swiss chard to immature and mature Swiss chard, and the ratio of turnip leaves to turnip roots of all rotations. BYI 02960-OH-glyc was the prominent compound in all samples of all rotations.

Overall, identification rates were high for all samples of all rotations. For some RACs (e.g., wheat straw and wheat grain), high identification rates were only shown for the 1st and 2nd rotation (or in the case of grains for the 1st rotation only) since exhaustive extraction and following analysis of the exhaustive extracts was only conducted exemplarily for these samples. Thus, lower identification rates in this study were generally linked to higher bound residues (wheat matrices) and no subsequent exhaustive extraction step. In the case of turnip roots of the 2nd rotation, the identification rate was also quite low (53%) since one unknown compound represented a high percentage of the TRR, but at a very low residue level (0.004 mg/kg).

Table 6.6.2-2 Distribution of parent compound and metabolites in wheat matrices after a 29 day plant back interval (1st rotation, [furanone-4-^{14}C]BYI 02960)

1st Rotation	**wheat forage**		**wheat hay**		**wheat straw**		**wheat grains**	
TRR [mg/kg]	0.783		2.003		6.290		0.478	
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Conventional extraction								
BYI 02960 (parent comp.)	46.6	0.365	33.6	0.672	33.9	2.135	0.4	0.002
glucose/carbohydrates	---	---	---	---	---	---	---	---
amino-furanone	1.9	0.015	3.8	0.076	1.9	0.120	0.5	0.002
mercapto-lactic acid	1.6	0.013	0.4	0.008	1.1	0.068	---	---
bromo-amino-furanone	2.0	0.016	1.6	0.033	2.6	0.161	---	---
difluoroethyl-amino-furanone-OH-glyc	3.2	0.025	5.8	0.116	3.5	0.217	---	---
difluoroethyl-amino-furanone	9.9	0.077	10.2	0.205	5.3	0.333	---	---
glyoxylic acid	15.8	0.124	11.3	0.227	14.7	0.925	5.1	0.024
acetic acid-glyc	---	---	1.2	0.024	0.7	0.043	---	---
acetic acid	1.7	0.013	1.6	0.031	1.7	0.106	0.6	0.003
OH-glyc	3.6	0.028	3.4	0.067	3.6	0.228	1.4	0.007
OH	1.3	0.010	1.9	0.038	2.3	0.147	2.3	0.011
bromo / chloro	0.3	0.003	---	---	0.2	0.011	---	---
Subtotal identified	**88.0**	**0.689**	**74.7**	**1.496**	**71.4**	**4.493**	**10.3**	**0.049**
unknown 1a[1]	1.5	0.012	3.7	0.075	3.6	0.227	2.3	0.011
unknown 2	---	---	---	---	0.3	0.018	---	---
unknown 3	---	---	---	---	0.1	0.008	---	---
unknown 4	---	---	---	---	0.2	0.011	---	---
unknown 5	---	---	---	---	0.2	0.010	---	---
unknown 6	---	---	---	---	0.3	0.020	---	---
unknown 7	---	---	0.3	0.007	0.5	0.032	---	---
unknown 8	---	---	---	---	---	---	---	---
unknown 9	---	---	---	---	---	---	1.2	0.006
unknown 10	---	---	---	---	---	---	---	---
unknown 11	---	---	---	---	---	---	0.7	0.003
unknown 12	---	---	---	---	---	---	---	---
unknown 13	---	---	---	---	---	---	---	---
unknown 14	---	---	---	---	---	---	---	---
unknown 15	---	---	---	---	---	---	---	---
unknown 16	---	---	---	---	0.3	0.022	---	---
unknown 17	---	---	2.0	0.041	---	---	---	---
Subtotal characterised	1.5	0.012	6.1	0.122	5.5	0.347	4.2	0.020
Total conventional extr.	**89.5**	**0.701**	**80.8**	**1.619**	**76.9**	**4.840**	**14.5**	**0.069**

Table continued on next page…

1st Rotation	wheat forage		wheat hay		wheat straw		wheat grains	
Microwave extraction I (ACN/water)								
BYI 02960 (parent comp.					1.6	0.102		
amino-furanone					0.2	0.013		
bromo-amino-furanone					0.2	0.011		
difluoroethyl-amino-furanone-OH-glyc					0.2	0.012		
difluoroethyl-amino-furanone					0.2	0.013		
glyoxylic acid					0.5	0.029		
acetic acid					0.1	0.003		
OH-glyc					0.1	0.007		
OH					0.1	0.007		
Subtotal identified					**3.1**	**0.196**		
unknown 1a[1]					1.4	0.085		
Subtotal characterised					1.4	0.085		
Total microwave extr. I					**4.5**	**0.282**		
Microwave extraction II (1% NaCl)								
BYI 02960 (parent comp.)					2.0	0.124		
amino-furanone					0.7	0.044		
difluoroethyl-amino-furanone					0.3	0.019		
glyoxylic acid					0.1	0.008		
acetic acid					<0.1	0.003		
OH-glyc					0.1	0.006		
OH					0.1	0.006		
Subtotal identified					**3.3**	**0.209**		
unknown 1a[1]					1.4	0.086		
Subtotal characterised					1.4	0.086		
Total 1% NaCl extraction					**4.7**	**0.295**		
Diastase digestion								
BYI 02960 (parent comp.)					0.7	0.042	**---**	**---**
glucose/carbohydrates					---	---	70.5	0.338
amino-furanone					0.3	0.016	---	---
difluoroethyl-amino-furanone					0.1	0.009	---	---
glyoxylic acid					0.1	0.003	---	---
OH					<0.1	0.001	---	---
Subtotal identified					**1.1**	**0.072**	**70.5**	**0.338**
unknown 1a[1]					0.8	0.050	---	---
Subtotal characterised					0.8	0.050	---	---
Total diastase digestion					**1.9**	**0.122**	**70.5**	**0.338**
EDTA + cellulase + 5N HCl extraction								
BYI 02960 (parent comp.)					0.9	0.057		
amino-furanone					0.5	0.032		
Subtotal identified					**1.4**	**0.089**		
unknown 1a[1]					3.6	0.229		
Subtotal characterised					3.6	0.229		

Table continued on next page…

1st Rotation	wheat forage		wheat hay		wheat straw		wheat grains	
Total EDTA + cellul.+ 5N HCl extraction					**5.1**	**0.318**		
5N NaOH extraction								
Subtotal characterised					4.6	0.291		
Total 5N NaOH extraction					**4.6**	**0.291**		
Total identified	**88.0**	**0.689**	**74.7**	**1.496**	**80.4**	**5.059**	**80.8**	**0.387**
Total characterised	**1.5**	**0.012**	**6.1**	**0.122**	**17.3**	**1.089**	**4.2**	**0.020**
Total extractable	**89.7**	**0.703**	**81.6**	**1.634**	**98.4**	**6.190**	**88.0**	**0.421**
Not analysed/losses	0.3	0.002	0.7	0.015	0.7	0.042	3.0	0.014
Unextractable (PES*)	10.3	0.081	18.4	0.369	1.6	0.099	12.0	0.058
Accountability	**100.0**	**0.783**	**100.0**	**2.003**	**100.0**	**6.290**	**100.0**	**0.478**

* post extraction solids

[1] polar unkown peak 1a in the conventional extract of wheat straw of the 1st rotation consisted of 4 different metabolites, all of them were minor according to TLC subquantification

Table 6.6.2-3 Distribution of parent compound and metabolites in wheat matrices after a 135 day plant back interval (2[nd] rotation, [furanone-4-^{14}C]BYI 02960)

2[nd] Rotation	wheat forage		wheat hay		wheat straw		wheat grains	
TRR [mg/kg]	0.193		1.081		1.519		0.103	
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Conventional extraction								
BYI 02960 (parent comp.)	63.9	0.124	29.1	0.314	28.5	0.433	0.5	0.001
glucose/carbohydrates	---	---	---	---	---	---	---	---
amino-furanone	2.0	0.004	6.2	0.067	4.1	0.062	1.3	0.001
mercapto-lactic acid	1.6	0.003	3.5	0.037	4.4	0.067	---	---
bromo-amino-furanone	3.3	0.006	9.9	0.107	6.1	0.093	---	---
difluoroethyl-amino-furanone-OH-glyc	1.3	0.003	7.3	0.078	4.2	0.064	---	---
difluoroethyl-amino-furanone	8.2	0.016	6.9	0.075	5.3	0.081	---	---
glyoxylic acid	0.3	<0.001	1.9	0.020	1.2	0.018	0.8	0.001
acetic acid-glyc	---	---	0.5	0.005	0.9	0.013	---	---
acetic acid	1.6	0.003	1.6	0.017	2.3	0.035	1.0	0.001
OH-glyc	3.4	0.007	3.4	0.037	5.0	0.076	2.1	0.002
OH	1.8	0.003	1.9	0.021	2.7	0.042	3.4	0.003
bromo / chloro	---	---	---	---	---	---	---	---
Subtotal identified	**87.3**	**0.169**	**71.9**	**0.778**	**64.7**	**0.982**	**9.2**	**0.009**
unknown 1a[1]	1.3	0.002	4.3	0.047	5.1	0.078	2.5	0.003
unknown 2	---	---	---	---	---	---	---	---
unknown 3	---	---	---	---	---	---	---	---
unknown 4	0.4	0.001	0.6	0.006	0.6	0.009	---	---
unknown 5	---	---	---	---	---	---	---	---
unknown 6	---	---	---	---	---	---	---	---
unknown 7	0.2	<0.001	0.5	0.006	---	---	---	---
unknown 8	---	---	---	---	---	---	---	---
unknown 9	---	---	---	---	---	---	0.7	0.001
unknown 10	---	---	---	---	---	---	---	---
unknown 11	---	---	---	---	---	---	0.9	0.001
unknown 12	0.3	0.001	---	---	---	---	---	---
unknown 13	---	---	---	---	---	---	---	---
unknown 14	---	---	---	---	---	---	---	---
unknown 15	---	---	---	---	---	---	---	---
unknown 16	---	---	---	---	---	---	---	---
unknown 17	---	---	---	---	---	---	---	---
Subtotal characterised	2.2	0.004	5.4	0.059	5.8	0.087	4.2	0.004
Total conventional extr.	**89.6**	**0.173**	**77.4**	**0.837**	**70.4**	**1.070**	**13.4**	**0.014**

Table continued on next page…

2nd Rotation	wheat forage		wheat hay		wheat straw		wheat grains	
Microwave extraction I (ACN/water)								
BYI 02960 (parent comp.					2.0	0.031	---	---
amino-furanone					0.7	0.011	---	---
difluoroethyl-amino-furanone-OH-glyc					0.1	0.002	---	---
difluoroethyl-amino-furanone					0.3	0.005	---	---
glyoxylic acid					0.1	0.001	---	---
acetic acid					0.1	0.001	---	---
OH-glyc					0.2	0.003	---	---
OH					0.2	0.004	---	---
Subtotal identified					3.8	0.057	---	---
unknown 1a[1]					1.0	0.015	---	---
Subtotal characterised					1.0	0.015	---	---
Total microwave extr. I	**---**	**---**	**---**	**---**	**4.8**	**0.073**	**[2]2.5**	**[2]0.003**
Microwave extraction II (1% NaCl)								
BYI 02960 (parent comp.)					2.3	0.035	**---**	**---**
amino-furanone					0.8	0.012	---	---
difluoroethyl-amino-furanone					0.3	0.004	---	---
acetic acid					<0.1	0.001	---	---
OH-glyc					0.1	0.001	---	---
OH					0.1	0.002	---	---
Subtotal identified					3.6	0.055	---	---
unknown 1a[1]					1.5	0.023	---	---
Subtotal characterised					1.5	0.023	---	---
Total 1% NaCl extraction	**---**	**---**	**---**	**---**	**5.2**	**0.078**	**[2]41.7**	**[2]0.043**
Diastase digestion								
BYI 02960 (parent comp.)					1.0	0.015	**---**	**---**
amino-furanone					0.4	0.006	---	---
Subtotal identified					1.4	0.021	---	---
unknown 1a[1]					0.9	0.014	---	---
Subtotal characterised					0.9	0.014	---	---
Total diastase digestion	**---**	**---**	**---**	**---**	**2.3**	**0.035**	**[2]23.7**	**[2]0.024**
EDTA + cellulase + 5N HCl extraction								
BYI 02960 (parent comp.)					1.6	0.024		
amino-furanone					1.3	0.019		
Subtotal identified					2.9	0.043		
unknown 1a[1]					3.3	0.050		
Subtotal characterised					3.3	0.050		

Table continued on next page…

2nd Rotation	**wheat forage**		**wheat hay**		**wheat straw**		**wheat grains**	
Total EDTA + cellul.+ 5N HCl extraction	**---**	**---**	**---**	**---**	**6.2**	**0.094**		
5N NaOH extraction								
Subtotal characterised					8.7	0.131		
Total 5N NaOH extraction					**8.7**	**0.131**		
Total identified	**87.3**	**0.169**	**71.9**	**0.778**	**76.4**	**1.159**	**9.2**	**0.009**
Total characterised	**2.2**	**0.004**	**5.4**	**0.059**	**12.5**	**0.102**	**4.2**	**0.004**
Total extractable	**89.6**	**0.173**	**77.9**	**0.842**	**97.8**	**1.485**	**82.6**	**0.085**
Not analysed/losses	---	---	0.5	0.006	0.3	0.005	69.2	0.071
Unextractable (PES*)	10.4	0.020	22.1	0.239	2.2	0.033	17.4	0.018
Accountability	**100.0**	**0.193**	**100.0**	**1.081**	**100.0**	**1.431**	**100.0**	**0.103**

* post extraction solids
[1] polar unkown peak 1a in the conventional extract of wheat straw of the 1st rotation consisted of 4 different metabolites, all of them were minor according to TLC subquantification
[2] no analysis performed, but presumably glucose/carbohydrates as identified in grains of 1st rotation

Table 6.6.2-4 Distribution of parent compound and metabolites in wheat matrices after a 296 day plant back interval (3rd rotation, [furanone-4-^{14}C]BYI 02960)

3rd Rotation	**wheat forage**		**wheat hay**		**wheat straw**		**wheat grains**	
TRR [mg/kg]	0.111		0.254		0.462		0.047	
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Conventional extraction								
BYI 02960 (parent comp.)	43.0	0.048	18.3	0.047	20.7	0.096	2.0	0.001
glucose/carbohydrates	---	---	---	---	---	---	---	---
amino-furanone	3.6	0.004	7.4	0.019	4.9	0.023	---	---
mercapto-lactic acid	2.6	0.003	5.1	0.013	1.5	0.007	---	---
bromo-amino-furanone	5.7	0.006	10.7	0.027	7.4	0.034	---	---
difluoroethyl-amino-furanone-OH-glyc	5.5	0.006	8.6	0.022	8.7	0.040	---	---
difluoroethyl-amino-furanone	12.1	0.013	8.3	0.021	5.2	0.024	---	---
glyoxylic acid	---	---	0.5	0.001	---	---	---	---
acetic acid	1.2	0.001	1.1	0.003	1.6	0.007	0.8	<0.001
OH-glyc	2.5	0.003	2.3	0.006	3.4	0.016	1.7	0.001
OH	0.8	0.001	1.6	0.004	2.1	0.010	2.8	0.001
bromo / chloro	---	---	---	---	---	---	---	---
Total identified	**77.1**	**0.085**	**64.0**	**0.163**	**55.6**	**0.257**	**7.4**	**0.003**
unknown 1a[1]	2.4	0.003	4.7	0.012	12.0	0.055	3.2	0.001
unknown 4	0.7	0.001	0.8	0.002	0.9	0.004	---	---
unknown 9	---	---	---	---	---	---	1.1	0.001
Total characterised	**3.1**	**0.003**	**5.5**	**0.014**	**12.9**	**0.060**	**4.3**	**0.002**
Total extractable	**80.2**	**0.089**	**69.5**	**0.177**	**70.3**	**0.325**	**20.4**	**0.010**
Not analysed/losses	---	---	---	---	1.8	0.008	8.8	0.004
Unextractable (PES*)	19.8	0.022	30.5	0.077	29.7	0.137	[2]79.6	[2]0.037
Accountability	**100.0**	**0.111**	**100.0**	**0.254**	**100.0**	**0.462**	**100.0**	**0.047**

* post extraction solids
[1] polar unkown peak 1a in the conventional extract of wheat straw of the 1st rotation consisted of 4 different metabolites, all of them were minor according to TLC subquantification
[2] no analysis performed, but presumably glucose/carbohydrates as identified in grains of 1st rotation

Table 6.6.2-5 Distribution of parent compound and metabolites in Swiss chard and turnip matrices after a 29 day plant back interval (1st rotation, [furanone-4-^{14}C]BYI 02960)

1st Rotation	**Swiss chard immature**		**Swiss chard mature**		**turnip leaves**		**turnip roots**	
TRR [mg/kg]	0.848		0.871		0.679		0.074	
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Conventional extraction								
BYI 02960 (parent comp.)	**54.3**	**0.460**	**42.6**	**0.371**	**64.3**	**0.437**	**55.9**	**0.041**
glucose/carbohydrates	---	---	---	---	---	---	3.4	0.003
amino-furanone	1.8	0.015	3.1	0.027	0.9	0.006	4.1	0.003
difluoroethyl-amino-furanone-OH-glyc	---	---	1.2	0.010	---	---	---	---
difluoroethyl-amino-furanone	16.6	0.141	16.6	0.145	1.0	0.007	---	---
glyoxylic acid	3.7	0.031	4.7	0.041	6.6	0.045	12.2	0.009
OH-glyc-SA, isomer 1	1.2	0.010	2.5	0.022	---	---	---	---
acetic acid-glyc	0.5	0.004	1.6	0.014	3.5	0.024	---	---
OH-glyc-SA, isomer 2	3.3	0.028	3.2	0.028	---	---	---	---
acetic acid	0.4	0.003	0.6	0.005	1.2	0.008	0.2	<0.001
OH-glyc	8.5	0.072	13.6	0.119	11.2	0.076	2.1	<0.001
OH	2.0	0.017	1.9	0.017	1.7	0.012	0.4	<0.001
bromo / chloro	0.6	0.005	0.4	0.003	1.1	0.007	1.3	0.001
Total identified	**92.8**	**0.787**	**92.0**	**0.802**	**91.5**	**0.621**	**79.6**	**0.058**
unknown 1a[1]	2.5	0.021	3.5	0.031	1.4	0.010	---	---
unknown 1b	---	---	---	---	---	---	6.0	0.004
unknown 6	---	---	---	---	0.8	0.006	---	---
unknown 7	---	---	---	---	0.8	0.005	---	---
unknown 8	---	---	---	---	0.5	0.003	---	---
unknown 10	---	---	---	---	0.5	0.003	---	---
unknown 11	---	---	---	---	0.2	0.002	---	---
unknown 14	---	---	0.3	0.002	0.8	0.006	---	---
unknown 17	---	---	---	---	---	---	2.4	0.002
Total characterised	**2.5**	**0.021**	**[1]3.8**	**0.033**	**5.1**	**0.035**	**8.4**	**0.006**
Total extractable	**95.7**	**0.812**	**96.1**	**0.838**	**96.6**	**0.656**	**88.1**	**0.065**
Not analysed/losses	0.4	0.003	0.3	0.002	---	---	---	---
Unextractable (PES*)	4.3	0.037	3.9	0.034	3.4	0.023	11.9	0.009
Accountability	**100.0**	**0.848**	**100.0**	**0.871**	**100.0**	**0.679**	**100.0**	**0.073**

* post extraction solids

[1] polar unkown peak 1a in Swiss chard consisted of 8 different metabolites, all of them were minor according to TLC subquantification

Table 6.6.2-6 Distribution of parent compound and metabolites in Swiss chard and turnip matrices after a 135 day plant back interval (2nd rotation, [furanone-4-^{14}C]BYI 02960)

2nd Rotation	**Swiss chard immature**		**Swiss chard mature**		**turnip leaves**		**turnip roots**	
TRR [mg/kg]	0.311		0.263		0.158		0.014	
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Conventional extraction								
BYI 02960 (parent comp.)	55.0	0.171	27.5	0.072	68.1	0.108	31.0	0.004
glucose/carbohydrates	---	---	---	---	---	---	16.0	0.002
amino-furanone	8.8	0.027	8.8	0.023	0.6	0.001	---	---
difluoroethyl-amino-furanone-OH-glyc	---	---	---	---	---	---	---	---
difluoroethyl-amino-furanone	10.3	0.032	17.4	0.046	1.0	0.002	---	---
glyoxylic acid	---	---	---	---	1.5	0.002	1.8	<0.001
OH-glyc-SA, isomer 1	2.9	0.009	3.5	0.009	---	---	---	---
acetic acid-glyc	1.8	0.006	1.1	0.003	0.8	0.001	---	---
OH-glyc-SA, isomer 2	2.0	0.006	3.2	0.008	---	---	---	---
acetic acid	0.5	0.002	0.8	0.002	1.3	0.002	0.2	<0.001
OH-glyc	11.7	0.036	18.0	0.047	12.7	0.020	2.3	<0.001
OH	2.0	0.006	2.4	0.006	1.1	0.002	---	---
bromo / chloro	0.5	0.001	---	---	1.3	0.002	1.6	<0.001
Total identified	**95.5**	**0.297**	**82.7**	**0.218**	**88.5**	**0.140**	**53.0**	**0.007**
unknown 1a[1]	0.9	0.003	9.3	0.025	1.4	0.002	---	---
unknown 1b	---	---	---	---	---	---	28.0	0.004
unknown 6	---	---	---	---	0.8	0.001	---	---
unknown 7	---	---	---	---	0.6	0.001	---	---
unknown 8	---	---	---	---	0.5	0.001	---	---
unknown 14	0.4	0.001	---	---	2.8	0.004	1.3	<0.001
unknown 15	0.4	0.001	---	---	---	---	---	---
Total characterised	**1.6**	**0.005**	**9.3**	**0.025**	**6.0**	**0.010**	**29.3**	**0.004**
Total extractable	**97.1**	**0.302**	**92.5**	**0.243**	**94.5**	**0.150**	**82.3**	**0.012**
Not analysed/losses	---	---	0.5	0.001	---	---	---	---
Unextractable (PES*)	2.9	0.009	7.5	0.020	5.5	0.009	17.7	0.003
Accountability	**100.0**	**0.311**	**100.0**	**0.263**	**100.0**	**0.158**	**100.0**	**0.014**

* post extraction solids

[1] polar unkown peak 1a in Swiss chard consisted of 8 different metabolites, all of them were minor according to TLC subquantification

Table 6.6.2-7 Distribution of parent compound and metabolites in Swiss chard and turnip matrices after a 296 day plant back interval (3rd rotation, [furanone-4-^{14}C]BYI 02960)

3rd Rotation	**Swiss chard immature**		**Swiss chard mature**		**turnip leaves**		**turnip roots**	
TRR [mg/kg]	0.180		0.152		0.090		0.008	
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Conventional extraction								
BYI 02960 (parent comp.)	**36.7**	**0.066**	**33.4**	**0.051**	**72.4**	**0.065**	**69.9**	**0.006**
glucose/carbohydrates	---	---	---	---	---	---	5.3	<0.001
amino-furanone	1.3	0.002	1.8	0.003	0.5	<0.001	5.0	<0.001
difluoroethyl-amino-furanone-OH-glyc	2.1	0.004	1.9	0.003	---	---	---	---
difluoroethyl-amino-furanone	13.7	0.025	15.6	0.024	1.6	0.001	---	---
glyoxylic acid	0.2	<0.001	---	---	1.7	0.002	---	---
OH-glyc-SA, isomer 1	1.7	0.003	2.4	0.004	---	---	---	---
acetic acid-glyc	0.2	<0.001	0.2	<0.001	0.5	<0.001	---	---
OH-glyc-SA, isomer 2	4.2	0.008	2.4	0.004	---	---	---	---
acetic acid	0.9	0.002	0.9	0.001	1.1	0.001	0.3	<0.001
OH-glyc	22.2	0.040	21.9	0.033	10.2	0.009	3.1	<0.001
OH	3.6	0.007	3.1	0.005	0.6	0.001	---	---
bromo / chloro	0.5	0.001	0.6	0.001	1.8	0.002	2.5	<0.001
Total identified	**87.3**	**0.157**	**84.2**	**0.128**	**90.2**	**0.081**	**86.2**	**0.007**
unknown 1a[1]	3.4	0.006	1.8	0.003	1.1	0.001	---	---
unknown 1b	---	---	---	---	---	---	9.2	0.001
unknown 3	0.5	0.001	0.6	0.001	---	---	---	---
unknown 4	0.8	0.001	0.8	0.001	---	---	---	---
unknown 5	0.6	0.001	0.2	<0.001	---	---	---	---
unknown 6	---	---	---	---	1.1	0.001	---	---
unknown 11	0.3	<0.001	0.2	<0.001	---	---	---	---
unknown 13	---	---	0.6	0.001	---	---	---	---
unknown 14	0.2	<0.001	---	---	---	---	---	---
unknown 15	0.8	0.001	0.8	0.001	---	---	---	---
Total characterised	**6.5**	**0.012**	**4.9**	**0.008**	**2.3**	**0.002**	**9.2**	**0.001**
Total extractable	**93.8**	**0.169**	**89.1**	**0.135**	**92.5**	**0.083**	**95.5**	**0.008**
Not analysed/losses	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**
Unextractable (PES*)	6.2	0.011	10.9	0.017	7.5	0.007	4.5	<0.001
Accountability	**100.0**	**0.180**	**100.0**	**0.152**	**100.0**	**0.090**	**100.0**	**0.008**

* post extraction solids

[1] polar unkown peak 1a in Swiss chard of 1st rotation consisted of 8 different metabolites, all of them were minor according to TLC subquantification

III. Conclusions

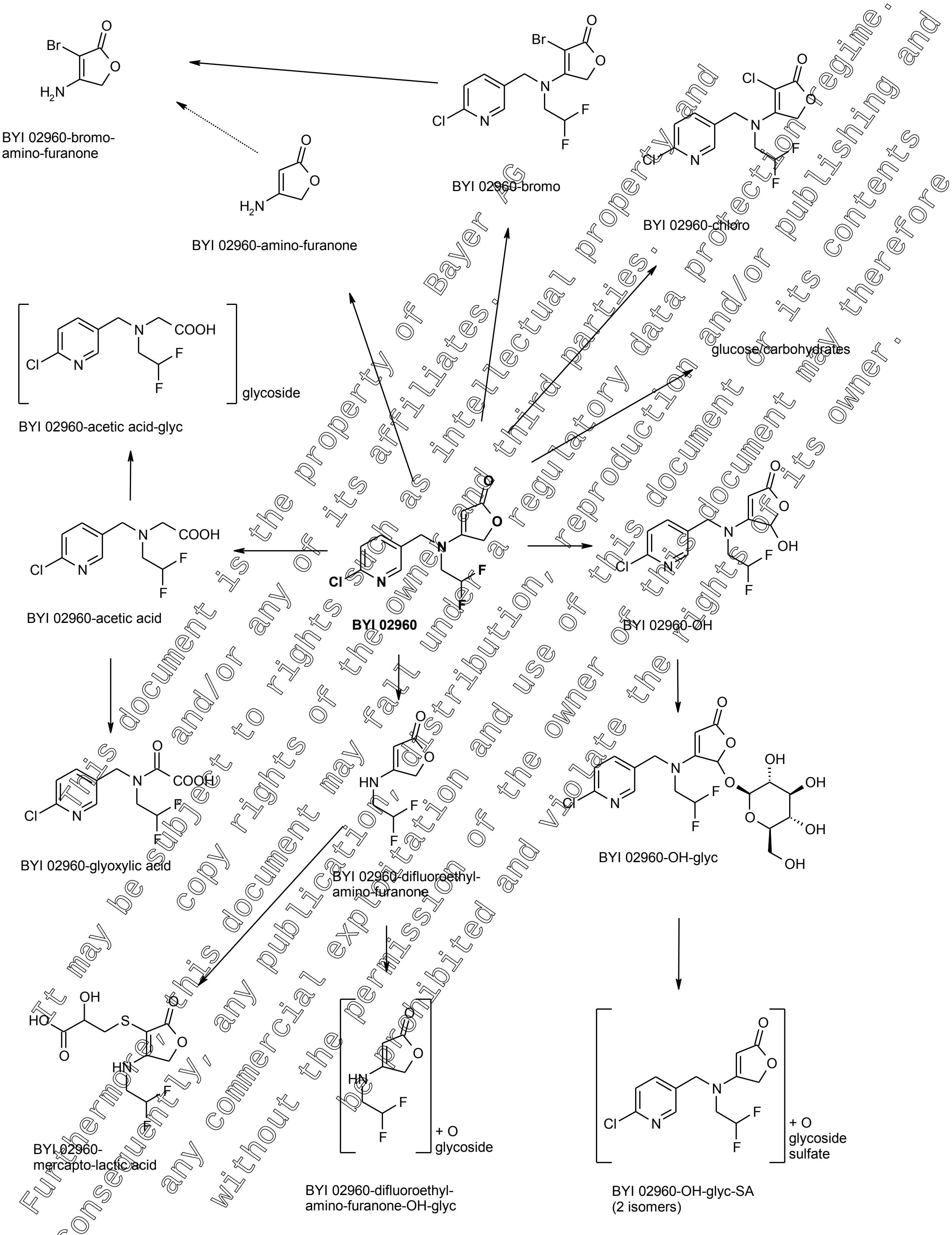
[Furanone-4-^{14}C] BYI 02960 was rather extensively metabolised in confined rotational crops. Parent compound and fourteen metabolites were identified. Parent compound was the main component in all samples of the three rotations, except for wheat grains. Four general metabolic transformation reactions were observed (cleavage, hydroxylation, conjugation and halogenation):

- cleavage of the pyridinylmethylamine bond and formation of metabolites based on difluoroethyl-amino-furanone and amino-furanone structures,
- BYI 02960-difluorethyl-amino-furanone was either conjugated with mercapto-lactic acid or hydroxylated and conjugated with carbohydrates,
- hydroxylation of the furanone moiety followed by conjugation with carbohydrates and sulphate,
- oxidative degradation of the furanone moiety to BYI 02960-acetic acid, which was further oxidized or conjugated with glucose
- complete degradation of the furanone moiety and incorporation of carbon atoms into the natural compound pool, i.e. into glucose/carbohydrates, and
- halogenation of the furanone ring with bromine or chlorine.

BYI 02960-glyoxylic acid, the oxidation product of BYI 02960-acetic acid, was presumably a transient soil metabolite that was taken up by the plants, since it was prominent in the samples of the 1st rotation, only. Halogenation of the furanone moiety of the active substance occurred most probably also in the soil which was supported by the fact that small amounts of halogenated parent compound were identified in the aerobic soil degradation studies.

On the basis of the results of this study it is concluded that the metabolism of [furanone-4-^{14}C]BYI 02960 in confined rotational crops is well understood and the following metabolic pathway is proposed:

Figure 6.6.2-1 Proposed metabolic pathway of [furanone-4-^{14}C]BYI 02960 in confined rotational crops



Report:	**KIIA 6.6.2/02, [redacted]; 2011**
Title:	Metabolism of [pyridinylmethyl-^{14}C]BYI 02960 in confined rotational crops
Report No & Edition No	MEF-10/892 M-419853-02-1
Guidelines:	OECD 502 Metabolism in Rotational Crops US EPA Residue Chemistry Test Guideline OPPTS 860.1850: Confined Accumulation in Rotational Crops European Parliament and Council Regulation (EC) No 1107/2009
GLP	yes

Executive Summary

The metabolism of the insecticide BYI 02960 was investigated in the representative rotational crops spring wheat, Swiss chard and turnips from three consecutive rotations. [Pyridinylmethyl-^{14}C]BYI 02960 was formulated as an SL 300 and used for one spray application onto the soil of a planting container (approx. 1 m^2). The actual application rate corresponded to 433 g a.s./ha, slightly above the anticipated maximum seasonal field rate of 400 g a.s./ha. The crops were each sown at 29, 135 and 296 days after the soil application, representing the first, the second and the third rotation.

Intermediate raw agricultural commodities (RACs) investigated were Swiss chard immature, wheat forage and wheat hay. All other RACs (wheat straw, wheat grain, Swiss chard, turnip leaves and turnip roots) were harvested at maturity.

The TRR values for all RACs are given in the following table.

Table 6.6.2-8 TRR values in the different RACs of the three rotations after soil application of [pyridinylmethyl-^{14}C]BYI 02960

TRR [mg/kg]	**Wheat**				**Swiss chard**		**Turnips**	
	forage	**hay**	**straw**	**grain**	**imm.**	**mature**	**leaves**	**roots**
1st rotation	1.407	2.409	9.015	0.177	1.358	1.483	0.815	0.072
2nd rotation	0.308	1.009	2.148	0.057	0.332	0.438	0.230	0.022
3rd rotation	0.117	0.321	0.491	0.017	0.135	0.130	0.083	0.008

The samples were conventionally extracted four times with acetonitrile/water mixtures releasing 35.5% (wheat grain, 2nd rotation) to 98.1% (immature Swiss chard and turnip leaves, 2nd rotation) of the TRR. To increase the extraction efficiency in wheat matrices additional exhaustive extraction steps were applied. Finally, the extraction efficiency in wheat grain was increased significantly from 52.2% to 83.8% of the TRR (1st rotation) and from 35.4% to 83.8% of the TRR (2nd rotation). In wheat forage, hay and straw, the additionally extracted portions ranged from 3.5% to 20.5% of the TRR, depending on the extraction steps applied.

Parent compound and metabolites in the extracts were analysed by HPLC. Identification was achieved by spectroscopic evidence (LC-MS/MS) after isolation and purification of the respective compounds from the conventional extracts of wheat straw or Swiss chard of the 1st rotation. HPLC co-chromatography with the isolated and identified radiolabelled metabolites and HPLC comparison of

metabolic profiles of the different extracts allowed the assignment of the compounds in all other extracts.

Parent compound was the most prominent compound in all RACs of all rotations, except in wheat grains of the 1st and the 2nd rotation, where it was detected as a minor compound. Seventeen metabolites were identified. Major metabolites were BYI 02960-6-CNA-glycerol-gluA, BYI 02960-glyoxylic acid and BYI 02960-OH in wheat matrices and BYI 02960-OH-glyc in Swiss chard and in turnip matrices. Compared to the confined rotational crop study performed with [furanone-4-^{14}C]BYI 02960, eight common metabolites were found.

BYI 02960 was rather extensively metabolised in confined rotational crops. The following metabolic routes were observed:

- cleavage of the pyridinylmethylamine bond followed by conjugation with carbohydrates or by oxidation of the methylene group to a carboxylic group,
- hydroxylation of the methylene group of the furanone moiety followed by conjugation with carbohydrates and sulphate,
- cleavage or loss of the furanone moiety followed by several oxidation and conjugation reactions, and
- halogenation of the furanone moiety with bromine or chlorine.

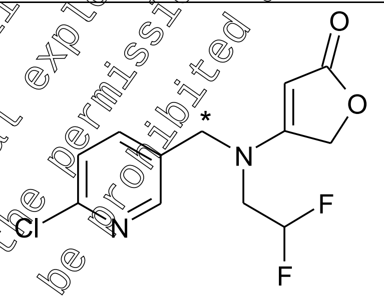
Halogenation of the furanone moiety of the active substance probably occurred in the soil. This assumption is supported by the fact that small amounts of halogenated parent compound were identified in the aerobic soil degradation studies.

On the basis of these results, a metabolic pathway of [pyridinylmethyl-^{14}C]BYI 02960 in confined rotational crops can be proposed.

I. Materials and Methods

A. Materials

1. Test Material:

Chemical structure	 * position of the radiolabel
Radiolabelled test material	[pyridinylmethyl-^{14}C]BYI 02960
Specific radioactivity (before radiodilution)	4.37 MBq/mg (118.08 µCi/mg)
Chemical Purity	> 99% (HPLC)
Radiochemical purity	> 99% (HPLC and TLC)

The supplied radiolabelled test compound [pyridinylmethyl-^{14}C]BYI 02960 was dissolved in acetonitrile. Formulation of the test compound was performed prior to the application: An appropriate amount of this stock solution was evaporated to dryness. The respective amount of blank formulation SL 300 was added and the mixture was homogenised using an ultrasonic bath (radioactive formulation). The sample was adjusted to a final volume of approx. 100 mL with water and homogenised by stirring (spray dilution).

2. Soil: "[redacted]4" (sandy loam soil from Germany), pH ($CaCl_2$) = 6.9, 58% sand, 28% silt and 14% clay, 2.1% organic carbon, cation exchange capacity (CEC) of 8.1 meq/100 g

3. Plants:

rotational crop	variety	representative for crop group
spring wheat	Thasos	small grain
Swiss chard	Lukullus	leafy vegetable
turnips	Rondo	root crop

B. Study Design

Experimental conditions:

BYI 02960 was applied as an SL formulation with a computer controlled track sprayer onto the bare soil of a planting container (surface area of approx. 1 m^2). The application rate was 433 g a.s./ha and was slightly above the anticipated maximum seasonal rate of BYI 02960. The treated soil remained undisturbed for an aging period of 29 days. After this period, the upper layer of the soil (approx. 15 cm) was intensively mixed and wheat, Swiss chard and turnips of the first rotation were sown. Wheat was sown on approx. 50% (0.5 m^2) of the soil area of the planting container. Swiss chard and turnips were each sown on 25% (0.25 m^2) of the soil area of the container. At day 135 and 296 after the application (after harvest of the mature wheat - the crop with the longest vegetation period) the soil was cultivated again and the crops of the second and third rotation were sown, respectively. With each rotation the plots of the crops in the container were changed. Wheat was sown on the plot where Swiss chard and turnips had been sown in the preceding rotation and Swiss chard and turnips were sown on the plot where wheat was sown before.

Sampling:

Raw agricultural commodities (RAC) sampled for this study included the immature samples forage and hay from wheat, and the immature samples from Swiss chard. All other samples (wheat straw and wheat grain, Swiss chard, turnip leaves and turnip roots) were harvested of each rotation at maturity.

About 20% of the wheat plants were cut shortly above the ground as forage sample at BBCH growth stage 29-31 (stem elongation). At BBCH 79-83 ("medium dough stage") again 20% of the wheat plants were cut as hay sample and dried at room temperature for three to five 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. A part of the Swiss chard plants were sampled at an immature stage (BBCH 44-46) and the remaining plants at maturity (BBCH 49). The Swiss chard plants were cut above the roots. The mature turnips plants were removed from soil, separated into leaves and roots. The plant materials were cut in pieces before homogenization with liquid nitrogen using a Polytron homogenizer.

Aliquots of the homogenized samples were used to estimate the TRR in the sample material by combustion and were used for extraction. Remaining homogenized sample material was stored in a freezer at approx. -18 °C.

C. Analytical Procedures

Extraction:

An aliquot of each homogenized RAC was extracted conventionally three to four times with ACN/water (8:2, v/v). The extracts were combined, purified using a pre-conditioned SPE RP 18 cartridge, concentrated and analysed by HPLC. The radioactivity in the extracts was determined by LSC, in the solids by combustion followed by LSC. The actual TRR values of the samples were determined by summing up the radioactivity measured in the extracts and in the remaining solids. If needed, solids were further extracted exhaustively using microwave conditions. Post-extraction solids of forage and hay (1st rotation) were extracted two times with an ACN/water mixture under microwave assistance at increased temperature. Post-extraction solids of wheat straw (1st rotation) were subjected to a sequential extraction procedure after one exhaustive extraction step with ACN/water (8:2, v/v) at increased temperature (60 °C) under microwave conditions. The solids of the microwave extraction step were subjected to a treatment with sodium chloride solution (2 h at 100 °C under microwave assistance), a diastase incubation (approx. 6 h at 26 °C), a treatment with EDTA solution (1 h at 100 °C under microwave assistance) and a cellulase treatment (approx. 12 h at 40 °C) at adjusted temperatures to break down the plant cell walls and liberate residues bound to cell walls or in the cells. The remaining solids of the sequential extraction were extracted finally in two steps with a 5N HCl and a 0.1N NaOH solution. Extracts of the EDTA, the cellulase and the HCl treatment were combined and adjusted to pH 7. The extract was concentrated, centrifuged and analysed by HPLC. The NaOH extract was not submitted to HPLC due to its high viscosity. Post-extraction solids of grains (1st rotation) were subjected to four subsequent exhaustive extraction steps under microwave conditions at increased temperature. Extraction was performed with ACN/water mixtures, 0.1N HCL and 0.1N NaOH.The ACN/water extracts were combined, concentrated and analysed by HPLC. The post-extraction solids of grains of the 2nd rotation were subjected to one exhaustive extraction step with ACN/water (8:2, v/v) at increased temperature under microwave assistance, followed by a diastase digestion (20 h at 26 °C) and a treatment with sodium chloride solution at 100 °C. HPLC analysis of the extracts was not performed due to the low radioactivity levels in the extracts.

Quantification:

Parent compound and metabolites in the extracts were analysed by reversed phase HPLC coupled to a radioactivity detector with a glass scintillator cell. The HPLC chromatograms (= metabolite profiles) were integrated for quantification of compounds.

Identification and characterisation:

Identification of parent compound and metabolites was based on the metabolite profiles of the conventional extracts of Swiss chard and wheat straw of the first rotation. These extracts showed all major and minor metabolites also detected in the other extracts. Therefore, parent compound, all major and most minor metabolites were isolated from these extracts, purified and identified by HPLC-MS/MS. Two metabolites were co-eluting in the extract of wheat straw when analysed with the profiling method. To ensure the right assignment in other extracts, the respective peak was isolated by semi-preparative HPLC and re-analysed with an acidic method which was able to separate the two compounds, if present. Based on these unambiguous assignments, the compounds in all conventional and exhaustive extracts of all rotations were identified by comparison with the metabolite patterns of Swiss chard and wheat straw. The presence of several metabolites was additionally confirmed by HPLC co-chromatography using the isolated compounds of Swiss chard or wheat straw as reference compounds.

Storage stability:

All conventional extraction experiments and the first HPLC analyses were performed within 9 days after harvest of the plants, with the exception for wheat grain of the second rotation which was extracted within 7 days after harvest, but analysed only 154 days after harvest. Therefore, the extract stability was investigated by re-analysing the grain extract after a storage time of more than 21 months in the freezer at ≤ -18 °C. No change in the metabolite pattern was detected indicating that the residues in the extracts are stability for at least 21 months.

Quantitative ^{14}C-HPLC analysis of the extracts was performed with the profiling method BYI02960_NEUTR. Only for wheat forage and hay, Swiss chard and turnips from the 1st rotation, the metabolic profile was measured with the preliminary profiling method BYI02960_CRC directly after extraction. The preliminary method was based on the same type of column and the same eluents but had a slightly shorter gradient. The metabolite profiles obtained from the two methods were comparable, however profiling method BYI02960_NEUTR showed an improved separation for some metabolites. For better comparison of metabolic pattern over all RACs of all rotations, the profiles of wheat forage and hay, Swiss chard and turnips of the 1st rotation were re-analysed with method BYI02960_NEUTR about 1 – 2 months after extract preparation. These new metabolic profiles were then considered as basis for quantification. Extract stability has been demonstrated for this time period.

Exhaustive extractions were started within approx. four to seven months after harvest. Since the compounds identified in the exhaustive extracts were identical with the compounds of the conventional extracts, it was concluded that the residues in the solids were stable and reflected the released residues at the time of exhaustive extraction.

Thus it can be concluded that the residues in all matrices were sufficiently stable during the experimental period of the study and that the first quantified profiles represented the metabolic pattern in the samples at harvest. Nevertheless, storage stability of BYI 02960 residues in frozen sample material was additionally demonstrated for Swiss chard and wheat straw for at least 20 or 18 months, respectively. Swiss chard and wheat straw samples were extracted and analysed for a second time after storage of the samples at ≤ -18 °C for at least 18 months. Comparison of the HPLC profiles showed no changes in the metabolite patterns.

As well, extract stability was proven for selected matrices (wheat forage, wheat grain, Swiss chard, turnip leaves and turnip roots) by re-analysis of stored extracts. All extracts were stable for at least 4 months (period tested for turnip roots). For wheat grain an extract stability of at least 21 months was demonstrated, as mentioned above.

II. Results and Discussion

The metabolism of [pyridinylmethyl-^{14}C]BYI 02960 was investigated in the representative rotational crops spring wheat, Swiss chard and turnips following one soil application. The active substance was applied as an SL formulation on the bare soil at a rate of 433 g/ha at 29 days before sowing of the crops representing the first rotation. Crops of the 2nd and 3rd rotation were sown 135 and 296 days after application. Immature Swiss chard, wheat forage and wheat hay were harvested as intermediate raw agricultural commodities (RACs). All other RACs (wheat straw, wheat grain, Swiss chard, turnip leaves and turnip roots) were harvested at maturity.

The TRR values of all RACs declined significantly (by a factor of 7 to 18) from the first to the third rotation. Highest residues were detected in the non-edible commodities of wheat and in the edible commodities of Swiss chard, as shown above in Table 6.6.2-8.

The radioactive residues were efficiently extracted from all commodities of all rotations with acetonitrile/water mixtures, except for wheat grain where only 35.4% to 52.2% of the TRR was detected after conventional extraction. For all wheat matrices additional exhaustive extraction steps were applied to the solids after conventional extraction. Exhaustive extraction comprised one to two extraction steps with acetonitrile/water mixtures at increased temperature (60 °C) under microwave assistance and in the case of wheat straw (1st and 2nd rotation) and wheat grain (2nd rotation) additional sequential extraction steps including enzymatic digestion steps. For wheat grain, exhaustive extraction released additional high amounts of radioactivity from the post-extraction solids. The extracted portions increased from 52.2% to 83.8% of the TRR (1st rotation) and from 35.4% to 89.4% of the TRR (2nd rotation). For the other wheat matrices, the additionally extracted portions ranged between 3.5% and 20.5% of the TRR depending on the exhaustive extraction steps applied. Thus, extraction efficiencies were increased significantly by exhaustive extraction steps, if applied – and extraction efficiencies above 80% resulted, even for wheat grain.

Parent compound BYI 02960 and about 50 metabolites were detected in the conventional and exhaustive extracts of the various samples of the three rotations. Of these the active substance and 17 metabolites were identified by LC-MS/MS. The other metabolites, none exceeding 5% of the TRR or 0.05 mg/kg, were characterised by their extraction behaviour and their retention time in radio-HPLC. The amounts of active substance and metabolites in all RACs are summarized in Table 6.6.2-9 to Table 6.6.2-14 for the three rotations.

Except in wheat grain, parent compound was by far the main component detected in all matrices of all rotations, accounting for 8% to 62% of the TRR in the commodities of the 1st rotation, 1% to 67% in the 2nd rotation and 14% to 69% in the 3rd rotation. The lowest percentage was always detected in wheat grain and the highest in turnip leaves.

Eight of the identified metabolites were specific to the radiolabel used: BYI 02960-CHMP, three different conjugates of this metabolite, the corresponding oxidation product 6-CNA and its glycerol-glucuronic acid conjugates (3 isomers) and two oxidation products of the postulated cleavage product BYI 02960-AMCP-difluoroethanamine. The isomers of 6-CNA-glycerol-gluA were detected as major metabolites in all matrices of wheat. In wheat grains they represented the highest proportion of the TRR. It is probable that the weak acid 6-CNA with its pronounced phloem mobility was transported into the seeds as a phloem sink, with conjugation occurring after transport. The 6-CNA conjugates were not identified in the matrices of Swiss chard or turnips.

Identified metabolites common to both radiolabels were BYI 02960-OH and its conjugates, BYI 02960-acetic acid, its conjugates and its successor molecule BYI 02960-glyoxylic acid and the chlorinated/brominated parent compound.

Overall, identification rates were high and ranged from 68% - 87% of the TRR in all RACs apart from wheat grains. In grains the identification rate was lower (29% - 58% of the TRR), but at least additional significant portions of the TRR were characterized by the extraction behaviour of the residues. The solids remaining after the conventional extraction of the grains of the 2nd rotation were subjected in a first step to microwave extraction with ACN/water (8:2, v/v) at increased temperature (15 min at 100 °C). An additional portion of approx. 5% of the TRR was released. Analysis of this extract showed the known major compounds of the conventional extract besides a high amount of a polar unknown compound. Enzymatic treatment of the post-extraction solids of the microwave extraction with diastase (approx. 20 h at 26 °C) solubilised a significant higher portion of the TRR (approx. 21% of the TRR), indicating that a quite polar residue was released. Subsequent extraction of the remaining solids with a sodium chloride solution (2 h at 100 °C) released another significant portion of the TRR (approx. 28% of the TRR). These extraction steps indicate that a major part of the residues in grain is of polar nature – and can be most probably assigned to natural compounds.

Table 6.6.2-9 Distribution of parent compound and metabolites in wheat matrices after a 29 day plant back interval (1st rotation, [pyridinylmethyl-^{14}C]BYI 02960)

1st Rotation	**wheat forage**		**wheat hay**		**wheat straw**		**wheat grains**	
TRR [mg/kg]	1.407		2.409		9.015		0.177	
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Conventional extraction								
BYI 02960 (parent comp.)	**43.8**	**0.619**	**25.0**	**0.601**	**31.4**	**2.834**	**1.8**	**0.003**
6-CNA	2.0	0.029	3.0	0.072	2.8	0.249	3.8	0.007
6-CNA-glycerol-gluA (1)	3.2	0.045	3.4	0.083	2.1	0.193	2.3	0.004
6-CNA-glycerol-gluA (2 + 3)	14.1	0.200	23.6	0.569	19.2	1.733	15.8	0.028
CHMP-glyc	1.7	0.024	5.0	0.120	2.4	0.213	---	---
CHMP	1.2	0.016	1.5	0.036	1.2	0.107	---	---
glyoxylic acid	12.3	0.173	7.3	0.176	5.6	0.508	6.0	0.011
acetic acid-glyc	0.6	0.009	---	---	0.8	0.072	---	---
OH-glyc	3.4	0.048	4.0	0.095	3.2	0.284	5.0	0.009
acetic acid	1.2	0.017	1.4	0.033	1.1	0.100	1.7	0.003
OH	1.4	0.020	2.2	0.052	2.4	0.212	6.8	0.012
bromo/chloro	---	---	0.9	0.021	0.4	0.036	---	---
Subtotal identified	**84.9**	**1.200**	**77.2**	**1.858**	**72.6**	**6.542**	**43.3**	**0.077**

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1st Rotation	**wheat forage**		**wheat hay**		**wheat straw**		**wheat grains**	
unknown 1	0.8	0.011	---	---	---	---	---	---
unknown 2	---	---	---	---	0.3	0.024	---	---
unknown 3	---	---	0.7	0.017	---	---	---	---
unknown 5	---	---	0.5	0.013	0.2	0.020	---	---
unknown 6	---	---	1.1	0.026	---	---	---	---
unknown 7	---	---	---	---	0.2	0.022	---	---
unknown 9	---	---	---	---	0.6	0.056	---	---
unknown 10	---	---	---	---	0.6	0.050	2.2	0.004
unknown 14	0.7	0.010	---	---	0.5	0.042	---	---
unknown 16	---	---	0.9	0.023	0.5	0.044	---	---
unknown 17	---	---	---	---	0.3	0.028	---	---
unknown 18	---	---	---	---	0.5	0.042	---	---
unknown 21	---	---	0.9	0.022	---	---	4.1	0.007
unknown 24	---	---	---	---	0.4	0.034	---	---
unknown 25	0.7	0.010	0.8	0.018	0.3	0.023	2.6	0.005
unknown 26	---	---	---	---	0.6	0.052	---	---
unknown 27	---	---	1.0	0.023	0.7	0.060	---	---
unknown 28	1.8	0.025	0.6	0.014	0.9	0.077	---	---
unknown 29	1.0	0.014	0.8	0.019	0.6	0.055	---	---
unknown 33	---	---	---	---	1.4	0.123	---	---
Subtotal characterised	5.0	0.071	7.3	0.176	8.4	0.754	8.9	0.016
Total conventional extr.	**89.9**	**1.271**	**84.5**	**2.034**	**81.0**	**7.296**	**52.2**	**0.093**
Microwave extraction I (ACN/water)								
BYI 02960 (parent comp.	**1.6**	**0.023**	**3.1**	**0.075**	**2.4**	**0.214**	**6.5**	**0.012**
6-CNA	---	---	---	---	0.1	0.012	---	---
6-CNA-glycerol-gluA (2 + 3)	---	---	---	---	1.4	0.123	4.4	0.008
glyoxylic acid	---	---	---	---	0.6	0.058	---	---
OH-glyc.	---	---	1.6	0.040	0.1	0.012	---	---
acetic acid	---	---	0.6	0.014	0.1	0.004	---	---
OH	---	---	---	---	0.2	0.017	3.6	0.006
Subtotal identified	1.6	0.023	5.3	0.129	4.9	0.440	14.5	0.026
unknown 1	0.5	0.007	2.7	0.065	0.4	0.036	4.9	0.009
unknown 29	1.3	0.019	---	---	0.1	0.011	---	---
Subtotal characterised	1.8	0.026	2.7	0.065	0.5	0.047	4.9	0.009
Total microwave extr. I	**3.5**	**0.049**	**8.0**	**0.193**	**5.4**	**0.487**	**19.4**	**0.034**
Microwave extraction II (1% NaCl)								
BYI 02960 (parent comp.)					1.0	0.087		
6-CNA					0.8	0.076		
6-CNA-glycerol-gluA (1)					0.2	0.016		
6-CNA-glycerol-gluA (2 + 3)					0.2	0.020		
OH					0.1	0.006		
Subtotal identified					2.3	0.205		
unknown 1					0.4	0.040		
unknown 29					0.2	0.015		
Subtotal characterised					0.6	0.055		

Table continued on next page…

1st Rotation	wheat forage		wheat hay		wheat straw		wheat grains	
Total microwave extr. II	**---**	**---**	**---**	**---**	**2.9**	**0.260**	**---**	**---**
Diastase digestion								
BYI 02960 (parent comp.)					0.7	0.064		
6-CNA					0.6	0.055		
6-CNA-glycerol-gluA (2 + 3)					0.1	0.005		
glyoxylic acid					0.2	0.020		
OH					<0.1	0.004		
Subtotal identified					**1.6**	**0.148**		
unknown 1					0.3	0.024		
unknown 5					0.1	0.006		
unknown 9					0.1	0.008		
unknown 29					0.1	0.013		
Subtotal characterised					0.6	0.051		
Total diastase digestion	**---**	**---**	**---**	**---**	**2.2**	**0.199**	**---**	**---**
EDTA + cellulase + 5N HCl extraction (wheat straw) or 0.1N HCl (wheat grain)								
BYI 02960 (parent comp.)					0.7	0.062		
6-CNA					0.7	0.066		
6-CNA-glycerol-gluA (2 + 3)					0.2	0.019		
glyoxylic acid					0.3	0.028		
Subtotal identified					**1.9**	**0.176**		
unknown 1					0.8	0.071		
unknown 29					1.0	0.088		
Subtotal characterised					1.8	0.159		
Total exhaustive extraction	**---**	**---**	**---**	**---**	**3.7**	**0.335**	**[1]2.3**	**0.004**
5N NaOH extraction								
Total NaOH extraction							**[1]9.9**	**0.018**
Total identified	**86.5**	**1.220**	**82.5**	**1.987**	**83.4**	**7.511**	**57.8**	**0.103**
Total characterised	**6.9**	**0.097**	**10.0**	**0.240**	**11.8**	**1.066**	**13.8**	**0.025**
Total extractable	**93.5**	**1.316**	**92.5**	**2.227**	**95.2**	**8.578**	**83.8**	**0.149**
Not analysed/losses	0.3	0.004	---	---	4.5	0.403	12.2	0.022
Unextractable (PES*)	6.2	0.087	7.5	0.181	0.4	0.035	16.2	0.029
Accountability	**100.0**	**1.407**	**100.0**	**2.409**	**100.0**	**9.015**	**100.0**	**0.177**

(1) isomer 1
(2 + 3) isomer 2 and/or isomer 3
* post extraction solids
[1] no analysis was feasible

Table 6.6.2-10 Distribution of parent compound and metabolites in wheat matrices after a 135 day plant back interval (2nd rotation, [pyridinylmethyl-^{14}C]BYI 02960)

2nd Rotation	**wheat forage**		**wheat hay**		**wheat straw**		**wheat grains**	
TRR [mg/kg]	0.308		1.009		2.148		0.057	
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Conventional extraction								
BYI 02960 (parent comp.)	**59.6**	**0.183**	**28.1**	**0.283**	**31.9**	**0.684**	**1.1**	**0.001**
6-CNA	1.6	0.005	3.2	0.032	4.0	0.086	---	---
6-CNA-glycerol-gluA (1)	4.4	0.014	2.4	0.024	2.4	0.051	2.5	0.001
6-CNA-glycerol-gluA (2 + 3)	14.4	0.044	23.9	0.242	22.0	0.472	11.9	0.007
CHMP-glyc	0.7	0.002	0.8	0.008	2.2	0.048	---	---
CHMP	---	---	0.5	0.005	---	---	---	---
glyoxylic acid	---	---	1.0	0.010	1.7	0.036	0.9	0.001
acetic acid-glyc	0.7	0.002	---	---	---	---	---	---
OH-glyc	2.6	0.008	4.5	0.045	5.3	0.112	4.6	0.003
acetic acid	0.9	0.003	1.6	0.016	1.8	0.039	1.6	0.001
OH	1.7	0.005	1.9	0.019	3.4	0.072	6.4	0.004
Subtotal identified	86.5	0.266	67.9	0.685	74.6	1.600	29.0	0.017
unknown 1	0.3	0.001	0.4	0.004	1.3	0.028	---	---
unknown 2	1.2	0.004	---	---	---	---	---	---
unknown 3	---	---	0.5	0.005	---	---	---	---
unknown 5	---	---	0.4	0.004	---	---	---	---
unknown 7	---	---	0.6	0.006	---	---	---	---
unknown 10	---	---	0.5	0.005	---	---	1.1	0.001
unknown 14	---	---	2.3	0.023	1.1	0.024	---	---
unknown 17	---	---	1.2	0.012	---	---	---	---
unknown 18	---	---	0.6	0.006	---	---	---	---
unknown 20	---	---	0.9	0.009	---	---	---	---
unknown 21	---	---	---	---	---	---	2.1	0.001
unknown 24	0.5	0.001	0.8	0.008	---	---	---	---
unknown 25	---	---	---	---	1.8	0.039	2.3	0.001
unknown 27	0.4	0.001	0.8	0.008	---	---	---	---
unknown 28	0.3	0.001	0.2	0.002	---	---	---	---
unknown 29	0.6	0.002	0.5	0.005	---	---	---	---
Subtotal characterised	3.3	0.010	9.8	0.099	4.2	0.091	5.6	0.003
Total conventional extr.	**89.9**	**0.276**	**77.6**	**0.784**	**78.8**	**1.692**	**34.6**	**0.020**
Microwave extraction I (ACN/water)								
BYI 02960 (parent comp.)					3.4	0.072		
6-CNA					1.5	0.032		
OH					0.3	0.007		
Subtotal identified					5.2	0.111		
unknown 1					1.6	0.034		
Subtotal characterised					1.6	0.034		

Table continued on next page…

2nd Rotation	**wheat forage**		**wheat hay**		**wheat straw**		**wheat grains**	
Total microwave extr. I					**6.7**	**0.145**		
Microwave extraction II (1% NaCl)								
BYI 02960 (parent comp.)					0.9	0.020		
6-CNA					0.9	0.019		
Subtotal identified					1.8	0.040		
unknown 1					0.3	0.006		
Subtotal characterised					0.3	0.006		
Total NaCl extraction					**2.1**	**0.046**		
Diastase digestion								
BYI 02960 (parent comp.)					0.6	0.013		
6-CNA					0.5	0.011		
Subtotal identified					1.1	0.024		
unknown 1					0.3	0.006		
unknown 29					0.1	0.002		
Subtotal characterised					0.4	0.008		
Total diastase digestion					**1.5**	**0.032**		
EDTA + cellulase + 5N HCl extraction								
BYI 02960 (parent comp.)					**0.7**	**0.013**		
6-CNA					0.5	0.011		
Subtotal identified					1.1	0.024		
unknown 1					0.7	0.014		
unknown 29					0.8	0.017		
Subtotal characterised					1.5	0.032		
Total EDTA + cellul.+ 5N HCl extraction					**2.6**	**0.056**		
Total identified	**86.5**	**0.266**	**67.9**	**0.685**	**83.8**	**1.799**	**29.0**	**0.017**
Total characterised	**3.3**	**0.010**	**9.8**	**0.099**	**8.0**	**0.171**	**5.6**	**0.003**
Total extractable	**89.9**	**0.276**	**77.6**	**0.784**	**91.8**	**1.970**	**34.6**	**0.020**
Not analysed/losses	---	---	---	---	7.9	0.169	54.8	0.032
Unextractable (PES*)	10.1	0.031	22.4	0.226	0.3	0.007	10.5	0.006
Accountability	**100.0**	**0.308**	**100.0**	**1.009**	**100.0**	**2.148**	**100.0**	**0.057**

(1) isomer 1
(2 + 3) isomer 2 and/or isomer 3
* post extraction solids

Table 6.6.2-11 Distribution of parent compound and metabolites in wheat matrices after a 296 day plant back interval (3rd rotation, [pyridinylmethyl-^{14}C]BYI 02960)

3rd Rotation	**wheat forage**		**wheat hay**		**wheat straw**		**wheat grains**	
TRR [mg/kg]	0.117		0.321		0.491		0.017	
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Conventional extraction								
BYI 02960 (parent comp.)	45.3	0.053	19.6	0.063	26.2	0.129	13.9	0.002
6-CNA	2.7	0.003	4.3	0.014	4.8	0.024	---	---
6-CNA-glycerol-gluA (1)	3.1	0.004	3.6	0.011	4.5	0.022	---	---
6-CNA-glycerol-gluA (2 + 3)	19.1	0.022	29.7	0.095	28.4	0.140	11.2	0.002
CHMP-glyc	3.1	0.004	4.9	0.016	2.9	0.014	---	---
CHMP	1.4	0.002	2.9	0.009	---	---	---	---
glyoxylic acid	0.8	0.001	---	---	2.6	0.013	---	---
OH-glyc	3.2	0.004	3.0	0.010	2.9	0.014	5.2	0.001
acetic acid	1.1	0.001	1.1	0.003	1.0	0.005	1.8	<0.001
OH	1.0	0.001	1.7	0.005	2.1	0.010	5.5	0.001
Total identified	**80.7**	**0.094**	**70.8**	**0.227**	**75.4**	**0.370**	**37.7**	**0.006**
unknown 1	---	---	0.7	0.002	---	---	---	---
unknown 7	---	---	0.5	0.002	---	---	---	---
unknown 10	---	---	1.1	0.003	---	---	---	---
unknown 16	---	---	1.3	0.004	---	---	---	---
unknown 21	---	---	---	---	---	---	2.4	<0.001
unknown 24	1.5	0.002	---	---	---	---	---	---
unknown 25	---	---	---	---	---	---	1.8	<0.001
unknown 27	---	---	0.6	0.002	---	---	---	---
unknown 28	---	---	---	---	---	---	2.8	0.001
Total characterised	**1.5**	**0.002**	**4.2**	**0.014**	**---**	**---**	**7.1**	**0.001**
Total extractable	**82.2**	**0.096**	**75.0**	**0.241**	**75.4**	**0.370**	**44.8**	**0.007**
Not analysed/losses	---	---	---	---	1.2	0.006	---	---
Unextractable (PES*)	17.8	0.021	25.0	0.080	23.4	0.115	55.2	0.009
Accountability	**100.0**	**0.117**	**100.0**	**0.321**	**100.0**	**0.491**	**100.0**	**0.017**

(1) isomer 1
(2 + 3) isomer 2 and/or isomer 3
* post extraction solids

Table 6.6.2-12 Distribution of parent compound and metabolites in Swiss chard and turnip matrices after a 29 day plant back interval (1st rotation, [pyridinylmethyl-14C]BYI 02960)

1st Rotation	**Swiss chard immature**		**Swiss chard mature**		**turnip leaves**		**turnip roots**	
TRR [mg/kg]	1.358		1.483		0.815		0.072	
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Conventional extraction								
BYI 02960 (parent comp.)	57.4	0.779	46.3	0.687	62.4	0.508	57.8	0.042
CHMP-glyc-tri-SA	1.8	0.025	2.3	0.034	---	---	---	---
6-CNA	7.3	0.099	7.0	0.103	1.0	0.008	8.5	0.006
CHMP-glyc-di-SA	2.5	0.035	3.0	0.045	---	---	---	---
CHMP-glyc	5.5	0.075	5.4	0.080	4.5	0.037	---	---
CHMP	---	---	---	---	---	---	4.1	0.003
glyoxylic acid	1.5	0.021	2.6	0.039	2.6	0.021	8.6	0.006
acetic acid-glyc	1.6	0.022	---	---	0.4	0.003	---	---
acetic acid-glyc/ OH-glyc-SA (2)	---	---	2.5	0.037	---	---	---	---
OH-glyc	7.4	0.101	10.9	0.162	9.4	0.076	2.5	0.002
OH-glyc-SA (1)	1.1	0.015	1.7	0.025	0.6	0.005	---	---
OH-glyc-SA (2)	0.5	0.006	---	---	1.7	0.014	---	---
N-formyl- /N-acetyl-AMCP-difluoroethanamine	4.0	0.055	2.9	0.043	3.6	0.030	3.5	0.003
OH	1.8	0.024	1.6	0.023	1.4	0.011	0.5	<0.001
bromo/chloro	0.7	0.009	0.5	0.008	1.3	0.011	1.4	0.001
Total identified	**93.2**	**1.266**	**86.6**	**1.285**	**88.9**	**0.724**	**86.8**	**0.063**
unknown 1	---	---	0.3	0.005	0.4	0.004	2.2	0.002
unknown 2	---	---	0.5	0.007	---	---	---	---
unknown 6	---	---	---	---	1.3	0.011	---	---
unknown 7	---	---	---	---	---	---	1.1	0.001
unknown 11	0.7	0.010	1.1	0.016	---	---	---	---
unknown 12	---	---	0.4	0.006	0.6	0.005	---	---
unknown 13	3.0	0.041	5.0	0.075	---	---	---	---
unknown 14	---	---	0.4	0.006	---	---	---	---
unknown 15	0.8	0.011	0.3	0.004	---	---	---	---
unknown 16	---	---	1.2	0.018	2.0	0.016	---	---
unknown 17	---	---	---	---	---	---	---	---
unknown 18	---	---	---	---	0.9	0.007	---	---
unknown 25	---	---	---	---	0.5	0.004	---	---
unknown 26	---	---	---	---	1.1	0.009	---	---
unknown 27	---	---	---	---	<0.1	<0.001	---	---
unknown 28	---	---	---	---	0.4	0.004	---	---
unknown 29	---	---	---	---	---	---	---	---
unknown 30	---	---	0.3	0.004	1.6	0.013	---	---
unknown 31	---	---	0.2	0.003	---	---	---	---
unknown 32	---	---	0.3	0.004	---	---	---	---
Total characterised	**4.5**	**0.062**	**9.9**	**0.146**	**8.8**	**0.071**	**3.2**	**0.002**

Table continued on next page…

1st Rotation	Swiss chard immature		Swiss chard mature		turnip leaves		turnip roots	
Total extractable	**97.7**	**1.327**	**96.5**	**1.431**	**97.7**	**0.796**	**90.0**	**0.065**
Not analysed/losses	0.3	0.004	0.5	0.008	---	---	---	---
Unextractable (PES*)	2.1	0.028	2.9	0.043	2.3	0.019	10.0	0.007
Accountability	**100.0**	**1.358**	**100.0**	**1.483**	**100.0**	**0.815**	**100.0**	**0.072**

(1) isomer 1
(2) isomer 2
* post extraction solids

Table 6.6.2-13 Distribution of parent compound and metabolites in Swiss chard and turnip matrices after a 135 day plant back interval (2nd rotation, [pyridinylmethyl-^{14}C]BYI 02960)

2nd Rotation	**Swiss chard immature**		**Swiss chard mature**		**turnip leaves**		**turnip roots**	
TRR [mg/kg]	0.332		0.438		0.230		0.022	
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Conventional extraction								
BYI 02960 (parent comp.)	51.2	0.170	24.6	0.108	66.8	0.153	48.4	0.011
CHMP-glyc-tri-SA	2.8	0.009	2.0	0.009	---	---	---	---
6-CNA	2.9	0.010	2.9	0.013	0.8	0.002	7.7	0.002
CHMP-glyc-di-SA	1.8	0.006	2.4	0.010	---	---	---	---
CHMP-glyc	5.1	0.017	1.3	0.006	4.9	0.011	2.0	<0.001
CHMP	---	---	---	---	---	---	1.1	<0.001
acetic acid-glyc	---	---	3.0	0.013	---	---	---	---
OH-glyc	17.4	0.058	25.3	0.111	11.1	0.025	2.4	0.001
OH-glyc-SA (1)	1.6	0.005	2.9	0.013	---	---	---	---
OH-glyc-SA (2)	2.5	0.008	6.3	0.028	---	---	---	---
N-formyl- /N-acetyl-AMCP-difluoroethanamine	1.6	0.005	---	---	1.2	0.003	---	---
OH	3.9	0.013	3.6	0.016	1.6	0.004	---	---
bromo/chloro	0.5	0.002	0.2	0.001	1.6	0.004	2.0	<0.001
Total identified	**91.4**	**0.303**	**74.6**	**0.327**	**88.0**	**0.202**	**63.6**	**0.013**
unknown 1	1.4	0.005	6.8	0.030	---	---	5.6	0.001
unknown 5	---	---	---	---	---	---	1.1	<0.001
unknown 11	---	---	1.5	0.006	---	---	---	---
unknown 13	3.6	0.012	4.3	0.019	---	---	0.6	<0.001
unknown 14	---	---	1.2	0.005	0.7	0.002	---	---
unknown 15	0.9	0.003	0.7	0.003	---	---	---	---
unknown 16	---	---	1.1	0.005	---	---	---	---
unknown 18	---	---	---	---	1.7	0.004	---	---
unknown 19	---	---	4.8	0.021	---	---	---	---
unknown 25	---	---	---	---	1.9	0.004	---	---
unknown 30	0.8	0.003	0.6	0.003	5.7	0.013	6.5	0.001
unknown 31	---	---	0.6	0.002	---	---	---	---
Total characterised	**6.7**	**0.022**	**14.7**	**0.064**	**10.0**	**0.023**	**13.9**	**0.003**
Total extractable	**98.1**	**0.325**	**96.1**	**0.421**	**98.1**	**0.225**	**77.5**	**0.015**
Not analysed/losses	---	---	0.7	0.003	---	---	0.6	<0.001
Unextractable (PES*)	1.9	0.006	3.2	0.014	1.9	0.004	21.9	0.005
Accountability	**100.0**	**0.332**	**100.0**	**0.438**	**100.0**	**0.230**	**100.0**	**0.022**

(1) isomer 1
(2) isomer 2
* post extraction solids

Table 6.6.2-14 Distribution of parent compound and metabolites in Swiss chard and turnip matrices after a 296 day plant back interval (3rd rotation, [pyridinylmethyl-^{14}C]BYI 02960)

3rd Rotation	**Swiss chard immature**		**Swiss chard mature**		**turnip leaves**		**turnip roots**	
TRR [mg/kg]	0.135		0.130		0.083		0.008	
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Conventional extraction								
BYI 02960 (parent comp.)	31.6	0.042	27.4	0.036	69.2	0.058	64.8	0.005
CHMP-glyc-tri-SA	2.5	0.003	0.4	0.001	---	---	---	---
6-CNA	5.3	0.007	5.1	0.007	0.8	0.001	4.7	<0.001
CHMP-glyc-di-SA	2.6	0.003	2.8	0.004	---	---	---	---
CHMP-glyc	5.1	0.007	6.2	0.008	5.9	0.005	---	---
CHMP	---	---	---	---	---	---	1.4	<0.001
glyoxylic acid	2.1	0.003	1.0	0.001	---	---	---	---
acetic acid-glyc/ OH-glyc-SA (2)	---	---	2.8	0.004	0.9	0.001	---	---
OH-glyc	24.6	0.033	28.1	0.036	9.6	0.008	3.8	<0.001
OH-glyc-SA (1)	5.3	0.007	2.9	0.004	0.5	<0.001	---	---
OH-glyc-SA (2)	0.5	0.001	---	---	---	---	---	---
N-formyl- /N-acetyl-AMCP-difluoroethanamine	0.8	0.001	1.8	0.002	2.2	0.002	---	---
OH	3.8	0.005	3.4	0.004	---	---	---	---
bromo/chloro	0.7	0.001	0.4	0.001	1.6	0.001	2.5	<0.001
Total identified	**84.9**	**0.114**	**82.4**	**0.107**	**90.7**	**0.075**	**77.1**	**0.005**
unknown 1	---	---	0.8	0.001	0.4	<0.001	8.4	0.001
unknown 2	---	---	---	---	0.2	<0.001	---	---
unknown 4	0.4	0.001	---	---	---	---	---	---
unknown 5	0.4	0.001	0.6	0.001	---	---	---	---
unknown 6	0.5	0.001	0.5	0.001	---	---	---	---
unknown 7	---	---	0.5	0.001	0.3	<0.001	---	---
unknown 11	1.0	0.001	1.4	0.002	---	---	---	---
unknown 12	---	---	---	---	1.2	0.001	---	---
unknown 13	4.4	0.006	---	---	---	---	3.2	<0.001
unknown 14	0.6	0.001	5.7	0.007	---	---	---	---
unknown 15	0.5	0.001	---	---	0.4	<0.001	---	---
unknown 16	0.2	<0.001	1.0	0.001	---	---	---	---
unknown 18	---	---	---	---	1.8	0.001	---	---
unknown 30	1.1	0.001	---	---	---	---	1.1	<0.001
unknown 32	---	---	1.2	0.002	---	---	---	---
Total characterised	**9.0**	**0.012**	**11.6**	**0.016**	**4.2**	**0.002**	**12.7**	**0.001**
Total extractable	**93.9**	**0.126**	**94.0**	**0.123**	**94.9**	**0.078**	**89.8**	**0.006**
Not analysed/losses	---	---	---	---	---	---	3.3	<0.001
Unextractable (PES*)	6.1	0.008	6.0	0.008	5.1	0.004	6.9	0.001
Accountability	**100.0**	**0.135**	**100.0**	**0.130**	**100.0**	**0.083**	**100.0**	**0.008**

(1) isomer 1
(2) isomer 2
* post-extraction solids

III. Conclusions

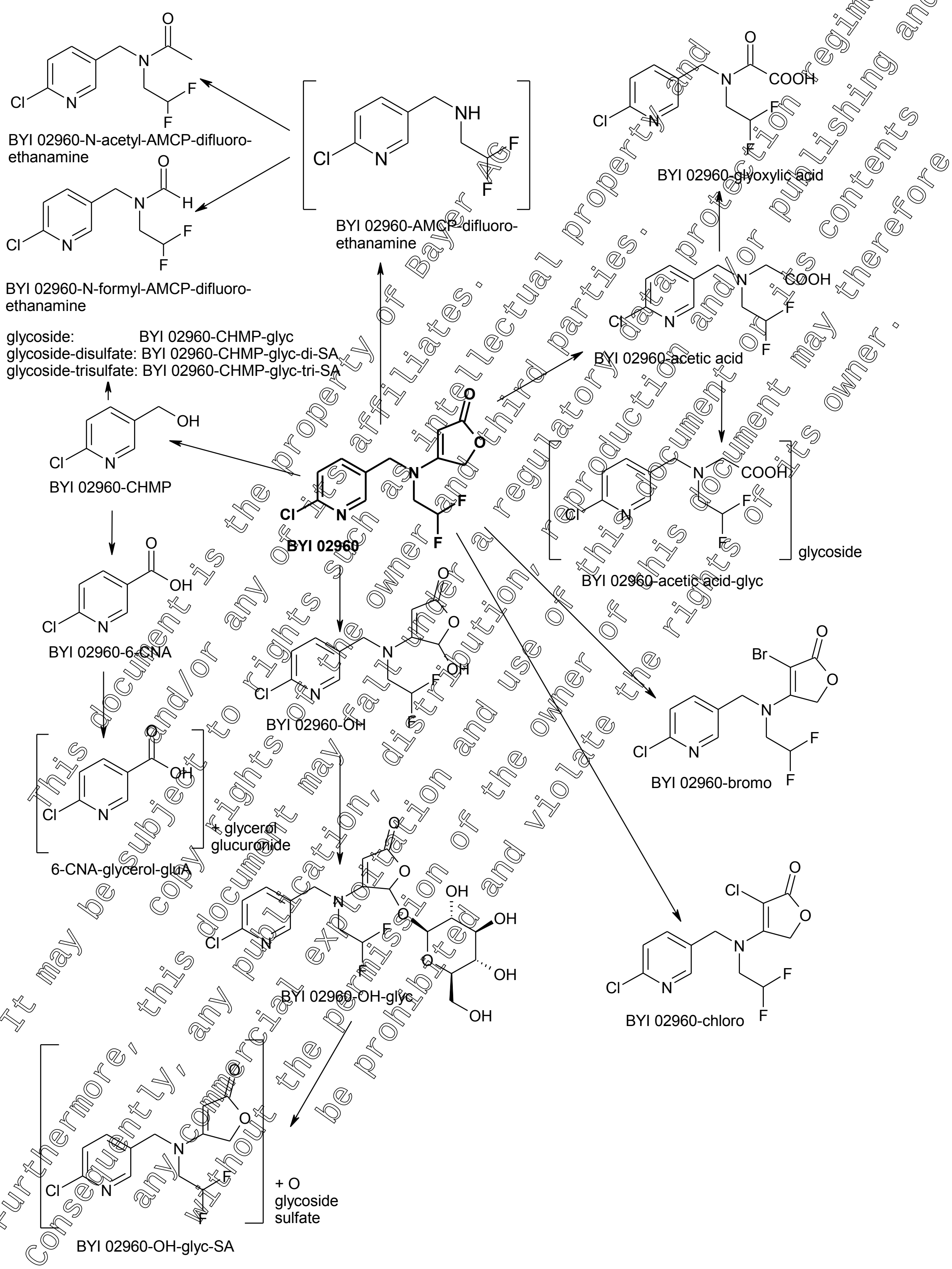
[Pyridinylmethyl-^{14}C]BYI 02960 was rather extensively metabolised in confined rotational crops. However, parent compound was detected as main component in all RACs of all rotations, except in wheat grain of the first and the second rotation. Considering all samples, BYI 02960-6-CNA-glycerol-gluA (a mixture of two isomers) was the main metabolite in the wheat matrices and BYI 02960-OH-glyc was the main metabolite detected in Swiss chard and turnips. The following main metabolic routes were observed:

- cleavage of the pyridinylmethylamine bond followed by conjugation with carbohydrates and sulphate or by oxidation of the methylene group to a carboxylic group,
- hydroxylation of the methylene group of the furanone moiety followed by conjugation with carbohydrates and sulphate,
- cleavage or complete degradation of the furanone moiety followed by several oxidation and conjugation reactions, and
- halogenation of the furanone moiety with bromine or chlorine.

Halogenation of the furanone moiety of the active substance probably occurred in the soil which is supported by the fact that small amounts of halogenated parent compound were identified in the aerobic soil degradation studies.

On the basis of the results of this study it is concluded that the metabolism of [pyridinylmethyl-^{14}C]BYI 02960 in confined rotational crops is well understood and the following metabolic pathway is proposed:

Figure 6.6.2-2 Proposed metabolic pathway of [pyridinylmethyl-^{14}C]BYI 02960 in confined rotational crops



Overall Conclusions for CRC

The metabolism of the insecticide BYI 02960 was investigated in the rotational crops wheat, Swiss chard and turnips from three consecutive rotations in two separate experiments with (1) [furanone-4-^{14}C]BYI 02960 or (2) [pyridinylmethyl-^{14}C]BYI 02960. In each study, parent compound was applied to the bare soil 29 days before sowing of the crops of the first rotation. The plant back intervals were 29, 135 and 296 days after the soil application, representing the first, second and third rotation. Sample materials under investigation were the immature raw agricultural commodities wheat forage, wheat hay and Swiss chard at an intermediate growth stage and the mature raw agricultural commodities wheat straw and wheat grain, Swiss chard and turnip leaves and roots.

(1) Label 1: [furanone-4-^{14}C]BYI 02960

The total radioactive residues (TRR) in all RACs declined significantly from the first to the third rotation. Parent compound was the main component detected in all RACs in all rotations (except for wheat grain), indicating that no major metabolites were formed in the soil and taken up by the plants. These results are in line with the aerobic soil degradation studies which show a quite high mineralization rate of BYI 02960, with only two major soil metabolites detected, both of them being label-specific and not possible to detect in the present study. The formation of BYI 02960-chloro and BYI 02960-bromo in soil was detected to a minor extent. Subsequent uptake of these soil metabolites is most probably the explanation for the trace levels detected in the different RACs. Further degradation of these halogenated compounds in the plant was probably the cause of metabolites such as BYI 02960-bromo-amino-furanone.

The main metabolite in wheat grains was assigned to a natural compound. Diastase digestion of the post extraction solids of the conventional extraction led to one polar metabolite which was identified as glucose by TLC co-chromatography. Radiolabelled glucose was also found in trace levels in turnip roots. Other label-specific metabolites identified were BYI 02960-difluoroethyl-amino-furanone, its conjugates BYI 02960-mercapto-lactic acid and BYI 02960-difluoroethyl-amino-furanone-OH-glyc, as well as the metabolites BYI 02960-amino-furanone and BYI 02960-bromo-amino-furanone. All other identified metabolites were not label specific and were detected at comparable residue levels in the CRC study performed with [pyridinylmethyl-^{14}C]BYI 02960.

On basis of the metabolites identified, the metabolic pathway was deduced. One major metabolic route was the cleavage of the pyridinylmethylamine bond and the formation of BYI 02960-difluoroethylamino-furanone and BYI 02960-amino-furanone after loss of the difluoroethyl moiety. The cleavage of the molecule was also detected in the CRC study conducted with [pyridinylmethyl-^{14}C]BYI 02960. BYI 02960-CHMP, 6-CNA and conjugates of these metabolites were identified as the corresponding counterparts. Oxidative degradation of the furanone moiety was also an important degradation path resulting in the metabolites BYI 02960-acetic acid, BYI 02960-glyoxylic and corresponding conjugates. Hydroxylation of the furanone moiety and subsequent conjugation with carbohydrates was an additional metabolic route resulting in metabolites common to both radiolabels tested. Complete degradation of the furanone moiety and incorporation of the carbon atoms into the natural compound pool, i.e. most probably into glucose was also observed. Halogenation of the furanone moiety of the active substance was most probably a process which occurred in the soil.

The results of the present metabolism study in confined rotation crops are in good conformity with the results of the corresponding study performed with [pyridinylmethyl-^{14}C]BYI 02960.

(2) Label 2: [pyridinylmethyl-^{14}C]BYI 02960
The total radioactive residues (TRR) in all RACs declined significantly from the first to the third rotation. Parent compound was the main component detected in most of the RACs in all rotation (not in wheat grain of the 1st rotation, not in wheat grain and mature Swiss chard in the 2nd rotation, and not in wheat hay, wheat straw and mature Swiss chard of the 3rd rotation). Other major metabolites were the glucuronic acid conjugates of 6-CNA-glycerol (which were detected in quite high amounts in all wheat matrices) and BYI 02960-OH-glyc (which were detected in significant amounts in Swiss chard). These results are in line with the aerobic soil degradation studies which show a quite high mineralization rate of BYI 02960, with only two major soil metabolites detected, one of them being label-specific and not possible to detect in the present study, and the other 6-CNA, which would be expected to be taken up by the plants and further metabolized (conjugated). The formation of 6-CNA is expected to also occur in the plant, supported by the fact that the preceding metabolite BYI 02960-CHMP - or conjugates of it - were also identified in several plant matrices. Metabolite 6-CNA and its preciding metabolite BYI 02960-CHMP, as well as their corresponding conjugates were the only label specific metabolites detected. All other metabolites identified were not label specific and were detected at comparable residue levels in the CRC study performed with [furanone-4-^{14}C]BYI 02960.

On basis of the metabolites identified, the metabolic pathway was deduced. Overall, three major metabolic routes were detected: (1) Cleavage of the pyridinylmethylamine bond followed by conjugation with carbohydrates and sulphate or by oxidation of the methylene group to a carboxylic group and further conjugation, (2) hydroxylation of the methylene group of the furanone moiety followed by conjugation with carbohydrates and sulphate, and (3) cleavage or complete degradation of the furanone moiety followed by several oxidation and conjugation reactions. Halogenation of the furanone moiety of the active substance was most probably a process which occurred in the soil. Most probably the metabolites were taken up by the roots and were not formed in the plants. This is in line with the finding of the aerobic soil degradation studies summarized in KAII 7.1.

The cleavage of the molecule was also detected in the CRC study conducted with [furanone-4-^{14}C]BYI 02960. BYI 02960-difluoroethyl-amino-furanone and BYI 02960-amino-furanone and conjugates of these metabolites were identified as the corresponding counterparts to BYI 02960-CHMP and 6-CNA or their conjugates. Thus, the results of the present metabolism study in confined rotation crops are in good conformity with the results of the corresponding study performed with [furanone-4-^{14}C]BYI 02960.

When considering the results from both confined rotational crop studies conducted, it can be concluded that BYI02960 is rather extensively metabolised in rotational crops. A total of 6 major and approx. 40 minor metabolites were found, and all major and 14 minor have been identified. The distribution of parent compound and metabolites in the edible matrices of confined rotational crops are shown in Table 6.6.2-15 to Table 6.6.2-20.

Table 6.6.2-15 TRR values and distribution of parent compound and metabolites in the edible matrix Swiss chard (rotational crop; 1st rotation)

	Confined rotational crops							
	Swiss chard, immature				Swiss chard, mature			
	[furanone-4-^{14}C]		[pyridinylmethyl-^{14}C]		[furanone-4-^{14}C]		[pyridinylmethyl-^{14}C]	
TRR [mg/kg] =		0.848		1.358		0.871		1.483
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
BYI 02960 (parent comp.)	54.3	0.460	57.4	0.779	42.6	0.371	46.3	0.687
glucose/carbohydrates	---	---			---	---		
amino-furanone	*1.8*	*0.015*			*3.1*	*0.027*		
CHMP-glyc-tri-SA			*1.8*	*0.025*			*2.3*	*0.034*
6-CNA			*7.3*	*0.099*			*7.0*	*0.103*
6-CNA-glycerol-gluA (1)			---	---			---	---
6-CNA-glycerol-gluA (2+3)			---	---			---	---
CHMP-glyc-di-SA			*2.5*	*0.035*			*3.0*	*0.045*
CHMP-glyc			*5.5*	*0.075*			*5.4*	*0.080*
CHMP			---	---			---	---
difluoroethyl-amino-furanone-OH-glyc	---	---			*1.2*	*0.010*		
difluoroethyl-amino-furanone	*16.6*	*0.141*			*16.6*	*0.145*		
glyoxylic acid	3.7	0.031	1.5	0.021	4.7	0.041	2.6	0.039
OH-glyc-SA (1)	1.2	0.010	1.1	0.015	2.5	0.022	1.7	0.025
acetic acid-glyc	0.5	0.004	1.6	0.022	1.6	0.014	---	---
OH-glyc-SA (2)	3.3	0.028	0.5	0.006	3.2	0.028	[1]2.5	[1]0.037
OH-glyc	8.5	0.072	7.4	0.101	13.6	0.119	10.9	0.162
acetic acid	0.4	0.003	---	---	0.6	0.005	---	---
N-formyl-/N-acetyl-AMCP-difluoroethanamine			4.0	0.055			2.9	0.043
OH	2.0	0.017	1.8	0.024	1.9	0.017	1.6	0.023
chloro/ bromo	0.6	0.005	0.7	0.009	0.4	0.003	0.5	0.008
Total identified	**92.8**	**0.787**	**93.2**	**1.266**	**92.0**	**0.802**	**86.6**	**1.285**
Total characterised	**2.5**	**0.021**	**4.5**	**0.062**	**3.8**	**0.033**	**9.9**	**0.146**
Analysed extract(s)	95.3	0.809	97.7	1.327	95.9	0.835	96.5	1.431
Extract(s) not analysed	0.4	0.003	0.3	0.004	0.3	0.002	0.5	0.008
Total extracted	95.7	0.812	97.7	1.327	96.1	0.838	96.5	1.431
Unextractable (PES*)	4.3	0.037	2.1	0.028	3.9	0.034	2.9	0.043
Accountability	**100.0**	**0.848**	**100.0**	**1.359**	**100.0**	**0.871**	**100.0**	**1.483**

* post extraction solids
[1] co-elution with BYI 02960-acetic-acid-glyc
(1) isomer 1 (2) isomer 2 (2 + 3) isomer 2 and/or isomer 3

Label specific metabolites are printed in *italic.*

Table 6.6.2-16 TRR values and distribution of parent compound and metabolites in the edible matrix Swiss chard (rotational crop; 2nd rotation)

	Confined rotational crops							
	Swiss chard, immature				Swiss chard, mature			
	[furanone-4-^{14}C]		[pyridinylmethyl-^{14}C]		[furanone-4-^{14}C]		[pyridinylmethyl-^{14}C]	
TRR [mg/kg] =		0.311		0.332		0.263		0.438
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
BYI 02960 (parent comp.)	55.0	0.171	51.2	0.170	27.5	0.072	24.6	0.108
glucose/carbohydrates	---	---			---	---		
amino-furanone	*8.8*	*0.027*			*8.8*	*0.023*		
CHMP-glyc-tri-SA			*2.8*	*0.009*			*2.0*	*0.009*
6-CNA			*2.9*	*0.010*			*2.9*	*0.013*
6-CNA-glycerol-gluA (1)			---	---			---	---
6-CNA-glycerol-gluA (2+3)			---	---			---	---
CHMP-glyc-di-SA			*1.8*	*0.006*			*2.4*	*0.010*
CHMP-glyc			*5.1*	*0.017*			*1.3*	*0.006*
CHMP			---	---			---	---
difluoroethyl-amino-furanone-OH-glyc	---	---			---	---		
difluoroethyl-amino-furanone	*10.3*	*0.032*			*17.4*	*0.046*		
glyoxylic acid	---	---	---	---	---	---	---	---
OH-glyc-SA (1)	2.9	0.009	1.6	0.005	3.5	0.009	2.9	0.013
acetic acid-glyc	1.8	0.006	---	---	1.1	0.003	3.0	0.013
OH-glyc-SA (2)	2.0	0.006	2.5	0.008	3.2	0.008	6.3	0.028
OH-glyc	11.7	0.036	17.4	0.058	18.0	0.047	25.3	0.111
acetic acid	0.5	0.002	---	---	0.8	0.002	---	---
N-formyl-/N-acetyl-AMCP-difluoroethanamine			*1.6*	*0.005*			---	---
OH	2.0	0.006	3.9	0.013	2.4	0.006	3.6	0.016
chloro/ bromo	0.5	0.001	0.5	0.002	---	---	0.2	0.001
Total identified	**95.5**	**0.297**	**91.4**	**0.303**	**82.7**	**0.218**	**74.6**	**0.327**
Total characterised	**1.6**	**0.005**	**6.7**	**0.022**	**9.3**	**0.025**	**14.7**	**0.064**
Analysed extract(s)	97.1	0.302	91.4	0.303	92.1	0.242	96.1	0.421
Extract(s) not analysed	---	---	---	---	0.5	0.001	0.7	0.003
Total extracted	97.1	0.302	98.1	0.325	92.5	0.243	96.1	0.421
Unextractable (PES*)	2.9	0.009	1.9	0.006	7.5	0.02	3.2	0.014
Accountability	**100.0**	**0.311**	**100.0**	**0.332**	**100.0**	**0.263**	**100.0**	**0.438**

* post extraction solids
(1) isomer 1 (2) isomer 2 (2 + 3) isomer 2 and/or isomer 3

Label specific metabolites are printed in *italic*.

Table 6.6.2-17 TRR values and distribution of parent compound and metabolites in the edible matrix Swiss chard (rotational crop; 3rd rotation)

	Confined rotational crops							
	Swiss chard, immature				Swiss chard, mature			
	[furanone-4-^{14}C]		[pyridinylmethyl-^{14}C]		[furanone-4-^{14}C]		[pyridinylmethyl-^{14}C]	
TRR [mg/kg] =		0.180		0.135		0.152		0.130
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
BYI 02960 (parent comp.)	36.7	0.066	31.6	0.042	33.4	0.051	27.4	0.036
glucose/carbohydrates	---	---			---	---		
amino-furanone	*1.3*	*0.002*			*1.8*	*0.003*		
CHMP-glyc-tri-SA			*2.5*	*0.003*			*0.4*	*0.001*
6-CNA			*5.3*	*0.007*			*5.1*	*0.007*
6-CNA-glycerol-gluA (1)			---	---			---	---
6-CNA-glycerol-gluA (2+3)			---	---			---	---
CHMP-glyc-di-SA			*2.6*	*0.003*			*2.8*	*0.004*
CHMP-glyc			*5.4*	*0.007*			*6.2*	*0.008*
CHMP			---	---			---	---
difluoroethyl-amino-furanone-OH-glyc	*2.1*	*0.004*			*1.9*	*0.003*		
difluoroethyl-amino-furanone	*13.7*	*0.025*			*15.6*	*0.024*		
glyoxylic acid	0.2	<0.001	2.1	0.003	---	---	1.0	0.001
OH-glyc-SA (1)	1.7	0.003	5.3	0.007	2.4	0.004	2.9	0.004
acetic acid-glyc	0.2	<0.001	---	---	0.2	<0.001	---	---
OH-glyc-SA (2)	4.2	0.008	0.5	0.001	2.4	0.004	[1]2.8	[1]0.004
OH-glyc	22.2	0.04	24.6	0.033	21.9	0.033	28.1	0.036
acetic acid	0.9	0.002	---	---	0.9	0.001	---	---
N-formyl-/N-acetyl-AMCP-difluoroethanamine			0.8	0.001			1.8	0.002
OH	3.6	0.007	3.8	0.005	3.1	0.005	3.4	0.004
chloro/ bromo	0.5	0.001	0.7	0.001	0.6	0.001	0.4	0.001
Total identified	**87.3**	**0.157**	**84.9**	**0.114**	**84.2**	**0.128**	**82.4**	**0.107**
Total characterised	**6.5**	**0.012**	**9.0**	**0.012**	**4.9**	**0.008**	**11.6**	**0.016**
Analysed extract(s)	93.8	0.169	84.9	0.114	89.1	0.135	82.4	0.107
Extract(s) not analysed	---	---	---	---	---	---	---	---
Total extracted	93.8	0.169	93.9	0.126	89.1	0.135	94.0	0.123
Unextractable (PES*)	6.2	0.011	6.1	0.008	10.9	0.017	6.0	0.008
Accountability	**100.0**	**0.180**	**100.0**	**0.134**	**100.0**	**0.152**	**100.0**	**0.130**

* post extraction solids
[1] co-elution with BYI 02960-acetic-acid-glyc
(1) isomer 1 (2) isomer 2 (2 + 3) isomer 2 and/or isomer 3

Label specific metabolites are printed in *italic*.

Table 6.6.2-18 TRR values and distribution of parent compound and metabolites in edible matrices wheat grains and turnip roots (rotational crops; 1st rotation)

	Confined rotational crops							
	wheat grains				turnip roots			
	[furanone-4-^{14}C]		[pyridinylmethyl-^{14}C]		[furanone-4-^{14}C]		[pyridinylmethyl-^{14}C]	
TRR [mg/kg] =		0.478		0.177		0.074		0.072
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
BYI 02960	0.4	0.002	8.3	0.015	55.9	0.041	57.8	0.042
glucose/carbohydrates	*70.5*	*0.338*			3.4	0.003		
amino-furanone	*0.5*	*0.002*			4.1	0.003		
CHMP-glyc-tri-SA			---	---			---	---
6-CNA			*3.8*	*0.007*			*8.5*	*0.006*
6-CNA-glycerol-gluA (1)			*2.3*	*0.004*			---	---
6-CNA-glycerol-gluA (2+3)			*20.2*	*0.036*			---	---
CHMP-glyc-di-SA			---	---			---	---
CHMP-glyc			---	---			---	---
CHMP			---	---			*4.1*	*0.003*
difluoroethyl-amino-furanone-OH-glyc	---	---			---	---		
difluoroethyl-amino-furanone	---	---			---	---		
glyoxylic acid	5.1	0.024	6.0	0.011	12.2	0.009	8.6	0.006
OH-glyc-SA (1)	---	---	---	---	---	---	---	---
acetic acid-glyc	---	---	---	---	---	---	---	---
OH-glyc-SA (2)	---	---	---	---	---	---	---	---
OH-glyc	1.4	0.007	5.0	0.009	2.1	<0.001	2.5	0.002
acetic acid	0.6	0.003	1.7	0.003	0.2	<0.001	---	---
N-formyl-/N-acetyl-AMCP-difluoroethanamine			---	---			3.5	0.003
OH	2.3	0.011	10.4	0.019	0.4	<0.001	0.5	<0.001
chloro/ bromo	---	---	---	---	1.3	0.001	1.4	0.001
Total identified	**80.8**	**0.387**	**57.8**	**0.103**	**79.6**	**0.058**	**86.8**	**0.063**
Total characterised	**4.2**	**0.020**	**13.8**	**0.025**	**8.4**	**0.006**	**3.2**	**0.002**
Analysed extract(s)	85.0	0.407	71.6	0.127	88.1	0.065	90.0	0.065
Extract(s) not analysed	3.0	0.014	12.2	0.022	---	---	---	---
Total extracted	88.0	0.421	83.8	0.149	88.1	0.065	90.0	0.065
Unextractable (PES*)	12.0	0.058	16.2	0.029	11.9	0.009	10.0	0.007
Accountability	**100.0**	**0.478**	**100.0**	**0.177**	**100.0**	**0.074**	**100.0**	**0.072**

* post extraction solids
(1) isomer 1 (2) isomer 2 (2 + 3) isomer 2 and/or isomer 3

Label specific metabolites are printed in *italic*.

Table 6.6.2-19 TRR values and distribution of parent compound and metabolites in edible matrices wheat grains and turnip roots (rotational crops; 2nd rotation)

	Confined rotational crops							
	wheat grains				turnip roots			
	[furanone-4-^{14}C]		[pyridinylmethyl-^{14}C]		[furanone-4-^{14}C]		[pyridinylmethyl-^{14}C]	
TRR [mg/kg] =		0.103		0.057		0.014		0.022
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
BYI 02960	0.5	0.001	1.1	0.001	31.0	0.004	48.4	0.011
glucose/carbohydrates	---	---			16.0	0.002		
amino-furanone	1.3	0.001			---	---		
CHMP-glyc-tri-SA			---	---			---	---
6-CNA			---	---			7.7	0.002
6-CNA-glycerol-gluA (1)			2.5	0.001			---	---
6-CNA-glycerol-gluA (2+3)			11.9	0.007			---	---
CHMP-glyc-di-SA			---	---			---	---
CHMP-glyc			---	---			2.0	<0.001
CHMP			---	---			1.1	<0.001
difluoroethyl-amino-furanone-OH-glyc	---	---			---	---		
difluoroethyl-amino-furanone	---	---			---	---		
glyoxylic acid	0.8	0.001	0.9	0.001	1.8	<0.001	---	---
OH-glyc-SA (1)	---	---	---	---	---	---	---	---
acetic acid-glyc	---	---	---	---	---	---	---	---
OH-glyc-SA (2)	---	---	---	---	---	---	---	---
OH-glyc	2.1	0.002	4.6	0.003	2.3	<0.001	2.4	0.001
acetic acid	1.0	0.001	1.6	0.001	0.2	<0.001	---	---
N-formyl-/N-acetyl-AMCP-difluoroethanamine			---	---			---	---
OH	3.4	0.003	6.4	0.004	---	---	---	---
chloro/ bromo	---	---	---	---	1.6	<0.001	2.0	<0.001
Total identified	**9.2**	**0.009**	**29.0**	**0.017**	**53.0**	**0.007**	**63.6**	**0.013**
Total characterised	**4.2**	**0.004**	**5.6**	**0.003**	**29.3**	**0.004**	**13.9**	**0.003**
Analysed extract(s)	13.4	0.014	34.6	0.02	82.3	0.012	77.5	0.015
Extract(s) not analysed	[1]69.2	[1]0.071	54.8	0.032	---	---	0.6	<0.001
Total extracted	82.6	0.085	34.6	0.020	82.3	0.012	77.5	0.015
Unextractable (PES*)	17.4	0.018	10.5	0.006	17.7	0.003	21.9	0.005
Accountability	**100.0**	**0.103**	**100.0**	**0.057**	**100.0**	**0.014**	**100.0**	**0.022**

* post extraction solids
[1] no analysis performed, but presumably glucose/carbohydrates as identified in grains of 1st rotation
(1) isomer 1 (2) isomer 2 (2 + 3) isomer 2 and/or isomer 3

Label specific metabolites are printed in *italic*.

Table 6.6.2-20 TRR values and distribution of parent compound and metabolites in edible matrices wheat grains and turnip roots (rotational crops; 3rd rotation)

	Confined rotational crops							
	wheat grains				turnip roots			
	[furanone-4-^{14}C]		[pyridinylmethyl-^{14}C]		[furanone-4-^{14}C]		[pyridinylmethyl-^{14}C]	
TRR [mg/kg] =		0.047		0.017		0.008		0.008
Compound (BYI 02960-)	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
BYI 02960	2.0	0.001	13.9	0.002	69.9	0.006	64.8	0.005
glucose/carbohydrates	---	---			5.3	<0.001		
amino-furanone	---	---			5.0	<0.001		
CHMP-glyc-tri-SA			---	---			---	---
6-CNA			---	---			4.7	<0.001
6-CNA-glycerol-gluA (1)			---	---			---	---
6-CNA-glycerol-gluA (2+3)			11.2	0.002			---	---
CHMP-glyc-di-SA			---	---			---	---
CHMP-glyc			---	---			---	---
CHMP			---	---			1.4	<0.001
difluoroethyl-amino-furanone-OH-glyc	---	---			---	---		
difluoroethyl-amino-furanone	---	---			---	---		
glyoxylic acid	---	---	---	---	---	---	---	---
OH-glyc-SA (1)	---	---	---	---	---	---	---	---
acetic acid-glyc	---	---	---	---	---	---	---	---
OH-glyc-SA (2)	---	---	---	---	---	---	---	---
OH-glyc	1.7	0.001	5.2	0.001	3.1	<0.001	3.8	<0.001
acetic acid	0.8	<0.001	1.8	<0.001	0.3	<0.001	---	---
N-formyl-/N-acetyl-AMCP-difluoroethanamine			---	---			---	---
OH	2.8	0.001	5.5	0.001	---	---	---	---
chloro/ bromo	---	---	---	---	2.5	<0.001	2.5	<0.001
Total identified	**7.4**	**0.003**	**37.7**	**0.006**	**86.2**	**0.007**	**77.1**	**0.005**
Total characterised	**4.3**	**0.002**	**7.1**	**0.001**	**9.2**	**0.001**	**12.7**	**0.001**
Analysed extract(s)	11.7	0.005	44.8	0.007	95.5	0.007	89.8	0.006
Extract(s) not analysed	8.8	0.004	---	---	---	---	3.3	<0.001
Total extracted	20.4	0.01	44.8	0.007	95.5	0.008	89.8	0.006
Unextractable (PES*)	[1]79.6	[1]0.037	55.2	0.009	4.5	<0.001	6.9	0.001
Accountability	**100.0**	**0.047**	**100.0**	**0.017**	**100.0**	**0.008**	**100.0**	**0.008**

* post extraction solids

[1] no analysis performed, but presumably glucose/carbohydrates as identified in grains of 1st rotation

(1) isomer 1 (2) isomer 2 (2 + 3) isomer 2 and/or isomer 3

Label specific metabolites are printed in *italic.*

In order to gain information on the fate of the difluoroethane moiety of BYI 02960, the extracts obtained in the CRC study with [furanone-4-^{14}C]BYI 02960 were additionally analysed for non-radiolabelled difluoroacetic acid by LC-MS/MS according to residue method 01304 (see KIIA 6.2./12). Significant levels of difluoroacetic acid were detected in all plant matrices of the first and second rotation. DFA represented the main proportion of the residues in the edible crops wheat grain, Swiss chard and turnip roots and as well as in the feed item wheat hay. In wheat forage and straw and turnip leaves, DFA was less prominent than parent, but it was still a major compound.

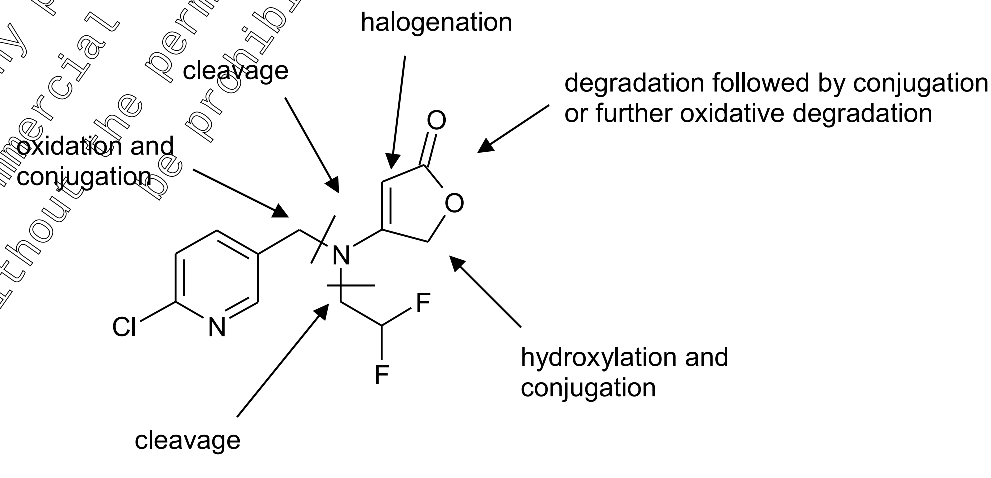
In corresponding crop samples from different plant back intervals, the DFA levels generally decreased significantly from the first to the third rotation, showing DFA levels slightly above or below the limit of quantification in all crops of the third rotation. The highest DFA concentrations were detected in wheat grains ranging from 4.45 mg a.s. equiv./kg in the first rotation to 0.15 mg a.s. equiv./kg in the third rotation.

On basis of the metabolites identified, biotransformation of BYI 02960 in confined rotational crops proceeds by the following main pathways:

- oxidative cleavage of the difluoroethylamine bond and formation of difluoroacetic acid
- cleavage of the pyridinylmethylamine bond and formation of BYI 02960-difluoroethyl-amino-furanone and the corresponding counterparts BYI 02960-CHMP and 6-CNA followed by several conjugation reactions
- cleavage of the furanone moiety followed by several oxidation and conjugation reactions
- complete degradation of the furanone moiety and incorporation of carbon atoms into the natural compound pool, e.g. into glucose/carbohydrates
- hydroxylation of the methylene group of the furanone moiety followed by conjugation with carbohydrates and sulphate
- halogenation (bromination and most probably chlorination, as well) of the furanone moiety

Halogenation of the furanone moiety of the active substance probably occurred in the soil which is supported by the fact that small amounts of halogenated parent compound were identified in the aerobic soil degradation studies.

The positions involved in the metabolic degradation are summarised in the following figure.



IIA 6.6.3 Field trials on representative crops

General remarks:

Metabolite naming:

In this summary section (KIIA 6.6.3), the name DFA and DFEAF will be used for the metabolites difluoroacetic acid and BYI 02960-difluoroethyl-amino-furanone, which are relevant to the tested residue definition:

Name	*Metab. No.*	*Standard "dossier name"*
DFEAF	M34	BYI 02960-difluoroethyl-amino-furanone

References:

In the first edition of this dossier, a report for the primary field rotational crop study was presented here – covering three crop groups (leafy, root, cereal) and three rotations – directly under point KIIA 6.6.3. That report has now been moved to KIIA 6.6.3.1.1.

IIA 6.6.3.1 Field trials on representative crops in the EU

Numerous field rotational crop trials have been conducted to support the use of BYI 02960. In the Annex II dossier, submitted in May 2012, only the "main" field study was described (containing data for three rotations with three crop groups: leafy, root, and cereal crops). In order to enable MRL-setting, further data on individual crops after one rotation ("small" rotational crop studies on tuber, stem, fruiting, bulb, and legume vegetables, as well as pulses and oilseeds) are also submitted in the Annex II dossier at hand.

The field rotational crop studies were conducted at seasonal application rates of 200 g a.s./ha ("main" field study) or 250 g a.s./ha (smaller rotational crop studies), which represent the maximum seasonal rate of BYI 02960 in Europe, or a rate slightly above the maximum seasonal rate. This European rate represents only 45-56% of the proposed maximum rate to be applied in a single crop according to the most critical global use rate in non-perennial crops (450 g a.s./ha = Australian use rate for fruiting vegetables, green beans, and potatoes), and does not account for possible accumulation of BYI 02960 soil residues following repeated annual use.

In order to evaluate the Australian situation, the APVMA has suggested extrapolating from the EU data using relevant factors. Assuming linearity of residues incurred relative to the application rate, a factor of 1.8 or 2.25 is required to account for the rate applied in rotational crop studies (250 or 200 g a.s./ha), compared with the proposed Australian use rate (up to a total of 450 g a.s./ha per crop).

APVMA also requested that soil accumulation of the higher, Australian dose be considered. Modelling of residue accumulation in soil based on an annual application of 450 g a.s./ha and the mean soil half-life of 204 days suggests a steady-state peak soil concentration of 1.4 times the initial concentration. However, the aged residue may not be fully available for uptake by plants. Calculations based on plant residues measured in the confined crop rotational (CRC) study, and the likely soil residues at the various sowing times in this study, support the declining availability of aged residues with time (KIIA 6.10/01, [redacted]; 2012). The analysis suggests that, rather than using a factor of 1.4 to account for potential residues from accumulated soil residue, a factor of 1.2 is appropriate, since not all this aged residue is available for uptake by plants.

IIA 6.6.3.1.1 Barley, carrot, lettuce, and turnip ("main" field study)

Both EU residue regions

Report:	**KIIA 6.6.3.1.1/01, [redacted]; [redacted] 2012**
Former Annex pt.:	KIIA 6.6.3/01
Title:	Determination of the residues of BYI 02960 in/on the field rotational crops barley, carrot, lettuce and turnip after spray application of BYI 02960 SL 200 on lettuce and soil in the field in Germany, the Netherlands, France (South) and Spain
Report No. & Document No.:	10-2503, dated April 11, 2012 M-429091-01-1
Guidelines:	– EU Council Directive 91/414/EEC amended by Commission Directive 96/68/EC – EU Guidance Working Document 7029/VI/95 rev. 5 – OECD Guideline for the Testing of Chemicals No. 504, Residues in Rotational Crops
GLP:	yes (certified laboratory)

I. Materials and Methods

Multi-crop/multi-plot/plantback field rotational crop residue trials were conducted in Europe, two in the northern and two in the southern residue region, as follows:

In 2010-11, 4 trials (one each in Germany, the Netherlands, Spain, and southern France) were conducted to support the use of BYI 02960 SL 200 in field-grown, non-perennial crops ([redacted] & [redacted], 2012, KIIA 6.6.3.1.1/01). A single application was made at a nominal rate of 1 L/ha, corresponding to 200 g/ha BYI 02960 a.s., which reflected the projected rate for soil treatment with BYI 02960 (via irrigation) in arable, non-perennial crops, such as lettuce. Water rates were 300-400 L/ha. Applications were either made to bare soil or to lettuce ("target crop"); in the latter case, the crop was then harvested from the field before further crops were planted. All treatments were made at the scheduled rates. All data pertaining to the application/use pattern are presented in table 6.6.3.1.1-1.

At various intervals, crops were planted back onto the test area in order to simulate a crop failure ("rotation 1", plant-back interval [PBI] 25-33 days), a second use of the plot in the same year ("rotation 2", PBI 60-200 days), or use of the same plot in the succeeding year ("rotation 3", PBI 260-330 days). In each rotation, 3 different crops representing different botanical groups were planted: a root crop (carrots or turnips), a leafy crop (lettuce), or a hard cereal (barley).

Samples of the rotational crops were taken at their respective harvest times, as well as at one earlier interval (immature RACs for lettuce and root crops, or fodder ["green material"] for barley). The samples were analyzed for the parent compound and its metabolites DFA and DFEAF using method 01304 (cf. KIIA 4.3/03). The respective LOQs for the 3 analytes were 0.01, 0.02, and 0.01 mg/kg (all in parent equivalents), yielding a calculated total-residue LOQ of 0.04 mg/kg.

II. Findings

Concurrent recoveries of BYI 02960 and its metabolites DFA and DFEAF were obtained from samples of carrots, turnips, lettuce, and barley. (Validation recoveries were conducted separately. Details of the validation recoveries are presented in chapter 4.3 of this dossier with method 01304.)

Root crops:
Concurrent recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg as well as at 0.10, 0.50, and 1.0 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries in root crop samples (carrot or turnip roots, turnip leaves) were 74-108%, with RSDs of the larger validations sets (n > 2, at the LOQ) of 7.1-16.0%; n=1-6. All values were within acceptable ranges.

For DFA, concurrent recovery samples were spiked at levels of 0.02 mg/kg, as well as at 0.20, 0.50, and 1.0 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries were 84-109%, with RSDs (of the larger validations sets [n > 2]) of 7.4-17.1%; n=1-6.

Details of recovery data are shown in table 6.6.3.1.1-5. All trial data are summarised below in table 6.6.3.1.1-2 and in greater detail in the Tier 1 summary forms. (Residues of parent BYI 02960 as well as its metabolites DFA and DFEAF are expressed in BYI 02960 equivalents.)

The total residues of BYI 02960 (parent compound plus DFA and DFEAF) in the harvested roots of carrots or turnips were generally highest in the first rotation, i.e. after the shortest plant-back interval (PBI) of 25-30 days, when they ranged at an "intermediate" growth stage (including "early harvest", BBCH 47-49) from 0.05-0.14 mg/kg, and at typical harvest ripeness (BBCH 49) from 0.05-0.12 mg/kg. In one trial, however, the residues in the 3rd and final rotation (PBI 284 days) were slightly higher than in the first rotation, at 0.06 mg/kg compared to 0.05 mg/kg. Thus, highest residues in roots in the entire study ranged from 0.06-0.14 mg/kg (median 0.08 mg/kg).

By the third rotation, residues in harvestable roots ranged from <0.04-0.06 mg/kg, with a median value of 0.05 mg/kg.

In turnip tops (=leaves; one trial only), highest residue levels were seen in the first rotation (0.24 mg/kg), but these were not significantly different from those seen in the third rotation (0.21 mg/kg).

Leafy crops:
Concurrent recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg and 0.10 mg/kg, as well as at 0.50, 1.0, and 5.0 mg/kg (expressed in BYI 02960 equivalents). Mean

recoveries in root crop samples (lettuce heads) were 91-105%, with RSDs of the larger validations sets (n > 2) of 2.2-10.7%; n=2-15.

For DFA, concurrent recovery samples were spiked at levels of 0.02, 0.05, and 0.50 mg/kg, as well as at 0.20, 1.0, and 5.0 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries were 90-98%, with RSDs (of the larger validations sets [n > 2]) of 4.3-10.2%; n=2-12.

Details of recovery data are shown in table 6.6.3.1.1-5. All trial data are summarised below in table 6.6.3.1.1-3 and in greater detail in the Tier 1 summary forms. (Residues of parent BYI 02960 as well as its metabolites DFA and DFEAF are expressed in BYI 02960 equivalents.)

The total residues of BYI 02960 (parent compound plus DFA and DFEAF) in the harvested heads of lettuce were highest in the first rotation, i.e. after the shortest plant-back interval (PBI) of 25-30 days, when they ranged at an "intermediate" growth stage (from BBCH 41-47, including "early harvest", BBCH 46-47) from 0.06-0.21 mg/kg, and at typical harvest ripeness (BBCH 49) from <0.04-0.16 mg/kg. Thus, highest residues in "marketable" heads in the entire study ranged from <0.04-0.16 mg/kg, with a median value of 0.08 mg/kg.

By the third rotation, total residues in lettuce heads ranged from <0.04-0.10 mg/kg (median <0.04 mg/kg).

<u>Cereal crops:</u>
Concurrent recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg as well as at 0.10 and 1.0 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries in cereal crop samples (green material, grain, and straw) were 76-110%, with RSDs of the larger validations sets (n > 2, at the LOQ) of 5.6-9.2%; n=1-4. All values were within acceptable ranges.

For DFA, concurrent recovery samples were spiked at levels of 0.02 mg/kg, as well as at 0.05, 0.20, 0.50, and 1.0 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries were 71-108%, with RSDs (of the larger validations sets [n > 2]) of 3.0-7.1%; n=1-3.

Details of recovery data are shown in table 6.6.3.1.1-5. All trial data are summarised below in table 6.6.3.1.1-4 and in greater detail in the Tier 1 summary forms. (Residues of parent BYI 02960 as well as its metabolites DFA and DFEAF are expressed in BYI 02960 equivalents.)

The total residues of BYI 02960 (parent compound plus DFA and DFEAF) in the harvested barley grain were highest in the first rotation, i.e. after the shortest plant-back interval (PBI) of 25-33 days, when they ranged from 0.11-0.65 mg/kg (median 0.35 mg/kg). In one trial, however, no grain samples could be taken due to damage by geese (trial 10-2503-02, Netherlands). Based on the data from straw, it is clear that the missing trial would have yielded residues well below the highest residues and probably below the current median. Residues in straw from the first rotation ranged from <0.07-0.39 mg/kg, with a median value of 0.12 mg/kg. (The level of residues in straw in the Dutch trial were the lowest of any trial.)

By the third rotation, residues in grain ranged from 0.08-0.39 mg/kg, with a median value of 0.12 mg/kg. In straw, they had dropped to <0.07-0.19 mg/kg (median <0.07 mg/kg).

Early in the respective growing periods of each rotation, samples were also taken of green material (forage). Again, residues were highest in the first rotation, in which they ranged from 0.05-0.41 mg/kg, with a median of 0.10 mg/kg. (Residue levels in green material in the Dutch trial were 0.06 mg/kg, below the median and the 2nd-lowest value in this study.)

III. Conclusions

In order to support the use in the EU of BYI 02960 in non-perennial crops, four multi-plant-back multi-crop rotational crop trials were conducted in Europe (2 each in the northern and southern residue regions) in the years 2010-2011. BYI 02960 was applied once as an SL 200 formulation either to bare soil or to a target crop (lettuce) at an active substance rate of 200 g/ha, the target crop was then harvested, and crops representing 3 different botanical groups (roots, leafy veg., cereals) were planted on the plots at 3 intervals thereafter.. All applications were at the required rates, and all trials were conducted according to GLP.

To evaluate the potential residues in following crops, samples of the rotated crops were taken at an intermediate stage and at usual full harvest ripeness. Samples were analyzed for the relevant residues of BYI 02960, comprising the parent compound and its metabolites DFA and DFEAF. The residues of all three analytes were summed to yield a calculated "total residue of BYI 02960". The results of the trials presented above demonstrate that:

– total residues of BYI 02960 in all rotational crops tended to be highest in the first, earliest rotation, i.e. grown after a plant-back interval (PBI) of 25-33 days.

– highest total residues of BYI 02960 in rotational root crops (here: carrot and turnip roots) ranged from 0.06-0.14 mg/kg (median 0.08 mg/kg; n=4). In one trial, residues were also determined in the leaves; the highest measured value was in the first rotation, at 0.24 mg/kg.

– highest total residues of BYI 02960 in marketable rotational leafy crops (here: lettuce) ranged from <0.04-0.16 mg/kg, with a median value of 0.08 mg/kg (n=4).

– in rotated cereals (here: barley), the highest total residues of BYI 02960 in grain ranged from 0.11-0.65 mg/kg. The median value here was 0.35 mg/kg, but only 3 trials could be evaluated as geese ate the grain in the 4th trial. Samples were also taken of the fodder-relevant commodities green material and straw. Residues in straw at harvest were <0.07-0.39 mg/kg (median 0.12 mg/kg; n=4), and in green material taken earlier in the rotation they ranged from 0.05-0.41 mg/kg (median 0.10 mg/kg; n=4).

– if data are re-assessed for assumptions relevant to Australia, based on a maximum global application rate of 450 g a.s./ha and a soil accumulation factor of 1.2, extrapolation of residues would result in the following highest total residues of BYI 02960: 0.38 mg/kg in rotational root crops, 0.43 mg/kg in rotational leafy crops, 1.76 mg/kg in rotational cereal grains, 1.11 mg/kg in

rotational green material of cereals, and 1.05 mg/kg in rotational straw of cereals.
(Cereal grains are considered to be one of the most important export commodities in Australia, and a significant commodity with regard to world trade to the EU; cf. section 6.7.2, including Table 6.7.2.2-67.)

Table 6.6.3.1.1-1: Application scenario in field rotational crop trials (study 10-2503): Spray treatment with BYI 02960 SL 200 to soil or a target crop

Trial No. **Plot No Country Location Region Year**	**Target Crop, Variety**	**FL**	**Application** **No.**	**kg/ha (a.s.)**	**kg/hl (a.s.)**	**GS**
10-2503-01 10-2503-01-T-1A Germany [redacted] EU-N 2010	soil	200 SL	1	0.20	0.067	
10-2503-01 10-2503-01-T-2A Germany [redacted] EU-N 2010	lettuce Argentines, Butterhead variety	200 SL	1	0.20	0.067	19
10-2503-01 10-2503-01-T-3A Germany [redacted] EU-N 2010	lettuce Argentines, Butterhead variety	200 SL	1	0.20	0.067	19
10-2503-02 10-2503-02-T-1A Netherlands [redacted] EU-N 2010	soil	200 SL	1	0.20	0.050	
10-2503-02 10-2503-02-T-2A Netherlands [redacted] EU-N 2010	lettuce Gisela, Butterhead variety	200 SL	1	0.20	0.050	19
10-2503-02 10-2503-02-T-3A Netherlands [redacted] EU-N 2010	lettuce Gisela, Butterhead variety	200 SL	1	0.20	0.050	19

FL = formulation
GS = growth stage (BBCH-code) at last treatment
EU-N = northern European residue region

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Table 6.6.3.1.1-1 (cont'd): Application scenario in field rotational crop trials (study 10-2503): Spray treatment with BYI 02960 SL 200 to soil or a target crop

Trial No. **Plot No Country Location Region Year**	**Target Crop, Variety**	**FL**	**Application**			**GS**
			No.	**kg/ha (a.s.)**	**kg/hl (a.s.)**	
10-2503-03 10-2503-03-T-1A France [redacted] EU-S 2010	soil	200 SL	1	0.20	0.050	
10-2503-03 0-2503-03-T-2A France [redacted] EU-S 2010	lettuce Pitice, Loose leaf	200 SL	1	0.20	0.050	19
10-2503-03 10-2503-03-T-3A France [redacted] EU-S 2010	lettuce Pitice, Loose leaf	200 SL	1	0.20	0.050	19
10-2503-04 10-2503-04-T-1A Spain [redacted] EU-S 2010	soil	200 SL	1	0.20	0.067	
10-2503-04 10-2503-04-T-2A Spain [redacted] EU-S 2010	lettuce Maravilla, Butterroot	200 SL	1	0.212	0.0667	19
10-2503-04 10-2503-04-T-3A Spain [redacted] EU-S 2010	lettuce Maravilla, Butterroot	200 SL	1	0.20	0.067	19

FL = formulation
GS = growth stage (BBCH-code) at last treatment
EU-S = southern European residue region

Table 6.6.3.1.1-2: Results of field rotational crop trials following spray treatment with BYI 02960 SL 200 to soil or a target crop and then planting back and sampling of various rotational crops
Here: **root crops**

Study No. **(Trial No.)** **Plot No** **Country** **GLP**	**Rotational Crop, Variety** **(rotation information)**	**Portion analysed**	**GS**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960** **BYI 02960**	 **difluoro-acetic acid**	 **BYI 02960-difluoro-ethylamino-furanone**	 **total residue of BYI 02960 calc.**
10-2503 (10-2503-01) 10-2503-01-T-1A Germany GLP: yes	Carrot, Cestas F1 (Rotation 1) PBI 25 days	root	47 49	95 109	<0.01 <0.01	0.03 0.03	<0.01 <0.01	0.05 0.05
10-2503 (10-2503-01) 10-2503-01-T-2A Germany GLP: yes	Carrot, Cestas F1 (Rotation 2) PBI 70 days	root	48 49	150 164	<0.01 <0.01	<0.02 <0.02	<0.01 <0.01	<0.04 <0.04
10-2503 (10-2503-01) 10-2503-01-T-3A Germany GLP: yes	Carrot, Cestas (Rotation 3) PBI 284 days	root	48 49	396 410	<0.01 <0.01	0.03 0.04	<0.01 <0.01	0.05 0.06
10-2503 (10-2503-02) 10-2503-02-T-1A Netherlands GLP: yes	Carrot, Nerja (Rotation 1) PBI 25 days	root	48 49	92 106	<0.01 <0.01	0.03 0.05	<0.01 <0.01	0.05 0.07
10-2503 (10-2503-02) 10-2503-02-T-2A Netherlands GLP: yes	Carrot, Nerja (Rotation 2) PBI 61 days	root	48 49	151 165	<0.01 <0.01	0.03 0.03	<0.01 <0.01	0.05 0.05
10-2503 (10-2503-02) 10-2503-02-T-3A Netherlands GLP: yes	Carrot, Nerja (Rotation 3) PBI 328 days	root	47 49	406 420	<0.01 <0.01	<0.02 <0.02	<0.01 <0.01	<0.04 <0.04

DALT = days after last treatment GS = growth stage (BBCH-code) at sampling
PBI = plant-back interval

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Table 6.6.3.1.1-2 (cont'd): Results of field rotational crop trials following spray treatment with BYI 02960 SL 200 to soil or a target crop and then planting back and sampling of various rotational crops
Here: **root crops**

Study No. (Trial No.) Plot No Country GLP	Rotational Crop, Variety (rotation information)	Portion analysed	GS	DALT (days)	Residues (mg/kg) expressed as BYI 02960 BYI 02960	difluoro-acetic acid	BYI 02960-difluoro-ethylamino-furanone	total residue of BYI 02960 calc.
10-2503 (10-2503-03) 10-2503-03-T-1A France GLP: yes	Turnip, edible Aramis (Rotation 1) PBI 25 days	body leaf	49 49 49 49	82 96 82 96	<0.01 <0.01 0.03 0.02	0.12 0.10 0.20 0.07	<0.01 <0.01 <0.01 <0.01	0.14 0.12 0.24 0.10
10-2503 (10-2503-03) 10-2503-03-T-2A France GLP: yes	Turnip, edible Aramis (Rotation 2) PBI 70 days	body leaf	49 49 49 49	127 141 127 141	<0.01 <0.01 0.02 <0.01	0.05 0.04 0.08 0.03	<0.01 <0.01 <0.01 <0.01	0.07 0.06 0.11 0.05
10-2503 (10-2503-03) 10-2503-03-T-3A France GLP: yes	Carrot, Turnip, edible Aramis (Rotation 3) PBI 314 days	body leaf	47 47 49 49	380 394 380 394	<0.01 <0.01 0.03 0.04	0.04 0.03 0.11 0.16	<0.01 <0.01 <0.01 <0.01	0.06 0.05 0.15 0.21
10-2503 (10-2503-04) 10-2503-04-T-1A Spain GLP: yes	Carrot, Coral Nantesa (Rotation 1) PBI 30 days	root	47 49	100 114	<0.01 <0.01	0.05 0.06	<0.01 <0.01	0.07 0.08
10-2503 (10-2503-04) 10-2503-04-T-2A Spain GLP: yes	Carrot, Coral Nantesa (Rotation 2) PBI 145 days	root	49 49	314 328	<0.01 <0.01	0.02 0.03	<0.01 <0.01	0.04 0.05
10-2503 (10-2503-04) 10-2503-04-T-3A Spain GLP: yes	Carrot, Coral Nantesa (Rotation 3) PBI 279 days	root	47 49	349 363	<0.01 <0.01	<0.02 0.03	<0.01 <0.01	<0.04 0.05

DALT = days after last treatment
PBI = plant-back interval
GS = growth stage (BBCH-code) at sampling

Table 6.6.3.1.1-3: Results of field rotational crop trials following spray treatment with BYI 02960 SL 200 to soil or a target crop and then planting back and sampling of various rotational crops
Here: **leafy crops**

Study No. (Trial No.) Plot No Country GLP	Rotational Crop, Variety (rotation information)	Portion analysed	GS	DALT (days)	Residues (mg/kg) expressed as BYI 02960 BYI 02960	difluoro-acetic acid	BYI 02960-difluoro-ethylamino-furanone	total residue of BYI 02960 calc.
10-2503 (10-2503-01) 10-2503-01-T-1B Germany GLP: yes	Lettuce, Argentines, Butterhead variety (Rotation 1) PBI 25 days	head	46 49	63 77	<0.01 <0.01	0.06 0.05	<0.01 <0.01	0.09 0.07
10-2503 (10-2503-01) 10-2503-01-T-2B Germany GLP: yes	Lettuce, Argentines, Butterhead variety (Rotation 2) PBI 77 days	head	46 49	124 138	<0.01 <0.01	<0.02 <0.02	<0.01 <0.01	0.04 0.04
10-2503 (10-2503-01) 10-2503-01-T-3B Germany GLP: yes	Lettuce, Aleppo, Loose leaf variety (Rotation 3) PBI 320 days	head	46 49	354 368	<0.01 <0.01	<0.02 <0.02	<0.01 <0.01	<0.04 <0.04
10-2503 (10-2503-02) 10-2503-02-T-1B Netherlands GLP: yes	Lettuce, Lucan, Butterhead variety (Rotation 1) PBI 25 days	head	41 49	46 60	0.03 <0.01	<0.02 <0.02	<0.01 <0.01	0.06 <0.04
10-2503 (10-2503-02) 10-2503-02-T-2B Netherlands GLP: yes	Lettuce, Lucan, Butterhead variety (Rotation 2) PBI 64 days	head	46 49	95 109	<0.01 <0.01	<0.02 <0.02	<0.01 <0.01	<0.04 <0.04
10-2503 (10-2503-02) 10-2503-02-T-3B Netherlands GLP: yes	Lettuce, Lucan, Butterhead variety (Rotation 3) PBI 329 days	head	45 49	358 372	<0.01 <0.01	<0.02 <0.02	<0.01 <0.01	<0.04 <0.04

DALT = days after last treatment GS = growth stage (BBCH-code) at sampling
PBI = plant-back interval

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Table 6.6.3.1.1-3 (cont'd): Results of field rotational crop trials following spray treatment with BYI 02960 SL 200 to soil or a target crop and then planting back and sampling of various rotational crops
Here: **leafy crops**

Study No. **(Trial No.) Plot No Country** **GLP**	**Rotational Crop, Variety** **(rotation information)**	**Portion analysed**	**GS**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960** **BYI 02960**	**difluoro-acetic acid**	**BYI 02960-difluoro-ethylamino-furanone**	**total residue of BYI 02960 calc.**
10-2503 (10-2503-03) 10-2503-03-T-1B France GLP: yes	Lettuce, Pitice, Loose leaf (Rotation 1) PBI 28 days	head	41 49	55 69	0.08 0.03	0.12 0.11	<0.01 <0.01	0.21 0.16
10-2503 (10-2503-03) 10-2503-03-T-2B France GLP: yes	Lettuce, Pitice, Loose leaf (Rotation 2) PBI 70 days	head	46 49	107 121	0.03 0.01	0.08 0.09	<0.01 <0.01	0.12 0.11
10-2503 (10-2503-03) 10-2503-03-T-3B France GLP: yes	Lettuce, Pitice, Loose leaf (Rotation 3) PBI 314 days	head	46 49	357 371	0.02 <0.01	0.08 0.05	<0.01 <0.01	0.10 0.07
10-2503 (10-2503-04) 10-2503-04-T-1B Spain GLP: yes	Lettuce, Murai, (leafy variety) (Rotation 1) PBI 30 days	head	47 49	72 85	0.03 0.01	0.03 0.03	<0.01 <0.01	0.07 0.06
10-2503 (10-2503-04) 10-2503-04-T-2B Spain GLP: yes	Lettuce, Pelican, Butterhead (Rotation 2) PBI 145 days	head	48 49	291 305	<0.01 <0.01	<0.02 <0.02	<0.01 <0.01	<0.04 <0.04
10-2503 (10-2503-04) 10-2503-04-T-3B Spain GLP: yes	Lettuce, Murai (leafy variety) (Rotation 3) PBI 279 days	head	47 49	321 334	<0.01 <0.01	<0.02 <0.02	<0.01 <0.01	<0.04 <0.04

DALT = days after last treatment GS = growth stage (BBCH-code) at sampling
PBI = plant-back interval

Table 6.6.3.1.1-4: Results of field rotational crop trials following spray treatment with BYI 02960 SL 200 to soil or a target crop and then planting back and sampling of various rotational crops
Here: **cereal crops**

Study No. **(Trial No.) Plot No Country GLP**	**Rotational Crop, Variety (rotation information)**	**Portion analysed**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
				BYI 02960	**difluoroacetic acid**	**BYI 02960-difluoro-ethylamino-furanone**	**total residue of BYI 02960 calc.**
10-2503 (10-2503-01) 10-2503-01-T-1C Germany GLP: yes	Barley, Simba (Rotation 1) PBI 25 days	green material	56	0.01	0.11	<0.01	0.14
		grain	116	<0.01	0.33	<0.01	0.35
		straw	116	0.02	0.13	<0.01	0.15
10-2503 (10-2503-01) 10-2503-01-T-2C Germany GLP: yes	Barley, Leibnitz (Rotation 2) PBI 116 days	green material	305	<0.01	0.03	<0.01	0.05
		grain	406	<0.01	0.10	<0.01	0.12
		straw	406	<0.01	<0.05	<0.01	<0.07
10-2503 (10-2503-01) 10-2503-01-T-3C Germany GLP: yes	Barley, Simba (Rotation 3) PBI 284 days	green material	333	<0.01	<0.02	<0.01	<0.04
		grain	420	<0.01	0.10	<0.01	0.12
		straw	420	<0.01	<0.05	<0.01	<0.07
10-2503 (10-2503-02*) 10-2503-02-T-1C Netherlands GLP: yes	Barley, Cervoise (Rotation 1) PBI 33 days	green material	226	<0.01	0.04	<0.01	0.06
		straw	329	<0.01	<0.05	<0.01	<0.07
10-2503 (10-2503-02) 10-2503-02-T-2C Netherlands GLP: yes	Barley, Cervoise (Rotation 2) PBI 137 days	green material	330	<0.01	0.03	<0.01	0.05
		grain	446	<0.01	0.04	<0.01	0.06
		straw	446	<0.01	<0.05	<0.01	<0.07
10-2503 (10-2503-02) 10-2503-02-T-3C Netherlands GLP: yes	Barley, Tripple (Rotation 3) PBI 295 days	green material	350	<0.01	0.02	<0.01	0.04
		grain	459	<0.01	0.06	<0.01	0.08
		straw	459	<0.01	<0.05	<0.01	<0.07

DALT = days after last treatment
PBI = plant-back interval
* grain could not be taken in the 1st rotation of this trial due to geese feeding on the field

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Table 6.6.3.1.1-4 (cont'd): Results of field rotational crop trials following spray treatment with BYI 02960 SL 200 to soil or a target crop and then planting back and sampling of various rotational crops
Here: **cereal crops**

Study No. **(Trial No.) Plot No Country GLP**	**Rotational Crop, Variety (rotation information)**	**Portion analysed**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
				BYI 02960	**difluoroacetic acid**	**BYI 02960-difluoro-ethylamino-furanone**	**total residue of BYI 02960 calc.**
10-2503 (10-2503-03) 10-2503-03-T-1C France GLP: yes	Barley, Attrction (Rotation 1) PBI 27 days	green material	126	0.02	0.37	<0.01	0.41
		grain	218	<0.01	0.63	<0.01	0.65
		straw	218	0.04	0.34	<0.01	0.39
10-2503 (10-2503-03) 10-2503-03-T-2C France GLP: yes	Barley, Attrction (Rotation 2) PBI 195 days	green material	294	0.01	0.10	<0.01	0.13
		grain	386	<0.01	0.26	<0.01	0.28
		straw	386	0.02	0.10	<0.01	0.12
10-2503 (10-2503-03) 10-2503-03-T-3C France GLP: yes	Barley, Attrction (Rotation 3) PBI 290 days	green material	324	0.03	0.15	<0.01	0.19
		grain	419	<0.01	0.37	<0.01	0.39
		straw	419	<0.01	0.17	<0.01	0.19
10-2503 (10-2503-04) 10-2503-04-T-1C Spain GLP: yes	Barley, Graphic (Rotation 1) PBI 27 days	green material	133	<0.01	0.03	<0.01	0.05
		grain	233	<0.01	0.09	<0.01	0.11
		straw	233	0.01	0.05	<0.01	0.08
10-2503 (10-2503-04) 10-2503-04-T-2C Spain GLP: yes	Barley, Graphic (Rotation 2) PBI 143 days	green material	249	<0.01	0.03	<0.01	0.05
		grain	349	<0.01	0.09	<0.01	0.11
		straw	349	<0.01	<0.05	<0.01	<0.07
10-2503 (10-2503-04) 10-2503-04-T-3C Spain GLP: yes	Barley, Graphic (Rotation 3) PBI 266 days	green material	306	<0.01	0.02	<0.01	0.04
		grain	363	<0.01	0.09	<0.01	0.11
		straw	363	<0.01	<0.05	<0.01	<0.07

DALT = days after last treatment
PBI = plant back interval

Table 6.6.3.1.1-5: Recovery data for BYI 02960 in rotational crop matrices (root, leafy, and cereal crops)

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analysed**	**a.s./metabolite**	**n**	**Fortification level** (mg/kg)	**Recovery (%)** Individual recoveries	Min	Max	Mean	RSD
10-2503 (10-2503-01), (10-2503-02) and (10-2503-04) Plots T-1A to T-3A GLP: yes 2010	carrot	root	BYI 02960	6	0.01	90;99;110;111;120;120	90	120	108	11.0
				1	0.10	87	87	87	87	
				2	0.50	99;107	99	107	103	
				1	1.0	80	80	80	80	
				10	overall		80	120	102	13.4
			difluoroacetic acid	6	0.02	91;99;109;114;114;114	91	114	107	9.1
				1	0.20	86	86	86	86	
				2	0.50	97;97	97	97	97	
				1	1.0	84	84	84	84	
				10	overall		84	114	101	11.6
			BYI 02960-difluoroethyl-aminofuranone	6	0.01	90;92;106;113;118;119	90	119	106	12.0
				1	0.10	95	95	95	95	
				2	0.50	101;105	101	105	103	
				1	1.0	91	91	91	91	
				10	overall		90	119	103	10.7
10-2503 (10-2503-03) Plots T-1A to T-3A GLP: yes 2010	turnip, edible	body	BYI 02960	3	0.01	77;95;100	77	100	91	13.3
				1	0.10	74	74	74	74	
				1	0.50	92	92	92	92	
				5	overall		74	100	88	13.1
			difluoroacetic acid	3	0.02	83;112;115	83	115	103	17.1
				1	0.20	85	85	85	85	
				1	0.50	86	86	86	86	
				5	overall		83	115	96	16.5
			BYI 02960-difluoroethyl-aminofuranone	3	0.01	84;105;116	84	116	102	16.0
				1	0.10	97	97	97	97	
				1	0.50	99	99	99	99	
				5	overall		84	116	100	11.7
		leaf	BYI 02960	3	0.01	94;104;108	94	108	102	7.1
				1	0.10	81	81	81	81	
				1	0.50	103	103	103	103	
				5	overall		81	108	98	11.0
			difluoroacetic acid	3	0.02	100;113;115	100	115	109	7.4
				1	0.20	87	87	87	87	
				1	0.50	88	88	88	88	
				5	overall		87	115	101	13.2

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Table 6.6.3.1.1-5 (cont'd): Recovery data for BYI 02960 in rotational crop matrices (root, leafy, and cereal crops)

Study No. Trial No. GLP Year	Crop	Portion analysed	a.s./metabolite	n	Fortification level (mg/kg)	Recovery (%) Individual recoveries	Min	Max	Mean	RSD
10-2503 (10-2503-03) Plots T-3A GLP: yes 2010 (cont.)	turnip, edible	leaf	BYI 02960-difluoroethyl-aminofuranone	3	0.01	90;99;108	90	108	99	9.1
				1	0.10	92	92	92	92	
				1	0.50	99	99	99	99	
				5	overall		90	108	98	7.3
10-2503 (10-2503-01) to (10-2503-04) Plots T-1B to T-3B GLP: yes 2010	lettuce	head	BYI 02960	15	0.01	79;87;102;106;107 109;110;116;92; 97;107;108;114; 116;117	79	117	104	10.7
				5	0.10	88;90;90;92;93	88	93	91	2.2
				2	0.50	103;106	103	106	105	
				2	1.0	92;94	92	94	93	
				2	5.0	90;98	90	98	94	
				26	overall		79	117	100	10.5
			difluoroacetic acid	12	0.02	90;93;94;95;97; 112;112;116;86; 89;93;95	86	116	98	10.2
				3	0.05	90;94;98	90	98	94	4.3
				2	0.20	92;94	92	94	93	
				5	0.50	93;101;90;91;92	90	101	93	4.7
				2	1.0	90;92	90	92	91	
				2	5.0	90;89	89	90	90	
				26	overall		86	116	95	7.9
			BYI 02960-difluoroethyl-aminofuranone	15	0.01	87;93;95;100;100; 104;105;107;83;83 86;88;90;92;96	83	107	94	8.4
				5	0.10	85;98;97;97;99	85	99	95	6.1
				2	0.50	97;109	97	109	103	
				2	1.0	86;101	86	101	94	
				2	5.0	97;96	96	97	97	
				26	overall		83	109	95	7.7

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Table 6.6.3.1.1-5 (cont'd): Recovery data for BYI 02960 in rotational crop matrices (root, leafy, and cereal crops)

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analysed**	**a.s./metabolite**	**n**	**Fortification level** (mg/kg)	**Recovery (%)** Individual recoveries	Min	Max	Mean	RSD
10-2503 (10-2503-01) to (10-2503-04) Plots T-1C to T-3C GLP: yes 2010	barley	green material	BYI 02960	2	0.01	92;104	92	104	98	
				1	0.10	88	88	88	88	
				1	1.0	85	85	85	85	
				4	overall		85	104	92	9.0
			difluoroacetic acid	2	0.02	88;97	88	97	93	
				1	0.20	87	87	87	87	
				1	1.0	82	82	82	82	
				4	overall		82	97	89	7.1
			BYI 02960-difluoroethyl-aminofuranone	2	0.01	91;93	91	93	92	
				1	0.10	99	99	99	99	
				1	1.0	95	95	95	95	
				4	overall		91	99	95	3.6
		grain	BYI 02960	4	0.01	86;91;98;89	86	98	91	5.6
				2	0.10	90;88	88	90	89	
				1	1.0	105	105	105	105	
				7	overall		86	105	92	7.3
			difluoroacetic acid	3	0.02	94;99;99	94	99	97	3.0
				1	0.05	82	82	82	82	
				1	0.20	72	72	72	72	
				1	0.50	74	74	74	74	
				1	1.0	71	71	71	71	
				7	overall		71	99	84	15.0
			BYI 02960-difluoroethyl-aminofuranone	4	0.01	92;95;95;82	82	95	91	6.8
				2	0.10	92;90	90	92	91	
				1	1.0	110	110	110	110	
				7	overall		82	110	94	9.0
		straw	BYI 02960	4	0.01	95;100;116;98	95	116	102	9.2
				2	0.10	65;92	65	92	79	
				1	1.0	76	76	76	76	
				7	overall		65	116	92	18.2
			difluoroacetic acid	3	0.02	101;106;116	101	116	108	7.1
				1	0.05	95	95	95	95	
				1	0.20	66	66	66	66	
				1	0.50	95	95	95	95	
				1	1.0	71	71	71	71	
				7	overall		66	116	93	19.6

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Table 6.6.3.1.1-5 (cont'd): Recovery data for BYI 02960 in rotational crop matrices (root, leafy, and cereal crops)

Study No. Trial No. GLP Year	Crop	Portion analysed	a.s./metabolite	n	Fortification level (mg/kg)	Recovery (%) Individual recoveries	Min	Max	Mean	RSD
10-2503 (10-2503-01) to (10-2503-04) Plots T-1C to T-3C GLP: yes 2010 contd.			BYI 02960-difluoroethyl-aminofuranone	4 2 1 7	0.01 0.10 1.0 overall	81;83;96;80 71;95 82	80 71 82 71	96 95 82 96	85 83 82 84	8.8 10.5

Table 6.6.3.1.1-6: Extrapolation of total residues of BYI 02960 in rotational crops after application of 450 g a.s./ha to soil or a target crop and then planting back and sampling of various rotational crops
Here: **root crops**

***Study No.* (Trial No.) Plot No Country GLP**	**Rotational Crop, Variety (rotation information)**	**Portion analysed**	**GS**	**DALT (days)**	**Total BYI 02960 residues (mg/kg) measured @ 200g a.s./ha**	**estimated @ 450g a.s./ha**	**estimated @ 450g a.s./ha plus soil accumulation**
10-2503 (10-2503-01) 10-2503-01-T-1A Germany GLP: yes	Carrot, Cestas F1 (Rotation 1) PBI 25 days	root	47 49	95 109	0.05 0.05	0.11 0.11	0.14 0.14
10-2503 (10-2503-01) 10-2503-01-T-2A Germany GLP: yes	Carrot, Cestas F1 (Rotation 2) PBI 70 days	root	48 49	150 164	<0.04 <0.04	<0.09 <0.09	<0.11 <0.11
10-2503 (10-2503-01) 10-2503-01-T-3A Germany GLP: yes	Carrot, Cestas (Rotation 3) PBI 284 days	root	48 49	396 410	0.05 0.06	0.11 0.14	0.14 0.16
10-2503 (10-2503-02) 10-2503-02-T-1A Netherlands GLP: yes	Carrot, Nerja (Rotation 1) PBI 25 days	root	48 49	92 106	0.05 0.07	0.11 0.16	0.14 0.19

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Table 6.6.3.1.1-6 (cont'd): Extrapolation of total residues of BYI 02960 in rotational crops after application of 450 g a.s./ha to soil or a target crop and then planting back and sampling of various rotational crops
Here: **root crops**

Study No. **(Trial No.) Plot No Country GLP**	**Rotational Crop, Variety (rotation information)**	**Portion analysed**	**GS**	**DALT (days)**	**Total BYI 02960 residues (mg/kg)**		
					measured @ 200g a.s./ha	**estimated @ 450g a.s./ha**	**estimated @ 450g a.s./ha plus soil accumulation**
10-2503 (10-2503-02) 10-2503-02-T-2A Netherlands GLP: yes	Carrot, Nerja (Rotation 2) PBI 61 days	root	48 49	151 165	0.05 0.05	0.11 0.11	0.14 0.14
10-2503 (10-2503-02) 10-2503-02-T-3A Netherlands GLP: yes	Carrot, Nerja (Rotation 3) PBI 328 days	root	47 49	406 420	<0.04 <0.04	<0.09 <0.09	<0.11 <0.11
10-2503 (10-2503-03) 10-2503-03-T-1A France GLP: yes	Turnip, edible Aramis (Rotation 1) PBI 25 days	body	49 49	82 96	0.14 0.12	0.32 0.27	0.38 0.32
		leaf	49 49	82 96	0.24 0.10	0.54 0.23	0.65 0.27
10-2503 (10-2503-03) 10-2503-03-T-2A France GLP: yes	Turnip, edible Aramis (Rotation 2) PBI 70 days	body	49 49	127 141	0.07 0.06	0.16 0.14	0.19 0.16
		leaf	49 49	127 141	0.11 0.05	0.25 0.11	0.30 0.14
10-2503 (10-2503-03) 10-2503-03-T-3A France GLP: yes	Carrot, Turnip, edible Aramis (Rotation 3) PBI 314 days	body	47 47	380 394	0.06 0.05	0.14 0.11	0.43 0.14
		leaf	49 49	380 394	0.15 0.21	0.34 0.47	0.41 0.57
10-2503 (10-2503-04) 10-2503-04-T-1A Spain GLP: yes	Carrot, Coral Nantesa (Rotation 1) PBI 90 days	root	47 49	100 114	0.07 0.08	0.16 0.18	0.19 0.22
10-2503 (10-2503-04) 10-2503-04-T-2A Spain GLP: yes	Carrot, Coral Nantesa (Rotation 2) PBI 145 days	root	49 49	314 328	0.04 0.05	0.09 0.11	0.11 0.14

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Table 6.6.3.1.1-6 (cont'd): Extrapolation of total residues of BYI 02960 in rotational crops after application of 450 g a.s./ha to soil or a target crop and then planting back and sampling of various rotational crops
Here: **root crops**

Study No. **(Trial No.)** **Plot No** **Country** **GLP**	**Rotational Crop, Variety** **(rotation information)**	**Portion analysed**	**GS**	**DALT (days)**	**Total BYI 02960 residues (mg/kg)** **measured @ 200g a.s./ha**	**estimated @ 450g a.s./ha**	**estimated @ 450g a.s./ha plus soil accumulation**
10-2503 (10-2503-04) 10-2503-04-T-3A Spain GLP: yes	Carrot, Coral Nantesa (Rotation 3) PBI 279 days	root	47 49	349 363	<0.04 0.05	<0.09 0.11	<0.11 0.14

DALT = days after last treatment
GS = growth stage (BBCH-code) at sampling
PBI = plant-back interval

Table 6.6.3.1.1-7: Extrapolation of total residues of BYI 02960 in rotational crops after application of 450 g a.s./ha to soil or a target crop and then planting back and sampling of various rotational crops
Here: **leafy crops**

Study No. **(Trial No.)** **Plot No** **Country** **GLP**	**Rotational Crop, Variety** **(rotation information)**	**Portion analysed**	**GS**	**DALT (days)**	**Total BYI 02960 residues (mg/kg)** **measured @ 200g a.s./ha**	**estimated @ 450g a.s./ha**	**estimated @ 450g a.s./ha plus soil accumulation**
10-2503 (10-2503-01) 10-2503-01-T-1B Germany GLP: yes	Lettuce, Argentines, Butterhead variety (Rotation 1) PBI 25 days	head	46 49	63 77	0.09 0.07	0.20 0.16	0.24 0.19
10-2503 (10-2503-01) 10-2503-01-T-2B Germany GLP: yes	Lettuce, Argentines, Butterhead variety (Rotation 2) PBI 77 days	head	46 49	124 138	0.04 0.04	0.09 0.09	0.11 0.11
10-2503 (10-2503-01) 10-2503-01-T-3B Germany GLP: yes	Lettuce, Aleppo, Loose leaf variety (Rotation 3) PBI 328 days	head	46 49	354 368	<0.04 <0.04	<0.09 <0.09	<0.11 <0.11
10-2503 (10-2503-02) 10-2503-02-T-1B Netherlands GLP: yes	Lettuce, Lucan, Butterhead variety (Rotation 1) PBI 25 days	head	41 49	46 60	0.06 <0.04	0.14 <0.09	0.16 <0.11

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Table 6.6.3.1.1-7 (cont'd): Extrapolation of total residues of BYI 02960 in rotational crops after application of 450 g a.s./ha to soil or a target crop and then planting back and sampling of various rotational crops
Here: **leafy crops**

Study No. **(Trial No.) Plot No Country GLP**	**Rotational Crop, Variety (rotation information)**	**Portion analysed**	**GS**	**DALT (days)**	**Total BYI 02960 residues (mg/kg)**		
					measured @ 200g a.s./ha	**estimated @ 450g a.s./ha**	**estimated @ 450g a.s./ha plus soil accumulation**
10-2503 (10-2503-02) 10-2503-02-T-2B Netherlands GLP: yes	Lettuce, Lucan, Butterhead variety (Rotation 2) PBI 64 days	head	46 49	95 109	<0.04 <0.04	<0.09 <0.09	<0.11 <0.11
10-2503 (10-2503-02) 10-2503-02-T-3B Netherlands GLP: yes	Lettuce, Lucan, Butterhead variety (Rotation 3) PBI 329 days	head	45 49	358 372	<0.04 <0.04	<0.09 <0.09	<0.11 <0.11
10-2503 (10-2503-03) 10-2503-03-T-1B France GLP: yes	Lettuce, Pitice, Loose leaf (Rotation 1) PBI 28 days	head	41 49	55 69	0.21 0.16	0.47 0.36	0.57 0.43
10-2503 (10-2503-03) 10-2503-03-T-2B France GLP: yes	Lettuce, Pitice, Loose leaf (Rotation 2) PBI 70 days	head	46 49	107 121	0.12 0.11	0.27 0.25	0.32 0.30
10-2503 (10-2503-03) 10-2503-03-T-3B France GLP: yes	Lettuce, Pitice, Loose leaf (Rotation 3) PBI 314 days	head	46 49	357 371	0.10 0.07	0.23 0.16	0.62 0.19
10-2503 (10-2503-04) 10-2503-04-T-1B Spain GLP: yes	Lettuce, Murai, (leafy variety) (Rotation 1) PBI 30 days	head	47 49	72 85	0.07 0.06	0.16 0.14	0.199 0.16
10-2503 (10-2503-04) 10-2503-04-T-2B Spain GLP: yes	Lettuce, Pelican, Butterhead (Rotation 2) PBI 145 days	head	48 49	291 305	<0.04 <0.04	<0.09 <0.09	<0.24 <0.24

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Table 6.6.3.1.1-7 (cont'd): Extrapolation of total residues of BYI 02960 in rotational crops after application of 450 g a.s./ha to soil or a target crop and then planting back and sampling of various rotational crops
Here: **leafy crops**

Study No. (Trial No.) Plot No Country GLP	Rotational Crop, Variety (rotation information)	Portion analysed	GS	DALT (days)	Total BYI 02960 residues (mg/kg) measured @ 200g a.s./ha	estimated @ 450g a.s./ha	estimated @ 450g a.s./ha plus soil accumulation
10-2503 (10-2503-04) 10-2503-04-T-3B Spain GLP: yes	Lettuce, Murai (leafy variety) (Rotation 3) PBI 279 days	head	47 49	321 234	<0.04 <0.04	<0.09 <0.09	<0.11 <0.11

DALT = days after last treatment
GS = growth stage (BBCH-code) at sampling
PBI = plant-back interval

Table 6.6.3.1.1-8: Extrapolation of total residues of BYI 02960 in rotational crops after application of 450 g a.s./ha to soil or a target crop and then planting back and sampling of various rotational crops
Here: **cereal crops**

Study No. (Trial No.) Plot No Country GLP	Rotational Crop, Variety (rotation information)	Portion analysed	DALT (days)	Total BYI 02960 residues (mg/kg) measured @ 200g a.s./ha	estimated @ 450g a.s./ha	estimated @ 450g a.s./ha plus soil accumulation
10-2503 (10-2503-01) 10-2503-01-T-1C Germany GLP: yes	Barley, Simba (Rotation 1) PBI 25 days	green material	56	0.14	0.32	0.38
		grain	116	0.35	0.79	0.95
		straw	116	0.15	0.34	0.41
10-2503 (10-2503-01) 10-2503-01-T-2C Germany GLP: yes	Barley, Leibnitz (Rotation 2) PBI 116 days	green material	305	0.05	0.11	0.14
		grain	406	0.12	0.27	0.32
		straw	406	<0.07	<0.16	<0.19
10-2503 (10-2503-01) 10-2503-01-T-3C Germany GLP: yes	Barley, Simba (Rotation 3) PBI 284 days	green material	333	<0.04	<0.09	<0.11
		grain	420	0.12	0.27	0.32
		straw	420	<0.07	<0.16	0.19
10-2503 (10-2503-02*) 10-2503-02-T-1C Netherlands GLP: yes	Barley, Cervoise (Rotation 1) PBI 33 days	green material	226	0.06	0.14	0.16
		straw	329	<0.07	<0.16	<0.19

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Table 6.6.3.1.1-8 (cont'd): Extrapolation of total residues of BYI 02960 in rotational crops after application of 450 g a.s./ha to soil or a target crop and then planting back and sampling of various rotational crops
Here: **cereal crops**

Study No. **(Trial No.) Plot No Country** **GLP**	**Rotational Crop, Variety** **(rotation information)**	**Portion analysed**	**DALT (days)**	**Total BYI 02960 residues (mg/kg)** measured @ 200g a.s./ha	**Total BYI 02960 residues (mg/kg)** estimated @ 450g a.s./ha	**Total BYI 02960 residues (mg/kg)** estimated @ 450g a.s./ha plus soil accumulation
10-2503 (10-2503-02) 10-2503-02-T-2C Netherlands GLP: yes	Barley, Cervoise (Rotation 2) PBI 137 days	green material	330	0.05	0.11	0.14
		grain	446	0.06	0.14	0.16
		straw	446	<0.07	<0.16	0.19
10-2503 (10-2503-02) 10-2503-02-T-3C Netherlands GLP: yes	Barley, Tripple (Rotation 3) PBI 295 days	green material	350	0.04	0.09	0.11
		grain	459	0.08	0.18	0.22
		straw	459	<0.07	<0.16	>0-19
10-2503 (10-2503-03) 10-2503-03-T-1C France GLP: yes	Barley, Attrction (Rotation 1) PBI 27 days	green material	126	0.41	0.92	1.11
		grain	218	0.65	1.46	1.76
		straw	218	0.39	0.88	1.05
10-2503 (10-2503-03) 10-2503-03-T-2C France GLP: yes	Barley, Attrction (Rotation 2) PBI 195 days	green material	294	0.13	0.29	0.35
		grain	386	0.28	0.63	0.76
		straw	386	0.12	0.27	0.32
10-2503 (10-2503-03) 10-2503-03-T-3C France GLP: yes	Barley, Attrction (Rotation 3) PBI 290 days	green material	324	0.19	0.43	0.51
		grain	419	0.39	0.88	1.05
		straw	419	0.19	0.43	0.51
10-2503 (10-2503-04) 10-2503-04-T-1C Spain GLP: yes	Barley, Graphic (Rotation 1) PBI 27 days	green material	133	0.05	0.11	0.14
		grain	233	0.11	0.25	0.30
		straw	233	0.08	0.18	0.22
10-2503 (10-2503-04) 10-2503-04-T-2C Spain GLP: yes	Barley, Graphic (Rotation 2) PBI 143 days	green material	249	0.05	0.11	0.14
		grain	349	0.11	0.25	0.30
		straw	349	<0.07	<0.16	<0.19

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Table 6.6.3.1.1-8 (cont'd): Extrapolation of total residues of BYI 02960 in rotational crops after application of 450 g a.s./ha to soil or a target crop and then planting back and sampling of various rotational crops
Here: **cereal crops**

Study No. **(Trial No.) Plot No Country** **GLP**	**Rotational Crop, Variety** **(rotation information)**	**Portion analysed**	**DALT (days)**	**Total BYI 02960 residues (mg/kg)**		
				measured @ 200g a.s./ha	**estimated @ 450g a.s./ha**	**estimated @ 450g a.s./ha plus soil accumulation**
10-2503 (10-2503-04) 10-2503-04-T-3C Spain GLP: yes	Barley, Graphic (Rotation 3) PBI 266 days	green material	306	0.04	0.09	0.24
		grain	363	0.11	0.25	0.30
		straw	363	<0.07	<0.16	0.19

DALT = days after last treatment
PBI = plant-back interval

IIA 6.6.3.1.2 Potato (tuber crops)

Both EU residue regions

Report:	**KIIA 6.6.3.1.2/01, [redacted], 2012**
Title:	Determination of the residues of BYI 02960 in/on the field rotational crop potato after spray application of BYI 02960 SL 200 to bare soil in the field in northern France, the Netherlands, Spain and Italy-Limited Rotational Crop Study
Report No. & Document No.:	11-2550, dated September 10, 2012 M-438341-01-1
Guidelines:	– EU Council Directive 91/414/EEC – EU Guidance Working Document 7029/VI/95 rev. 5 – OECD Guideline for the Testing of Chemicals No. 504: Residues in Rotational Crops
GLP:	yes (certified laboratory)

I. Materials and Methods

Smaller (single-crop, single-rotation) field rotational crop residue trials were conducted in Europe, two in the northern and two in the southern residue regions, as follows:

In 2011, 4 trials (one each in northern France, the Netherlands, Spain, and Italy) were conducted to support the use of BYI 02960 SL 200 in field-grown, non-perennial tuber crops ([redacted], 2012, KIIA 6.6.3.1.2/01). The product was applied twice with an application interval of 10 days (9 days in one trial) at a nominal rate of 0.625 L/ha, corresponding to 125 g/ha BYI 02960 a.s. The application scenario was designed to approximate the situation in which the original crop failed, and the field was used again very shortly thereafter, in the same season, to grow a subsequent crop. As such, the use pattern used reflected a typical use in non-perennial (vegetable) crops, such as lettuce, followed by a defined interval before re-planting. Water rates were 300-400 L/ha. Applications were made to bare soil. At the second application, the test item was incorporated into the soil. All treatments were made at the scheduled rates with the exception of the Spanish trial, in which the second application was overdosed by 8.9%, which is well within the EU's tolerance of 25%. All data pertaining to the application/use pattern are presented in table 6.6.3.1.2-1.

After a plant-back interval of 25-33 days, potatoes were planted. Samples of potato tuber were taken at typical harvest maturity (BBCH growth stage 45-49). The samples were analyzed for the parent compound and its metabolites DFA and DFEAF using method 01304 (cf. KIIA 4.3/03). The respective LOQs for the 3 analytes were 0.01 mg/kg, 0.02 mg/kg, and 0.01 mg/kg (all in parent equivalents), yielding a calculated total-residue LOQ of 0.04 mg/kg.

II. Findings

Method validation of sample material potato tuber was conducted within the present study for BYI 02960 and its metabolites DFA and DFEAF. Concurrent recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg as well as at 0.10 mg/kg and 1.0 mg/kg (expressed in

BYI 02960 equivalents). Mean recoveries in potato tuber were 92-101%, with RSDs of the larger validations sets (n > 2) of 5.5-6.4%; n = 1-7. All values were within acceptable ranges.

For DFA, concurrent recovery samples were spiked at levels of 0.02 mg/kg, as well as at 0.20 and 1.0 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries were 88-100%, with RSDs of the larger validations sets (n > 2) of 5.0-12.6%; n = 1-7. All values were within acceptable ranges.

Details of recovery data are shown in table 6.6.3.1.2-3. All trial data are summarised below in table 6.6.3.1.2-2 and in greater detail in the Tier 1 summary forms. (Residues of parent BYI 02960 as well as its metabolites DFA and DFEAF are expressed in BYI 02960 equivalents.)

In rotational potatoes sampled at harvest in this study, the total residues of BYI 02960 in tubers ranged from 0.048-0.27 mg/kg, with a median value of 0.13 mg/kg (n=4).

III. Conclusions

In order to support the use in the EU of BYI 02960 in non-perennial crops, four single-rotation, single-crop rotational crop trials were conducted in Europe (2 each in the northern and southern residue regions) in 2011 on potatoes, representing tuber vegetables. BYI 02960 was applied twice as an SL 200 formulation to bare soil at an active substance rate of 125 g/ha followed by incorporation at the second application. 25–33 days after the second application, potatoes were planted. All applications were at the required rates, except in one trial, in which the 2nd application was overdosed by approx. 9%; this deviation was well within the EU's tolerance of 25%. All trials were conducted according to GLP.

To evaluate the potential residues in following crops, samples of the rotated crop were taken at harvest time (BBCH growth stage 45-49). Samples were analyzed for the relevant residues of BYI 02960, comprising the parent compound and its metabolites DFA and DFEAF. The residues of all three analytes were summed to yield a calculated "total residue of BYI 02960". The total residues of BYI 02960 in potato tuber ranged from 0.048-0.27 mg/kg with a median value of 0.13 mg/kg (n=4).

If data are re-assessed for assumptions relevant to Australia, based on a maximum global application rate of 450 g a.s./ha and a soil accumulation factor of 1.2, extrapolation of residues would result in highest total residues of BYI 02960 in potato tuber of 0.58 mg/kg. This residue value corresponds to the highest residue value estimated in rotational potatoes grown outside of Europe.
(Potatoes are considered to be a relevant commodity with regard to world trade to the EU; cf. section 6.7.2.2, including Table 6.7.2.2-67.)

Table 6.6.3.1.2-1: Application scenario in field rotational crop trials (study 11-2550): Spray treatment with BYI 02960 SL 200 to soil followed by planting of **potato**

Trial No. **Plot No Country Location Region Year**	**Target Test System**	**FL**	**Application**		
			No.	**kg/ha (a.s.)**	**kg/hl (a.s.)**
11-2550-01 11-2550-01 northern France [redacted] EU-N 2011	soil	200 SL	2	0.125	0.0417
11-2550-02 11-2550-02 Netherlands [redacted] EU-N 2011	soil	200 SL	2	0.125	0.0313
11-2550-03 11-2550-03 Spain [redacted] EU-S 2011	soil	200 SL	2	0.125-0.136*	0.0417
11-2550-04 11-2550-04 Italy [redacted] EU-S 2011	soil	200 SL	2	0.125	0.0417

FL=formulation
GS=growth stage (BBCH-code) at last treatment
EU-N=northern European residue region
EU-S=southern European residue region

* the second application was overdosed by 8.9%

Table 6.6.3.1.2-2: Results of field rotational crop trials following spray treatment with BYI 02960 SL 200 to soil and then planting back and sampling of **potato tuber**

Study No. **(Trial No.) Plot No Country GLP**	**Rotational Crop, Variety (rotation information)**	**Portion analyzed**	**GS**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
					BYI 02960	**DFA**	**BYI 02960-DFEAF**	**total residue of BYI 02960 calc.**
11-2550 (11-2550-01) northern France GLP: yes	potato Resy (early variety) (Rotation 1) PBI: 31 days	tuber	49	122	<0.01	0.19	<0.01	0.21
11-2550 (11-2550-02) Netherlands GLP: yes	potato Riviera (Rotation 1) PBI: 33 days	tuber	48	98	<0.01	0.028	<0.01	0.048
11-2550 (11-2550-03) Spain GLP: yes	potato Red Pontiac (cooking potatoes) (Rotation 1) PBI: 25 days	tuber	49	126	<0.01	0.25	<0.01	0.27
11-2550 (11-2550-04) Italy GLP: yes	potato Arinda (Rotation 1) PBI: 30 days	tuber	45	137	<0.01	0.036	<0.01	0.056

DALT=days after last treatment GS=growth stage (BBCH-code) at sampling
PBI=plant-back interval

Table 6.6.3.1.2-3: Recovery data for BYI 02960 in rotational crop matrix **potato tuber**

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortifi-cation level** (mg/kg)	**Recovery (%)**				
						Individual recoveries	**Min**	**Max**	**Mean**	**RSD**
11-2550 (11-2550-01), to (11-2550-04) GLP: yes 2011	potato	tuber	BYI 02960	7	0.01	89; 90; 93; 94; 96; 101; 106	89	106	96	6.4
				4	0.10	83; 92; 96; 98	83	98	92	7.2
				1	1.0	94	94	94	94	
				12	overall		89	106	94	6.3
			DFA	7	0.02	79; 88; 101; 104; 105; 110; 115	79	115	100	12.6
				4	0.20	86; 92; 94; 97	86	97	92	5.0
				1	1.0	88	88	88	88	
				12	overall		79	115	97	11.1
			BYI 02960-DFEAF	7	0.01	89; 91; 92; 94; 94; 94; 105	89	105	94	5.5
				4	0.10	87; 98; 99; 100	87	100	96	6.3
				1	1.0	101	101	101	101	
				12	overall		87	105	95	5.6

Table 6.6.3.1.2-4: Extrapolation of total residues of BYI 02960 in rotational potatoes after application of 450 g a.s./ha to soil and then planting back

Study No. **(Trial No.) Plot No Country GLP**	**Rotational Crop, Variety (rotation information)**	**Portion analysed**	**GS**	**DALT (days)**	**Total BYI 02960 residues (mg/kg)**		
					measured @ 250g a.s./ha	**estimated @ 450g a.s./ha**	**estimated @ 450g a.s./ha plus soil accumulation**
11-2550 (11-2550-01) northern France GLP: yes	potato Resy (early variety) (Rotation 1) PBI: 31 days	tuber	49	122	0.21	0.38	0.45
11-2550 (11-2550-02) Netherlands GLP: yes	potato Riviera (Rotation 1) PBI: 33 days	tuber	48	98	0.048	0.09	0.10
11-2550 (11-2550-03) Spain GLP: yes	potato Red Pontiac (cooking potatoes) (Rotation 1) PBI: 25 days	tuber	49	126	0.27	0.49	0.58
11-2550 (11-2550-04) Italy GLP: yes	potato Arinda (Rotation 1) PBI: 30 days	tuber	45	137	0.056	0.10	0.12

DALT=days after last treatment GS=growth stage (BBCH-code) at sampling
PBI=plant-back interval

IIA 6.6.3.1.3 Leek (stem vegetables)

Both EU residue regions

Report:	**KIIA 6.6.3.1.3/01, [redacted], 2012**
Title:	Determination of the residues of BYI 02960 in/on the field rotational crop leek after spray application of BYI 02960 SL 200 to bare soil in the field in northern France, Germany, Spain and Italy-Limited Rotational Crop Study
Report No. & Document No.:	11-2551, dated September 13, 2012 M-438384-01-1
Guidelines:	– EU Council Directive 91/414/EEC amended by Commission Directive 96/68/EC – EU Guidance Working Document 7029/VI/95 rev. 5 – OECD Guideline for the Testing of Chemicals No. 504, Residues in Rotational Crops
GLP:	yes (certified laboratory)

I. Materials and Methods

Smaller (single-crop, single-rotation) field rotational crop residue trials were conducted in Europe, two in the northern and two in the southern residue regions, as follows:

In 2011-11, 4 trials (one each in northern France, Germany, Spain, and Italy) were conducted to support the use of BYI 02960 SL 200 in field-grown, non-perennial stem vegetable crops ([redacted], 2012, KIIA 6.6.3.1.3/01). The product was applied twice with an application interval of 10 days (13 days in one trial) at a nominal rate of 0.625 L/ha, corresponding to 125 g/ha BYI 02960 a.s. The application scenario was designed to approximate the situation in which the original crop failed, and the field was used again very shortly thereafter, in the same season, to grow a subsequent crop. As such, the use pattern used reflected a typical use in non-perennial (vegetable) crops, such as lettuce, followed by a defined interval before re-planting. Water rates were 300-400 L/ha. Applications were made to bare soil. At the second application, the test item was incorporated into the soil. All treatments were made at the scheduled rates. All data pertaining to the application/use pattern are presented in table 6.6.3.1.3-1.

After a plant-back interval of 26-33 days, leeks were planted. Samples of leek (whole plant without root) were taken at typical harvest maturity (BBCH growth stage 48-49). The samples were analyzed for the parent compound and its metabolites DFA and DFEAF using method 01304 (cf. KIIA 4.3/03). The respective LOQs for the 3 analytes were 0.01 mg/kg, 0.02 mg/kg, and 0.01 mg/kg (all in parent equivalents), yielding a calculated total-residue LOQ of 0.04 mg/kg.

II. Findings

Method validations for the sample material leek (whole plant without root) for BYI 02960 and its metabolites DFA and DFEAF were done during the conduct of study 10-2503 (KIIA cf. 6.6.3.1/01) and within the present study 11-2551. Concurrent recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg as well as at 0.10 mg/kg (expressed in BYI 02960 equivalents).

Mean recoveries in leek, whole plant without root were 86-89%, with RSDs of the larger validations sets (n > 2) of 3.0-9.9%; n=3-5. All values were within acceptable ranges.

For DFA, concurrent recovery samples were spiked at levels of 0.02 mg/kg, as well as at 0.20 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries were 85-88%, with RSDs of the larger validations sets (n > 2) of 2.7-13.2%; n=3-5. All values were within acceptable ranges.

Details of recovery data are shown in table 6.6.3.1.3-3. All trial data are summarised below in table 6.6.3.1.3-2 and in greater detail in the Tier 1 summary forms. (Residues of parent BYI 02960 as well as its metabolites DFA and DFEAF are expressed in BYI 02960 equivalents.)

In rotational leeks sampled at harvest in this study, the total residues of BYI 02960 in whole plant without root ranged from 0.040-0.25 mg/kg, with a median value of 0.085 mg/kg (n=4).

III. Conclusions

In order to support the use in the EU of BYI 02960 in non-perennial crops, four single-rotation, single-crop rotational crop trials were conducted in Europe (2 each in the northern and southern residue regions) in 2011 on leeks, representing stem vegetables. BYI 02960 was applied twice as an SL 200 formulation to bare soil at an active substance rate of 125 g/ha, followed by incorporation at the second application. 26-33 days after the second application, leeks were planted. All applications were at the required rates, and all trials were conducted according to GLP.

To evaluate the potential residues in following crops, samples of the rotated crop were taken at typical harvest maturity (BBCH growth stage 48-49). Samples were analyzed for the relevant residues of BYI 02960, comprising the parent compound and its metabolites DFA and DFEAF. The residues of all three analytes were summed to yield a calculated "total residue of BYI 02960". The total residues of BYI 02960 in leek (whole plant without root) ranged from 0.040-0.25 mg/kg, with a median value of 0.085 mg/kg (n=4).

If data are re-assessed for assumptions relevant to Australia, based on a maximum global application rate of 450 g a.s./ha and a soil accumulation factor of 1.2, extrapolation of residues would result in highest total residues of BYI 02960 in stem vegetables of 0.54 mg/kg. This residue value corresponds to the highest residue value estimated in rotational stem vegetables grown outside of Europe.

(Stem vegetables, with the exception of celery, are not considered to be commodities which are imported in significant quantities to the EU, thus the extrapolated values shown here will not play a role in the evaluation and proposal of an EU MRL; cf. section 6.7.2.2.)

Table 6.6.3.1.3-1: Application scenario in field rotational crop trials (study 11-2551): Spray treatment with BYI 02960 SL 200 to soil followed by planting of **leek**

Trial No. **Plot No Country Location Region Year**	**Target Test System**	**FL**	**Application**		
			No.	**kg/ha (a.s.)**	**kg/hl (a.s.)**
11-2551-01 11-2551-01 northern France [redacted] EU-N 2011	soil	200 SL	2	0.125	0.0417
11-2551-02 11-2551-02 Germany [redacted] EU-N 2011	soil	200 SL	2	0.125	0.0417
11-2551-03 11-2551-03 Spain [redacted] EU-S 2011	soil	200 SL	2	0.125	0.0417
11-2551-04 11-2551-04 Italy [redacted] EU-S 2011	soil	200 SL	2	0.125	0.0313

FL=formulation
GS=growth stage (BBCH-code) at last treatment
EU-N=northern European residue region
EU-S=southern European residue region

Table 6.6.3.1.3-2: Results of field rotational crop trials following spray treatment with BYI 02960 SL 200 to soil and then planting back and sampling of **leek** (**whole plant without root)**

Study No. **(Trial No.) Plot No Country** **GLP**	**Rotational Crop, Variety** **(rotation information)**	**Portion analyzed**	**GS**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
					BYI 02960	**DFA**	**BYI 02960-DFEAF**	**total residue of BYI 02960 calc.**
11-2551 (10-2551-01) France GLP: yes	leek, Bleu de Solaize leek (Rotation 1) PBI 26 days	whole plant without root	49	103	<0.01	0.23	<0.01	0.25
11-2551 (11-2551-02) Germany GLP: yes	leek, Prelina (Rotation 1) PBI 33 days	whole plant without root	48	130	<0.01	0.095	<0.01	0.11
11-2551 (11-2551-03) Spain GLP: yes	leek, Atal Temprano – early variety (Rotation 1) PBI 28 days	whole plant without root	49	97	<0.01	0.020	<0.01	0.040
11-2551 (11-2551-04) Italy GLP: yes	leek, Libertas (Rotation 1) PBI 31 days	whole plant without root	49	112	<0.01	0.039	<0.01	0.059

DALT=days after last treatment GS=growth stage (BBCH-code) at sampling
PBI=plant-back interval

Table 6.6.3.1.3-3: Recovery data for BYI 02960 in rotational crop matrix **leek (whole plant without root)**

Study No. **Trial No.** **GLP Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortification level** (mg/kg)	**Recovery (%)**				
						Individual recoveries	**Min**	**Max**	**Mean**	**RSD**
11-2551 (11-2551-01), to (11-2551-04) GLP: yes 2011	leek	whole plant without root	BYI 02960	5	0.01	73; 87; 90; 91; 96	73	96	87	9.9
				3	0.10	83; 88; 89	83	89	87	3.7
				8	overall		73	96	87	7.8
			DFA	5	0.02	68; 86; 94; 95; 95	68	95	88	13.2
				3	0.20	82; 86; 86	82	86	85	2.7
				8	overall		68	95	87	10.4
			BYI 02960-DFEAF	5	0.01	71; 88; 88; 90; 91	71	91	86	9.7
				3	0.10	86; 90; 91	86	91	89	3.0
				8	overall		71	91	87	7.6

Table 6.6.3.1.3-4: Extrapolation of total residues of BYI 02960 in rotational stem vegetables (leek) after application of 450 g a.s./ha to soil and then planting back

Study No. **(Trial No.) Plot No Country GLP**	**Rotational Crop, Variety (rotation information)**	**Portion analysed**	**GS**	**DALT (days)**	**Total BYI 02960 residues (mg/kg)**		
					measured @ 250g a.s./ha	**estimated @ 450g a.s./ha**	**estimated @ 450g a.s./ha plus soil accumulation**
11-2551 (10-2551-01) France GLP: yes	leek, Bleu de Solaize leek (Rotation 1) PBI 26 days	whole plant without root	49	103	0.25	0.45	0.54
11-2551 (11-2551-02) Germany GLP: yes	leek, Prelina (Rotation 1) PBI 33 days	whole plant without root	48	130	0.11	0.20	0.24
11-2551 (11-2551-03) Spain GLP: yes	leek, Atal Temprano – early variety (Rotation 1) PBI 28 days	whole plant without root	49	97	0.040	0.07	0.09
11-2551 (11-2551-04) Italy GLP: yes	leek, Libertas (Rotation 1) PBI 31 days	whole plant without root	49	112	0.059	0.11	0.13

DALT=days after last treatment GS=growth stage (BBCH code) at sampling
PBI=plant-back interval

IIA 6.6.3.1.4 Cucumber (fruiting vegetables)

Both EU residue regions

Report:	**KIIA 6.6.3.1.4/01, [redacted], 2012**
Title:	Determination of the residues of BYI 02960 in/on the field rotational crop cucumber after spray application of BYI 02960 SL 200 to bare soil in the field in northern France, Germany, Spain and Italy-Limited Rotational Crop Study
Report No. & Document No.:	11-2552, dated September 13, 2012 M-438343-01-1
Guidelines:	– EU Council Directive 91/414/EEC – EU Guidance Working Document 7029/VI/95 rev. 5 – OECD Guideline for the Testing of Chemicals No. 504: Residues in Rotational Crops
GLP:	yes (certified laboratory)

I. Materials and Methods

Smaller (single-crop, single-rotation) field rotational crop residue trials were conducted in Europe, two in the northern and two in the southern residue regions, as follows:

In 2011, 4 trials (one each in northern France, Germany, Spain, and Italy) were conducted to support the use of BYI 02960 SL 200 in field-grown, non-perennial fruiting vegetable crops ([redacted], 2012, KIIA 6.6.3.1.4/01). The product was applied twice with an application interval of 10 days at a nominal rate of 0.625 L/ha, corresponding to 125 g/ha BYI 02960 a.s. The application scenario was designed to approximate the situation in which the original crop failed, and the field was used again very shortly thereafter, in the same season, to grow a subsequent crop. As such, the use pattern used reflected a typical use in non-perennial (vegetable) crops, such as lettuce, followed by a defined interval before re-planting. Water rates were 300-400 L/ha. Applications were made to bare soil. At the second application the test item was incorporated into the soil. All treatments were made at the scheduled rates. All data pertaining to the application/use pattern are presented in table 6.6.3.1.4-1.

After a plant-back interval of 25-30 days, cucumbers were planted. Samples of cucumber fruit were taken at typical harvest maturity (BBCH growth stage 71-79). The samples were analyzed for the parent compound and its metabolites DFA and DFEAF using method 01304 (cf. KIIA 4.3/03). The respective LOQs for the 3 analytes were 0.01, 0.02, and 0.01 mg/kg (all in parent equivalents), yielding a calculated total-residue LOQ of 0.04 mg/kg.

II. Findings

Method validation work for the sample material cucumber fruit for BYI 02960 and its metabolites DFA and DFEAF was conducted during study 10-2189 (cf. KIIA 6.3.1.7/03) Concurrent recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg as well as at 0.10 mg/kg and 1.0 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries in cucumber fruit were 90-102%, with RSDs of the larger validations sets (n > 2) of 0.6-6.2%; n=2-5. All values were within acceptable ranges.

For DFA, concurrent recovery samples were spiked at levels of 0.02 mg/kg, as well as at 0.20 and 1.0 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries were 87-96%, with RSDs of the larger validations sets (n > 2) of 6.6-11.9%; n=2-5. All values were within acceptable ranges.

Details of recovery data are shown in table 6.6.3.1.4-3. All trial data are summarised below in table 6.6.3.1.4-2 and in greater detail in the Tier 1 summary forms. (Residues of parent BYI 02960 as well as its metabolites DFA and DFEAF are expressed in BYI 02960 equivalents.)

In rotational cucumbers sampled at harvest in this study, the total residues of BYI 02960 in samples of fruit ranged from 0.067-0.43 mg/kg, with a median value of 0.32 mg/kg (n=4).

III. Conclusions

In order to support the use in the EU of BYI 02960 in non-perennial crops, four single-rotation, single-crop rotational crop trials were conducted in Europe (2 each in the northern and southern residue regions) in 2011 on cucumbers, representing fruiting vegetables. BYI 02960 was applied twice as an SL 200 formulation to bare soil at an active substance rate of 125 g/ha, followed by incorporation at the second application. 25–30 days after the second application, cucumbers were planted. All applications were at the required rates, and all trials were conducted according to GLP.

To evaluate the potential residues in following crops, samples of the rotated crop were taken at typical harvest maturity (BBCH growth stage 71-79). Samples were analyzed for the relevant residues of BYI 02960, comprising the parent compound and its metabolites DFA and DFEAF. The residues of all three analytes were summed to yield a calculated "total residue of BYI 02960". The total residues of BYI 02960 in cucumber fruit ranged from 0.067-0.43 mg/kg, with a median value of 0.32 mg/kg (n=4).

If data are re-assessed for assumptions relevant to Australia, based on a maximum global application rate of 450 g a.s./ha and a soil accumulation factor of 1.2, extrapolation of residues would result in highest total residues of BYI 02960 in fruiting vegetables of 0.93 mg/kg. This residue value corresponds to the highest residue value estimated in rotational fruting vegetables grown outside of Europe.
(Some fruit vegetables – e.g. tomatoes and chili peppers – are considered to be relevant commodities with regard to world trade to the EU, while others are not traded significantly to Europe; cf. section 6.7.2.2, including Table 6.7.2.2-67.)

Table 6.6.3.1.4-1: Application scenario in field rotational crop trials (study 11-2552): Spray treatment with BYI 02960 SL 200 to soil followed by planting of **cucumbers**

Trial No. **Plot No Country Location Region Year**	**Target Test System**	**FL**	**Application**		
			No.	**kg/ha (a.s.)**	**kg/hl (a.s.)**
11-2552 (11-2552-01) northern France [redacted] EU-N 2011	soil	200 SL	2	0.125	0.0417
11-2552 (11-2552-02) Germany [redacted] EU-N 2011	soil	200 SL	2	0.125	0.0417
11-2552 (11-2552-03) Spain [redacted] EU-S 2011	soil	200 SL	2	0.125	0.0417
11-2552 (11-2552-04) Italy [redacted] EU-S 2011	soil	200 SL	2	0.125	0.0313

FL=formulation
GS=growth stage (BBCH-code) at last treatment
EU-N=northern European residue region
EU-S=southern European residue region

Table 6.6.3.1.4-2: Results of field rotational crop trials following spray treatment with BYI 02960 SL 200 to soil and then planting back and sampling of **cucumber fruit**

Study No. **(Trial No.) Plot No Country GLP**	**Rotational Crop, Variety (rotation information)**	**Portion analyzed**	**GS**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
					BYI 02960	**DFA**	**BYI 02960-DFEAF**	**total residue of BYI 02960 calc.**
11-2552 (11-2552-01) northern France GLP: yes	cucumber Raider (R1) (Rotation 1) PBI: 29 days	fruit	71	79	<0.01	0.28	<0.01	0.30
11-2552 (11-2552-02) Germany GLP: yes	cucumber Melody cucumber (R1) (Rotation 1) PBI: 25 days	fruit	71	73	<0.01	0.32	<0.01	0.34
11-2552 (11-2552-03) Spain GLP: yes	cucumber Dasher Hibrido ciclo corto (R1) (Rotation 1) PBI: 28 days	fruit	79	83	<0.01	0.047	<0.01	0.067
11-2552 (11-2552-04) Italy GLP: yes	cucumber Marketmore (R1) (Rotation 1) PBI: 30 days	fruit	71	69	<0.01	0.41	<0.01	0.43

DALT=days after last treatment GS=growth stage (BBCH-code) at sampling
PBI=plant-back interval

Table 6.6.3.1.4-3: Recovery data for BYI 02960 in rotational crop matrix **cucumber fruit**

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortifi-cation level** (mg/kg)	**Recovery (%)**				
						Individual recoveries	**Min**	**Max**	**Mean**	**RSD**
11-2552 (11-2552-01), to (11-2552-04) GLP: yes 2011	cucumber	fruit	BYI 02960	5	0.01	97; 104; 112; 98; 98	97	112	102	6.2
				4	0.10	93; 93; 94; 94	93	94	94	0.6
				2	1.0	89; 90	89	90	90	
				11	overall		89	112	97	6.8
			DFA	5	0.02	77; 101; 106; 95; 102	77	106	96	11.9
				4	0.20	81; 91; 95; 89	81	95	89	6.6
				2	1.0	87; 86	86	87	87	
				11	overall		77	106	92	9.8
			BYI 02960-DFEAF	5	0.01	95; 99; 101; 94; 96	94	101	97	3.0
				4	0.10	90; 94; 97; 97	90	97	95	3.5
				2	1.0	90; 101	90	101	96	
				11	overall		90	101	96	3.9

Table 6.6.3.1.4-4: Extrapolation of total residues of BYI 02960 in rotational fruiting vegetables (cucumber) after application of 450 g a.s./ha to soil and then planting back

Study No. **(Trial No.) Plot No Country** **GLP**	**Rotational Crop, Variety** **(rotation information)**	**Portion analysed**	**GS**	**DALT (days)**	**Total BYI 02960 residues (mg/kg)** measured @ 250g a.s./ha	estimated @ 450g a.s./ha	estimated @ 450g a.s./ha plus soil accumulation
11-2552 (11-2552-01) northern France GLP: yes	cucumber Raider (R1) (Rotation 1) PBI: 29 days	fruit	71	79	0.30	0.54	0.65
11-2552 (11-2552-02) Germany GLP: yes	cucumber Melody cucumber (R1) (Rotation 1) PBI: 25 days	fruit	71	73	0.34	0.61	0.73
11-2552 (11-2552-03) Spain GLP: yes	cucumber Dasher Hibrido ciclo corto (R1) (Rotation 1) PBI: 28 days	fruit	79	83	0.067	0.12	0.14
11-2552 (11-2552-04) Italy GLP: yes	cucumber Marketmore (R1) (Rotation 1) PBI: 30 days	fruit	71	69	0.43	0.77	0.93

DALT=days after last treatment
PBI=plant-back interval
GS=growth stage (BBCH-code) at sampling

IIA 6.6.3.1.5 Onion (bulb vegetables)

Both EU residue regions

Report:	**KIIA 6.6.3.1.5/01, [redacted], 2012**
Title:	Determination of the residues of BYI 02960 in/on the field rotational crop onion after spray application of BYI 02960 SL 200 on bare soil in the field in France (North), Germany, Italy and Spain-Limited Rotational Crop Study
Report No. & Document No.:	11-2553, dated September 14, 2012 M-438397-01-1
Guidelines:	– EU Council Directive 91/414/– EU Guidance Working Document 7029/VI/95 rev. 5 – OECD Guideline for the Testing of Chemicals No. 504, Residues in Rotational Crops
GLP:	yes (certified laboratory)

I. Materials and Methods

Smaller (single-crop, single-rotation) field rotational crop residue trials were conducted in Europe, two in the northern and two in the southern residue regions, as follows:

In 2011, 4 trials (one each in northern France, Germany, Italy, and Spain) were conducted to support the use of BYI 02960 SL 200 in field-grown, non-perennial bulb vegetable crops ([redacted], 2012, KIIA 6.6.3.1.5/01). The product was applied twice with an application interval of 10 days (11 days in one trial) at a nominal rate of 0.625 L/ha, corresponding to 125 g/ha BYI 02960 a.s. The application scenario was designed to approximate the situation in which the original crop failed, and the field was used again very shortly thereafter, in the same season, to grow a subsequent crop. As such, the use pattern used reflected a typical use in non-perennial (vegetable) crops, such as lettuce, followed by a defined interval before re-planting. Water rates were 300-317 L/ha. Applications were made to bare soil. At the second application the test item was incorporated into the soil. All treatments were made at the scheduled rates with the exception of the Spanish trial, in which the second application was overdosed by 6%, which is well within the EU's tolerance of 25%. All data pertaining to the application/use pattern are presented in table 6.6.3.1.5-1.

After a plant-back interval of 25-33 days, onions were sown (northern Europe) or planted (southern Europe). Samples of onion bulb were taken at typical harvest maturity (BBCH growth stage 47-49). The samples were analyzed for the parent compound and its metabolites DFA and DFEAF using method 01304 (cf. KIIA 4.3/03). The respective LOQs for the 3 analytes were 0.01, 0.02, and 0.01 mg/kg (all in parent equivalents), yielding a calculated total-residue LOQ of 0.04 mg/kg.

II. Findings

Method validation for the sample material onion bulb, for BYI 02960 and its metabolites DFA and DFEAF, was conducted in the present study 11-2553. Recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg as well as at 0.10 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries in onion bulb were 88-97%, with RSDs of the larger validations sets (n > 2) of 3.2-6.8%; n=3-5. All values were within acceptable ranges.

For DFA, recovery samples were spiked at levels of 0.02 mg/kg as well as at 0.20 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries were 79-80%, with RSDs of the larger validations sets (n > 2) of 1.9-4.2%; n=4-5. All values were within acceptable ranges.

Details of recovery data are shown in table 6.6.3.1.5-3. All trial data are summarised below in table 6.6.3.1.5-2 and in greater detail in the Tier 1 summary forms. (Residues of parent BYI 02960 as well as its metabolites DFA and DFEAF are expressed in BYI 02960 equivalents.)

In rotational onions sampled at harvest in this study, the total residues of BYI 02960 in bulbs ranged from <0.04-0.18 mg/kg, with a median value of 0.085 mg/kg (n=4).

III. Conclusions

In order to support the use in the EU of BYI 02960 in non-perennial crops, four single-rotation, single-crop rotational crop trials were conducted in Europe (2 each in the northern and southern residue regions) in 2011 on onions, representing bulb vegetables. BYI 02960 was applied twice as an SL 200 formulation to bare soil at an active substance rate of 125 g/ha, followed by incorporation at the second application. 25–33 days after the second application, onions were sown (northern Europe) or planted (southern Europe). All applications were at the required rates, except in one trial, in which the 2nd application was overdosed by approx. 6%; this deviation was well within the EU's tolerance of 25%. All trials were conducted according to GLP.

To evaluate the potential residues in following crops, samples of the rotated crop were taken at typical harvest maturity (BBCH growth stage 47-49). Samples were analyzed for the relevant residues of BYI 02960, comprising the parent compound and its metabolites DFA and DFEAF. The residues of all three analytes were summed to yield a calculated "total residue of BYI 02960". The total residues of BYI 02960 in onion bulb ranged from <0.04-0.18 mg/kg, with a median value of 0.085 mg/kg (n=4).

If data are re-assessed for assumptions relevant to Australia, based on a maximum global application rate of 450 g a.s./ha and a soil accumulation factor of 1.2, extrapolation of residues would result in highest total residues of BYI 02960 in bulb vegetables of 0.39 mg/kg. This residue value corresponds to the highest residue value estimated in rotational bulb vegetables grown outside of Europe. (Onions are considered to be a relevant commodity with regard to world trade to the EU; cf. section 6.7.2.2, including Table 6.7.2.2-67.)

Table 6.6.3.1.5-1: Application scenario in field rotational crop trials (study 11-2553): Spray treatment with BYI 02960 SL 200 to soil followed by sowing/planting of **onions**

Trial No. **Plot No Country Location Region Year**	**Target Test System**	**FL**	**Application No.**	**Application kg/ha (a.s.)**	**Application kg/hl (a.s.)**
11-2553 (11-2553-01) northern France [redacted] EU-N 2011	soil	200 SL	2	0.125	0.0417
11-2553 (11-2553-02) Germany [redacted] EU-N 2011	soil	200 SL	2	0.125	0.0417
11-2553 (11-2553-03) Italy [redacted] EU-S 2011	soil	200 SL	2	0.125	0.0417
11-2553 (11-2553-04) Spain [redacted] EU-S 2011	soil	200 SL	2	0.125-0.132*	0.0416-0.0417

FL=formulation
GS=growth stage (BBCH-code) at last treatment
EU-N=northern European residue region
EU-S=southern European residue region

* The second application was overdosed by 6%.

Table 6.6.3.1.5-2: Results of field rotational crop trials following spray treatment with BYI 02960 SL 200 to soil and then planting back and sampling of **onion bulb**

Study No. **(Trial No.) Plot No Country** **GLP**	**Rotational Crop, Variety** **(rotation information)**	**Portion analyzed**	**GS**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
					BYI 02960	**DFA**	**BYI 02960-DFEAF**	**total residue of BYI 02960 calc.**
11-2553 (11-2553-01) France GLP: yes	onion, Paille des vertus (yellow onion) (Rotation 1) PBI: 30 days	bulb	49	175	<0.01	0.16	<0.01	0.18
11-2553 (11-2553-02) Germany GLP: yes	onion, Sherpa F1 (Rotation 1) PBI: 33 days	bulb	47	133	<0.01	0.071	<0.01	0.091
11-2553 (11-2553-03) Italy GLP: yes	onion, Dorata di Parma (Rotation 1) PBI: 25 days	bulb	49	116	<0.01	0.058	<0.01	0.078
11-2553 (11-2553-04) Spain GLP: yes	onion, Figueras (bulb onion) (Rotation 1) PBI: 28 days	bulb	48	118	<0.01	<0.02	<0.01	<0.04

DALT=days after last treatment GS=growth stage (BBCH-code) at sampling
PBI=plant-back interval

Table 6.6.3.1.5-3: Recovery data for BYI 02960 in rotational crop matrix **onion bulb**

Study No. **Trial No.** **GLP Year**	**Crop**	**Portion analyzed**	**a.s./metabolite**	**n**	**Fortification level (mg/kg)**	**Recovery (%)**				
						Individual recoveries	**Min**	**Max**	**Mean**	**RSD**
11-2553 (11-2553-01), to (11-2553-04) GLP: yes 2011	onion	bulb	BYI 02960	5	0.01	88; 90; 93; 93; 96	88	96	92	3.4
				4	0.10	93; 96; 101	93	101	97	4.2
				11	overall		88	101	94	4.3
			DFA	5	0.02	76; 77; 79; 82; 84	76	84	80	4.2
				4	0.20	78; 79; 81	78	81	79	1.9
				11	overall		76	84	80	3.4
			BYI 02960-DFEAF	5	0.01	81; 84; 89; 92; 96	81	96	88	6.8
				3	0.10	91; 95; 97	91	97	94	3.2
				8	overall		81	97	91	6.3

Table 6.6.3.1.5-4: Extrapolation of total residues of BYI 02960 in rotational bulb vegetables (onion) after application of 450 g a.s./ha to soil and then planting back

Study No. **(Trial No.) Plot No Country** **GLP**	**Rotational Crop, Variety** **(rotation information)**	**Portion analysed**	**GS**	**DALT (days)**	**Total BYI 02960 residues (mg/kg)**		
					measured @ 250g a.s./ha	**estimated @ 450g a.s./ha**	**estimated @ 450g a.s./ha plus soil accumulation**
11-2553 (11-2553-01) France GLP: yes	onion, Paille des vertus (yellow onion) (Rotation 1) PBI: 30 days	bulb	49	175	0.18	0.32	0.39
11-2553 (11-2553-02) Germany GLP: yes	onion, Sherpa F1 (Rotation 1) PBI: 33 days	bulb	47	133	0.091	0.16	0.20
11-2553 (11-2553-03) Italy GLP: yes	onion, Dorata di Parma (Rotation 1) PBI: 25 days	bulb	49	116	0.078	0.17	0.17
11-2553 (11-2553-04) Spain GLP: yes	onion, Figueras (bulb onion) (Rotation 1) PBI: 28 days	bulb	48	118	<0.04	<0.07	<0.09

DALT=days after last treatment GS=growth stage (BBCH-code) at sampling
PBI=plant-back interval

IIA 6.6.3.1.6 Bean (legume vegetables)

Both EU residue regions

Report:	**KIIA 6.6.3.1.6/01, [redacted] 2012**
Title:	Determination of the residues of BYI 02960 in/on the field rotational crop French bean after spray application of BYI 02960 SL 200 to bare soil in the field in northern France, Germany, Italy and Spain – Limited rotational crop study
Report No. & Document No.:	11-2555, dated September 14, 2012 M-438394-01-1
Guidelines:	– EU Council Directive 91/414/EEC amended by Commission Directive 96/68/EC – EU Guidance Working Document 7029/VI/95 rev. 5 – OECD Guideline for the Testing of Chemicals No. 504, Residues in Rotational Crops
GLP:	yes (certified laboratory)

I. Materials and Methods

Smaller (single-crop, single-rotation) field rotational crop residue trials were conducted in Europe, two in the northern and two in the southern residue regions, as follows:

In 2011, 4 rotational crop trials were conducted on French beans (one trial each in northern France, Germany, Italy, and Spain) to support the use of BYI 02960 SL 200 in field-grown, non-perennial legume vegetable crops ([redacted], 2012, KIIA 6.6.3.1.6/01). The product was applied twice with an application interval of 10-12 days at a nominal rate of 0.625 L/ha, corresponding to 125 g/ha BYI 02960 a.s. The application scenario was designed to approximate the situation in which the original crop failed, and the field was used again very shortly thereafter, in the same season, to grow a subsequent crop. Therefore, the use pattern used reflected a typical use in non-perennial (vegetable) crops, such as lettuce, followed by a defined interval before replanting. Water rates were 300-400 L/ha. Applications were made to bare soil. At the second application the test item was incorporated into the soil. All treatments were made at scheduled rates. All data pertaining to the application/use pattern are presented in table 6.6.3.1.6-1.

After a plant-back interval of 25-30 days, French beans were sown. Samples of bean pods were taken at BBCH growth stage 73-79 (85–105 DALT). All samples were analyzed for the parent compound and its metabolites DFA and DFEAF using method 01304 (cf. KIIA 4.3/03). The respective LOQs for the 3 analytes were 0.01 mg/kg, 0.02 mg/kg, and 0.01 mg/kg (all in parent equivalents), yielding a calculated total-residue LOQ of 0.04 mg/kg.

II. Findings

Method validation work for the sample material bean pod, for BYI 02960 and its metabolites DFA and DFEAF, was done in the present study 11-2555. For French beans, recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg as well as at 0.10 mg/kg and 5.0 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries were 84-104%, with RSDs of the larger validation sets (n > 2) of 1.9-5.8%; n=2-6. All values were within acceptable ranges.

For DFA, recovery samples were spiked at levels of 0.02 mg/kg, as well as 0.20 and 5.0 mg/kg (expressed as BYI 2960). Mean recoveries were 82-94%, with RSDs of the larger validation sets (n > 2) of 2.9-4.5%, n=2-6. All values were within acceptable ranges.

Details of recovery data are shown in table 6.6.3.1.6-3. All trial data are summarised below in table 6.6.3.1.6-2 and in greater detail in the Tier 1 summary forms. (Residues of parent BYI 02960 as well as its metabolites DFA and DFEAF are expressed in BYI 02960 equivalents.)

In rotational French beans sampled at appropriate maturity in this study, the total residues of BYI 02960 in pods were in the range of 0.28–1.1 mg/kg, with a median value of 0.50 mg/kg (n=4).

III. Conclusions

In order to support the use in the EU of BYI 02960 in non-perennial crops, four single-rotation, single-crop rotational crop trials were conducted in Europe (one trial in northern France, Germany, Italy, and Spain) in 2011 in French beans, representing legume vegetables. BYI 02960 was applied twice as an SL 200 formulation to bare soil at an active substance rate of 0.625 L/ha, corresponding to 125 g/ha BYI 02960 a.s., followed by incorporation at the second application. 25-30 days after the second application, French beans were sown. All applications were made at scheduled rates and all trials were conducted according to GLP.

To evaluate the potential residues in following crops, samples of the rotated crop were taken at typical harvest maturity (BBCH growth stage 73-79). Samples were analyzed for the relevant residues of BYI 02960, comprising the parent compound and its metabolites DFA and DFEAF. The residues of all three analytes were summed to yield a calculated "total residue of BYI 02960". The total residues of BYI 0290 in bean pods ranged from 0.28-1.1 mg/kg, with a median value of 0.50 mg/kg (n=4).

If data are re-assessed for assumptions relevant to Australia, based on a maximum global application rate of 450 g a.s./ha and a soil accumulation factor of 1.2, extrapolation of residues would result in highest total residues of BYI 02960 in legume vegetables of 2.38 mg/kg. This residue value corresponds to the highest residue value estimated in rotational legume vegetables grown outside of Europe.

(Legume vegetables are not considered to be commodities which are imported in significant quantities to the EU, thus the extrapolated values shown here will not play a role in the evaluation and proposal of an EU MRL; cf. section 6.7.2.2.)

Table 6.6.3.1.6-1: Application scenario in field rotational crop trials (study 11-2555): Spray treatment with BYI 02960 SL 200 to soil followed by sowing of **French beans**

Trial No. **Plot No Country Location Region Year**	**Target Test System**	**FL**	**Application**		
			No.	**kg/ha (a.s.)**	**kg/hl (a.s.)**
11-2555 11-2555-01 northern France [redacted] EU-N 2011	soil	200 SL	2	0.125	0.042
11-2555 11-2555-02 Germany [redacted] EU-N 2011	soil	200 SL	2	0.125	0.042
11-2555 11-2555-03 Italy [redacted] EU-S 2011	soil	200 SL	2	0.125	0.031
11-2555 11-2555-04 Spain [redacted] EU-S 2011	soil	200 SL	2	0.125	0.042

FL=formulation
GS=growth stage (BBCH-code) at last treatment
EU-N=northern European residue region
EU-S=southern European residue region

Table 6.6.3.1.6-2: Results of field rotational crop trials following spray application of BYI 02960 SL 200 to soil and then planting back and sampling of **French beans**

Study No. **(Trial No.) Plot No Country GLP**	**Rotational Crop, Variety (rotation information)**	**Portion analyzed**	**GS**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
					BYI 02960	**DFA**	**BYI 02960-DFEAF**	**total residue of BYI 02960 calc.**
11-2555 11-2555-01 Northern France GLP: yes	bean, climbing French Banga (Rotation 1) PBI: 29 days	pods	73	93	<0.01	1.1	<0.01	1.1
11-2555 11-2555-02 Germany GLP: yes	bean, climbing French Saxa (Rotation 1) PBI: 25 days	pods	79	105	<0.01	0.57	<0.01	0.59
11-2555 11-2555-03 Italy GLP: yes	bean, climbing French OR Arno (Rotation 1) PBI: 30 days	pods	73	85	<0.01	0.38	<0.01	0.40
11-2555 11-2555-04 Spain GLP: yes	bean, climbing French Cleo Temprana (Rotation 1) PBI: 28 days	pods	79	90	<0.01	0.26	<0.01	0.28

DALT=days after last treatment GS=growth stage (BBCH-code) at sampling
PBI=plant-back interval

Table 6.6.3.1.6-3: Recovery data for BYI 02960 in rotational crop matrix **French bean pod**

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analyzed**	**a.s./metabolite**	**n**	**Fortifi-cation level** (mg/kg)	**Recovery (%)**				
						Individual recoveries	**Min**	**Max**	**Mean**	**RSD**
11-2555 (11-2555-01), to (11-2555-04) GLP: yes 2011	bean, climbing French	pod	BYI 02960	6	0.01	89; 90; 91; 91; 92; 94	89	94	91	1.9
				4	0.10	85; 88; 88; 91	85	91	88	2.8
				2	5.0	82; 86	82	86	84	
				12	overall		82	94	89	3.8
			DFA	6	0.02	89; 89; 93; 96; 97; 99	89	99	94	4.5
				4	0.20	79; 80; 83; 84	79	84	82	2.9
				2	5.0	81; 85	81	85	83	
				12	overall		79	99	88	7.9
			BYI 02960-DFEAF	6	0.01	80; 86; 89; 89; 92; 95	80	95	89	5.8
				4	0.10	92; 93; 93; 97	92	97	94	2.4
				2	5.0	102; 106	102	106	104	
				12	overall		80	106	93	7.4

Table 6.6.3.1.6-4: Extrapolation of total residues of BYI 02960 in legume vegetables (green bean) after application of 450 g a.s./ha to soil and then planting back

Study No. (Trial No.) Plot No Country GLP	Rotational Crop, Variety (rotation information)	Portion analysed	GS	DALT (days)	Total BYI 02960 residues (mg/kg) measured @ 250g a.s./ha	estimated @ 450g a.s./ha	estimated @ 450g a.s./ha plus soil accumulation
11-2555 11-2555-01 Northern France GLP: yes	bean, climbing French Banga (Rotation 1) PBI: 29 days	pods	73	93	1.1	1.98	2.38
11-2555 11-2555-02 Germany GLP: yes	bean, climbing French Saxa (Rotation 1) PBI: 25 days	pods	79	105	0.59	1.06	1.27
11-2555 11-2555-03 Italy GLP: yes	bean, climbing French OR Arno (Rotation 1) PBI: 30 days	pods	73	85	0.40	0.72	0.86
11-2555 11-2555-04 Spain GLP: yes	bean, climbing French Cleo Temprana (Rotation 1) PBI: 28 days	pods	79	90	0.28	0.50	0.60

DALT=days after last treatment
PBI=plant-back interval
GS=growth stage (BBCH-code) at sampling

IIA 6.6.3.1.7 Field pea (pulses)

Both EU residue regions

Report:	**KIIA 6.6.3.1.7/02, [redacted] 2012**
Title:	Determination of the residues of BYI 02960 in/on the field rotational crop pea after spray application of BYI 02960 SL 200 on bare soil in the field in France (North), Germany, Italy and Spain – Limited rotational crop study
Report No. & Document No.:	11-2556, dated September 17, 2012 M-438582-01-1
Guidelines:	– EU Council Directive 91/414/EEC amended by Commission Directive 96/68/EC – EU Guidance Working Document 7029/VI/95 rev. 5 – OECD Guideline for the Testing of Chemicals No. 504, Residues in Rotational Crops
GLP:	yes (certified laboratory)

I. Materials and Methods

Smaller (single-crop, single-rotation) field rotational crop residue trials were conducted in Europe, two in the northern and two in the southern residue regions, as follows:

In 2011, 4 rotational crop trials were conducted on field peas (one each in northern France, Germany, Italy and Spain) to support the use of BYI 02960 SL 200 in field-grown, non-perennial pulses ([redacted], 2012, KIIA 6.6.3.1.7/01). The product was applied twice with an interval of 10-12 days at a nominal rate of 0.625 L/ha, corresponding to 125 g a.s./ha BYI 02960 a.s. The application scenario was designed to approximate the situation in which the original crop failed, and the field was used again very shortly thereafter, in the same season, to grow a subsequent crop. Therefore, the use pattern used reflected a typical use in non-perennial (vegetable) crops, such as lettuce, followed by a defined interval before replanting. Water rates were 300-400 L/ha. Applications were made to bare soil. At the second application, the test item was incorporated into the soil. All treatments were made at the scheduled rates. All data pertaining to the application/use pattern are presented in table 6.6.3.1.7-1.

After a plant-back interval of 25-35 days, peas were sown. Samples of dry pea seeds were taken at BBCH growth stage 89 (100–144 DALT). All samples were analyzed for the parent compound and its metabolites DFA and DFEAF using method 01304 (cf. KIIA 4.3/03). The respective LOQs for the 3 analytes were 0.01 mg/kg, 0.02 mg/kg, and 0.01 mg/kg (all in parent equivalents), yielding a calculated total-residue LOQ of 0.04 mg/kg.

II. Findings

Method validation for the sample material dry pea seed, for BYI 02960 and its metabolites DFA and DFEAF, was conducted in the present study 11-2556. For dry pea seed, recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg as well as at 0.10 mg/kg, 1.0 mg/kg, and 5.0 mg/kg (expressed in BYI 02960 equivalents). Mean recoveries were 85-101%, with RSDs of the larger validation sets (n > 2) of 2.2-3.0%, n=2-7. All values were within acceptable ranges.

For DFA, dry pea seed recovery samples were spiked at levels of 0.02 mg/kg, as well as 0.20 mg/kg, 1.0°mg/kg, and 5.0 mg/kg (expressed as BYI 2960). Mean recoveries were 66-92%, with RSDs of the larger validation sets (n > 2) of 7.8-4.5%, n=2-5. The mean recoveries at 0.20 mg/kg and 1.0 mg/kg for DFA (68% and 66%, respectively) are considered to be acceptable because the overall mean value is >70% and the overall RSD is <20%. Additionally, concurrent recoveries at 5.0 mg/kg were found >70%. Therefore, all values were within acceptable ranges.

Details of recovery data are shown in table 6.6.3.1.7-3. All trial data are summarised below in table 6.6.3.1.7-2 and in greater detail in the Tier 1 summary forms. (Residues of parent BYI 02960 as well as metabolites DFA and DFEAF are expressed in BYI 02960 equivalents.)

In rotational field peas sampled at appropriate harvest maturity in this study, the total residues of BYI 02960 in dry seeds were in the range of 0.67–2.3 mg/kg, with a median value of 1.55 mg/kg (n=4).

III. Conclusions

In order to support the use of BYI 02960 SL 200 in field-grown, non-perennial crops, four limited rotational crop trials were conducted in Europe (one trial in northern France, Germany, Italy and Spain) in 2011 on field peas, representing pulses. BYI 02960 was applied twice as an SL 200 formulation to bare soil at an active substance rate of 125 g a.s./ha, followed by incorporation into the soil after the second application. 25-35 days after the second application, peas were sown. All applications were at the required rates, and all trials were conducted according to GLP.

To evaluate the potential residues in following crops, samples of the rotated crop were taken at typical harvest maturity (BBCH growth stage 89). Samples were analyzed for the relevant residues of BYI 02960, comprising the parent compound and its metabolites DFA and DFEAF. The residues of all three analytes were summed to yield a calculated "total residue of BYI 02960". The total residues of BYI 0290 in dry pea seeds ranged from 0.67–2.3 mg/kg, with a median value of 1.55 mg/kg (n=4).

If data are re-assessed for assumptions relevant to Australia, based on a maximum global application rate of 450 g a.s./ha and a soil accumulation factor of 1.2, extrapolation of residues would result in highest total residues of BYI 02960 in pulses of 4.97 mg/kg. This residue value corresponds to the highest residue value estimated in rotational pulses grown outside of Europe.
(Pulses are considered to be one of the most important export crops in Australia, as well as being a significant commodity with regard to world trade to the EU; cf. section 6.7.2.2, including Table 6.7.2.2-67.)

Table 6.6.3.1.7-1: Application scenario in field rotational crop trials (study 11-2556): Spray treatment with BYI 02960 SL 200 to soil followed by sowing of **field peas**

Trial No. **Plot No Country Location Region Year**	**Target Test System**	**FL**	**Application**		
			No.	**kg/ha (a.s.)**	**kg/hl (a.s.)**
11-2556 11-2556-01 northern France [redacted] EU-N 2011	soil	200 SL	2	0.125	0.042
11-2556 11-2556-02 Germany [redacted] EU-N 2011	soil	200 SL	2	0.125	0.042
11-2556 11-2556-03 Italy [redacted] EU-S 2011	soil	200 SL	2	0.125	0.031
11-2556 11-2556-04 Spain [redacted] EU-S 2011	soil	200 SL	2	0.125	0.042

FL=formulation
EU-N=northern European residue region
GS=growth stage (BBCH-code) at last treatment
EU-S=southern European residue region

Table 6.6.3.1.7-2: Results of field rotational crop trials following spray application of BYI 02960 SL 200 to soil and then planting back and sampling of **peas**

Study No. **(Trial No.) Plot No Country** **GLP**	**Rotational Crop, Variety** **(rotation information)**	**Portion analyzed**	**GS**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
					BYI 02960	**DFA**	**BYI 02960-DFEAF**	**total residue of BYI 02960 calc.**
11-2556 11-2556-01 Northern France GLP: yes	pea, field Montana (Rotation 1) PBI: 25 days	dry seeds	89	136	<0.01	2.3	<0.01	2.3
11-2556 11-2556-02 Germany GLP: yes	pea, field Mascara (Rotation 1) PBI: 28 days	dry seeds	89	144	<0.01	0.99 (0.11*)	<0.01	1.0
11-2556 11-2556-03 Italy GLP: yes	pea, field Lambado (Rotation 1) PBI: 30 days	dry seeds	89	100	<0.01	0.65 (0.031*)	<0.01	0.67
11-2556 11-2556-04 Spain GLP: yes	pea, field Lincoln (Rotation 1) PBI: 35 days	dry seeds	89	132	<0.01	2.1	<0.01	2.1

DALT=days after last treatment GS=growth stage (BBCH-code) at sampling
PBI=plant-back interval

*=residues in control

Table 6.6.3.1.7-3: Recovery data for BYI 02960 in rotational crop matrix **dry pea seed**

Study No. Trial No. GLP Year	Crop	Portion analyzed	a.s./ metabolite	n	Fortification level (mg/kg)	Recovery (%)				
						Individual recoveries	Min	Max	Mean	RSD
11-2556 (11-2556-01), to (11-2556-04) GLP: yes 2011	pea, field	seed, dry	BYI 02960	7	0.01	88; 91; 93; 94; 94; 95; 96	88	96	93	2.9
				3	0.10	85; 86; 90	85	90	87	3.0
				2	1.0	84; 86	84	86	85	
				2	5.0	90; 101	90	101	96	
				14	overall		84	101	91	5.4
			DFA	5	0.02	83; 86; 93; 97; 100	83	100	92	7.8
				3	0.20	65; 69; 71	65	71	68	4.5
				2	1.0	65; 67	65	67	66	
				2	5.0	72; 82	72	82	77	
				12	overall		65	100	79	16.1
			BYI 02960-DFEAF	7	0.01	89; 89; 90; 91; 93; 95; 95	89	95	92	2.9
				3	0.10	94; 95; 98	94	98	96	2.2
				2	1.0	93; 96	93	96	95	
				2	5.0	100; 101	100	101	101	
				14	overall		89	101	94	4.0

Table 6.6.3.1.7-4: Extrapolation of total residues of BYI 02960 in rotational pulsed (dry peas) after application of 450 g a.s./ha to soil and then planting back

Study No. **(Trial No.) Plot No Country GLP**	**Rotational Crop, Variety (rotation information)**	**Portion analysed**	**GS**	**DALT (days)**	**Total BYI 02960 residues (mg/kg)**		
					measured @ 250g a.s./ha	**estimated @ 450g a.s./ha**	**estimated @ 450g a.s./ha plus soil accumulation**
11-2556 11-2556-01 Northern France GLP: yes	pea, field Montana (Rotation 1) PBI: 25 days	dry seeds	89	136	2.3	4.14	4.97
11-2556 11-2556-02 Germany GLP: yes	pea, field Mascara (Rotation 1) PBI: 28 days	dry seeds	89	144	1.0	1.80	2.16
11-2556 11-2556-03 Italy GLP: yes	pea, field Lambado (Rotation 1) PBI: 30 days	dry seeds	89	100	0.67	1.21	1.45
11-2556 11-2556-04 Spain GLP: yes	pea, field Lincoln (Rotation 1) PBI: 35 days	dry seeds	89	132	2.1	3.78	4.54

DALT=days after last treatment
GS=growth stage (BBCH-code) at sampling
PBI=plant-back interval

IIA 6.6.3.1.8 Oilseed rape (oilseeds)

Both EU residue regions

Report:	**KIIA 6.6.3.1.8/01, [redacted] 2012**
Title:	Determination of the residues of BYI 02960 in/on the field rotational crop winter rape after spray application of BYI 02960 SL 200 on bare soil in the field in northern France, Germany, Italy and Spain – Limited rotational crop study
Report No. & Document No.:	11-2554, dated December 07, 2012 M-443092-01-1
Guidelines:	– EU Council Directive 91/414/EEC – EU Guidance Working Document 7029/VI/95 rev. 5 – OECD Guideline for the Testing of Chemicals No. 504, Residues in Rotational Crops
GLP:	yes (certified laboratory)

I. Materials and Methods

Smaller (single-crop, single-rotation) field rotational crop residue trials were conducted in Europe, two in the northern and two in the southern residue regions, as follows:

In 2011, 4 rotational crop trials were conducted on oilseed rape (one trial in northern France, Germany, Italy and Spain) to support the use of BYI 02960 SL 200 in field-grown, non-perennial crops ([redacted], 2012, KIIA 6.6.3.1.8/01). The product was applied twice with an interval of 9-10 days at a nominal rate of 0.625 L/ha, corresponding to 125 g a.s./ha BYI 02960 a.s. The application scenario was designed to approximate the situation in which the original crop failed, and the field was used again very shortly thereafter, in the same season, to grow a subsequent crop. Therefore, the use pattern used reflected a typical use in non-perennial (vegetable) crops, such as lettuce, followed by a defined interval before replanting. Water rates were 300-400 L/ha. Applications were made to bare soil. At the second application the test item was incorporated into the soil. All treatments were made at the scheduled rates. After a plant-back interval of 27-41 days, rape seeds were sown. All data pertaining to the application/use pattern are presented in table 6.6.3.1.8-1.

Samples of rape seeds were taken at BBCH growth stage 89 (290–369 DALT). All samples were analyzed for the parent compound and its metabolites DFA and DFEAF using method 01304 (cf. KIIA 4.3/03). The respective LOQs for the 3 analytes were 0.01 mg/kg, 0.02 mg/kg, and 0.01 mg/kg (all in parent equivalents), yielding a calculated total-residue LOQ of 0.04 mg/kg.

II. Findings

Validation of sample material rape seed for BYI 02960 and its metabolites DFA and DFEAF was conducted within the present study 11-2554.

Rape seed recovery samples for parent compound and DFEAF were spiked at levels of 0.01 mg/kg as well as at 1.0 mg/kg (expressed in BYI 02960 equivalents). Recoveries were not corrected for apparent residues in the control samples used. Mean recoveries were 97-102%, with RSDs of the larger validation sets (n > 2) of 3.1-4.8%, n=3-7). All values were within acceptable ranges.

For DFA, rape seed recovery samples were spiked at levels of 0.02 mg/kg, as well as at 2.0°mg/kg (expressed as BYI 2960). The recoveries for DFA at the LOQ level were corrected for the apparent residues found in the used control samples. Mean recoveries were 70-90%, with RSDs of the larger validation sets (n > 2) of 3.2-14.8% (n=3-7). Mean values and overall mean values were within acceptable ranges.

Details of recovery data are shown in table 6.6.3.1.8-3. All trial data are summarised below in table 6.6.3.1.8-2 and in greater detail in the Tier 1 summary forms. (Residues of parent BYI 02960 as well as the metabolites DFA and DFEAF are expressed in BYI 02960 equivalents.)

For oilseed rape, the total residues of BYI 02960 in seeds were in the range of 0.070-0.17 mg/kg, with a median value of 0.101 mg/kg (n=4).

III. Conclusions

In order to support the use in the EU of BYI 02960 in non-perennial crops, four single-rotation, single-crop rotational crop trials were conducted in Europe (one trial in northern France, Germany, Italy and Spain) in 2011. BYI 02960 was applied twice as an SL 200 formulation to bare soil at an active substance rate of 125 g a.s./ha followed by incorporation into the soil after the second application. 27-41 days after the second application oilseed rape was sown. All applications were at the required rates, and all trials were conducted according to GLP.

To evaluate the potential residues in following crops, seed samples of the rotated crop rape were taken at harvest time (BBCH growth stage 89). Samples were analyzed for the relevant residues of BYI 02960, comprising the parent compound and its metabolites DFA and DFEAF. The residues of all three analytes were summed to yield a calculated "total residue of BYI 02960". The residues of the total residue of BYI 02960 in seeds ranged from 0.070-0.17 mg/kg, with a median value of 0.101 mg/kg (n=4).

If data are re-assessed for assumptions relevant to Australia, based on a maximum global application rate of 450 g a.s./ha and a soil accumulation factor of 1.2, extrapolation of residues would result in highest total residues of BYI 02960 in oilseeds of 0.37 mg/kg. This residue value corresponds to the highest residue value estimated in rotational oilseeds grown outside of Europe.
(Oilseeds and products thereof are considered to be among the most important export crops in Australia, as well as being a significant commodity with regard to world trade to the EU; cf. section 6.7.2.2, including Table 6.7.2.2-67.)

Table 6.6.3.1.8-1: Application scenario in field rotational crop trials (study 11-2554): Spray treatment with BYI 02960 SL 200 to soil followed by sowing of **oilseed rape**

Trial No. **Plot No Country Location Region Year**	**Target Crop, Variety**	**FL**	**Application**		
			No.	**kg/ha (a.s.)**	**kg/hl (a.s.)**
11-2554 11-2554-01 northern France [redacted] EU-N 2011	soil (T)	200 SL	2	0.125	0.042
11-2554 11-2554-02 Germany [redacted] EU-N 2011	soil (T)	200 SL	2	0.125	0.042
11-2554 11-2554-03 Italy [redacted] EU-S 2011	soil (T)	200 SL	2	0.125	0.031
11-2554 11-2554-04 Spain [redacted] EU-S 2011	soil (T)	200 SL	2	0.125	0.042

FL=formulation
EU-N=northern Europe
GS=growth stage (BBCH-code) at last treatment
EU-S=southern Europe

Table 6.6.3.1.8-2: Results of field rotational crop trials following spray application of BYI 02960 SL 200 to soil and then planting back and sampling of **oilseed rape**

Study No. **(Trial No.) Plot No Country GLP**	**Rotational Crop, Variety (rotation information)**	**Portion analyzed**	**GS**	**DALT (days)**	**Residues (mg/kg) expressed as BYI 02960**			
					BYI 02960	**DFA**	**BYI 02960-DFEAF**	**total residue of BYI 02960 calc.**
11-2554 11-2554-01 northern France GLP: yes	rape, winter Dynastie hybrid 00 (Rotation 1) PBI: 41 days	seeds	89	369	<0.01	0.090	<0.01	0.11
11-2554 11-2554-02 Germany GLP: yes	rape, winter ES-Astrid Rape (Rotation 1) PBI: 34 days	seeds	89	361	<0.01	0.15	<0.01	0.17
11-2554 11-2554-03 Italy GLP: yes	rape, winter Primus winter variety (Rotation 1) PBI: 27 days	seeds	89	307	<0.01	0.050	<0.01	0.070
11-2554 11-2554-04 Spain GLP: yes	rape, winter Pacific winter rape (Rotation 1) PBI: 39 days	seeds	89	290	<0.01	0.072	<0.01	0.092

DALT=days after last treatment
PBI=plant-back interval
GS=growth stage (BBCH-code) at sampling

Table 6.6.3.1.8-3: Recovery data for BYI 02960 in rotational crop matrix **oilseed rape**

Study No. **Trial No.** **GLP** **Year**	**Crop**	**Portion analyzed**	**a.s./ metabolite**	**n**	**Fortifi-cation level** (mg/kg)	**Recovery (%)** **Individual recoveries**	**Min**	**Max**	**Mean**	**RSD**
11-2554 (11-2554-01), to (11-2554-04) GLP: yes 2011	rape, winter	seed	BYI 02960	7	0.01	93; 93; 98; 99; 99; 100; 100	93	100	97	3.2
				3	1.0	93; 100; 102	93	102	98	4.8
				10	overall		93	102	98	3.5
			DFA	7	0.02	72* (106**)‡; 74* (108**)‡; 56* (108**)†; 62* (112**)†; 63* (114**)†; 81* (115**)‡; 84* (118**)‡	56	84	70	14.8
				3	2.0	87; 92; 92	87	92	90	3.2
				10	overall				76	17.0
			BYI 02960-DFEAF	7	0.01	96; 99; 102; 103; 103; 104; 107	96	107	102	3.5
				3	1.0	95; 99; 101	95	101	98	3.1
				10	overall		95	107	101	3.7

* Recovery after correction which was used for calculation of mean and RSD values.

** Recovery before correction which was not used for calculation purposes.

† The control sample used yielded residue levels of more than 30% of the LOQ (0.020 mg/kg) and therefore the recovery results were background-corrected for this signal present in the control sample used.

‡ The control sample used yielded residue levels of more than 30% of the LOQ (0.0068 mg/kg) and therefore the recovery results were background-corrected for this signal present in the control sample used.

Table 6.6.3.1.8-4: Extrapolation of total residues of BYI 02960 in rotational oilseeds (oilseed rape) after application of 450 g a.s./ha to soil and then planting back

Study No. (Trial No.) Plot No Country GLP	Rotational Crop, Variety (rotation information)	Portion analysed	GS	DALT (days)	Total BYI 02960 residues (mg/kg) measured @ 250g a.s./ha	estimated @ 450g a.s./ha	estimated @ 450g a.s./ha plus soil accumulation
11-2554 11-2554-01 northern France GLP: yes	rape, winter Dynastie hybrid 00 (Rotation 1) PBI: 41 days	seeds	89	369	0.11	0.20	0.24
11-2554 11-2554-02 Germany GLP: yes	rape, winter ES-Astrid Rape (Rotation 1) PBI: 34 days	seeds	89	361	0.17	0.31	0.37
11-2554 11-2554-03 Italy GLP: yes	rape, winter Primus winter variety (Rotation 1) PBI: 27 days	seeds	89	307	0.070	0.13	0.15
11-2554 11-2554-04 Spain GLP: yes	rape, winter Pacific winter rape (Rotation 1) PBI: 39 days	seeds	89	290	0.092	0.17	0.20

DALT=days after last treatment
PBI=plant-back interval
GS=growth stage (BBCH-code) at sampling

IIA 6.6.3.2 Field trials on representative crops in the USA

Field rotational crop trials in sugar cane have been conducted to support the use of BYI 02960 in Florida.

Report:	**KIIA 6.6.3.2/01, [redacted]; [redacted] 2012**
Title:	BYI 02960, fenamidone, fluopyram, and spiromesifen - magnitude of the residue in sugar cane in Florida (rotational crop regional tolerance)
Report No. & Document No.:	RARVP030, dated May 25, 2012 M-432179-01-2
Guidelines:	– EPA Ref.: OPPTS 860.1500, Crop Field Trials – PMRA Ref.: DACO 7.4.1. Supervised Residue Field Trial Study – PMRA Ref.: DACO 7.4.2. Residue Decline Study – OECD Test Guideline 509: Crop Field Trial (Adopted Sept. 7, 2009)
GLP:	yes

Four field rotational crop trials were conducted to measure the magnitude of BYI 02960 residues in/on sugar cane at a target 14-day plant-back interval (PBI) following a single broadcast spray application of BYI 02960 200 SL to bare ground. BYI 02960 200 SL is a soluble concentrate formulation containing 200 g BYI 02960/L. BYI 02960 200 SL was applied at target rates and timings as shown below.

Three other active ingredients (fenamidone, fluopyram, and spiromesifen) were also applied to the treated plot. Data associated with those treatments and the analysis of samples for those active ingredients will be reported at a later date.

Two additional trials were performed in the 2012 growing seasons, and the analysis of samples for all active ingredients will be reported at a later date.

The purpose for these trials was to establish a registered tolerance for on sugar cane in EPA Region 3.

The number and location of field trials are given in Table 6.6.3.2-1.

Table 6.6.3.2-1: Trial numbers and geographical locations for BYI 02960 in/on sugar cane

NAFTA Growing Region	Submitted [a]	Requested
3	4	4
Total	4	4

Material and Methods

Individual application rates ranged from 0.356 to 0.373 lb BYI 02960/A (0.399 to 0.418 kg BYI 02960/ha. Sugar cane was planted into the treated plot 13 to 14 days following the application. All applications were made to bare ground using ground-based equipment.

Trial site conditions, including soil characteristics are summarized in Table 6.6.3.2-2. Study use patterns are summarized in Table 6.6.3.2-3.

Table 6.6.3.2-2: Trial site conditions for BYI 02960 on sugar cane

Trial Location	Trial Identification	Soil Characteristics[a]				Meteorological Data[b]	
		Type	OM (%)	pH	CEC (meq/100g soil)	Total Rainfall (in)	Temp. Range (°F)
[redacted], FL	RV286-10RA	Tavares Sand	0.5-2.0	3.5-5.5	0.1-2.3	44.5	20-104
[redacted], FL	RV287-10RB	Sand	0.8	6.2	3	48.66	48-94
[redacted], FL	RV001-11RA	Sand	0.8	6.2	3	48.66	48-94
[redacted], FL	RV002-11RA	Fine Sandy Loam	0.5-3.0	4.5-6.0	0.2-1.3	34.48	28-101

[a] Abbreviations used: %OM = percent organic matter; CEC = cation exchange capacity .

[b] Data is for the interval of the month of first application through the month of last sampling. Meteorological data were obtained from nearby government weather stations.

Table 6.6.3.2-3: Study use pattern for BYI 02960 200 SL on sugar cane

Trial Identification	Location (City, State, NAFTA Region, and Year)	End-use Product (Formulation)	Application							Tank Mix Adjuvants
			Plot Name	Method	PBI (Plant Back Interval, days)	Spray Volume GPA (L/ha)	Rate lb a.i./A (kg a.i./ha)	Total Rate lb a.i./A (kg a.i./ha)		
RV286-10RA	[redacted], FL Region 3 2010	BYI 02960 200 SL	TRTD1	Broadcast spray	14	19 (176)	0.369 (0.414)	0.369 (0.414)		None
RV287-10RB	[redacted], FL Region 3 2011	BYI 02960 200 SL	TRTD1	Broadcast spray	14	19 (175)	0.356 (0.399)	0.356 (0.399)		None
RV001-11RA	[redacted], FL Region 3 2011	BYI 02960 200 SL	TRTD1	Broadcast spray	14	19 (177)	0.366 (0.411)	0.366 (0.411)		None
RV002-11RA	[redacted], FL Region 3 2010	BYI 02960 200 SL	TRTD1	Broadcast spray	13	18 (173)	0.373 (0.418)	0.373 (0.418)		None

[a] NA = Not applicable.

Duplicate composite samples of sugar cane (cane), along with an untreated control sample, were collected at crop maturity.

The residue(s) of BYI 02960, DFA, and DFEAF were quantitated by LC/MS/MS using stable isotopically labeled internal standards standards. The individual analyte residues were summed to give a total BYI 02960 residue. Residue measurements below the analyte LOQ were summed into the total BYI 02960 residue value as the analyte LOQ value.

Findings

Concurrent recoveries of BYI 02960, DFA, and DFEAF were measured with each set of samples to verify method performance. All recoveries were corrected for any interferences in corresponding controls. The overall mean of the recoveries at each fortification level was within the acceptable range of 70 to 110%, and the standard deviation values were ≤ 20% (Table 6.6.3.2-4).

Table 6.6.3.2-4: Summary of recoveries of BYI 02960 from sugar cane

Crop Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean Recovery (%) [a]	Std Dev (%)
Sugar cane[b]	BYI 02960	0.010	7	70, 109, 88, 87, 105, 71, 68	85%	17%
		0.10	4	111, 106, 99, 87	101%	11%
	DFA	0.05	7	72, 85, 78, 81, 84, 94, 75	81%	7%
		0.10	4	90, 106, 91, 82	92%	10%
	DFEAF	0.010	7	83, 96, 86, 115, 71, 96, 94	92%	14%
		0.10	4	103, 111, 96, 89	100%	9%

[a] Mean Recovery = mathematical average of all recoveries.

The freezer storage stability study indicates that BYI 02960 residues were stable in sugarcane commodities during frozen storage for at least 18 months (559 days) prior to analysis. The maximum storage period of frozen samples in this study for BYI 02960 was 178 days (6 months). A summary of the storage conditions are shown in Table 6.6.3.2-5.

Table 6.6.3.2-5: Summary of storage conditions for sugar cane

Residue Component(s)	Matrix (RAC)	Maximum Average Storage Temperatur (°C) [a]	Actual Storage Duration months (days) [b]	Interval of Demonstrated Storage Stability months (days) [c]
BYI 02960	Sugar cane	< -20	6 (178)	18 (559)
DFEAF	Sugar cane	< -20	6 (178)	18 (559)
DFA	Sugar cane	< -20	6 (178)	18 (559)

[a] The maximum average storage temperature is from the time of sample receipt at BRP until sample extraction and is the maximum of all average freezer temperatures at BRP. While preparing for sample analysis, the samples were maintained in a laboratory freezer.

[b] The storage duration is the time from field sampling through the last sample extraction.

[c] [redacted], [redacted] [redacted]. 2012. Storage stability of BYI 02960, difluoroacetic acid, and difluoroethyl-amino-furanone in plant matrices. Bayer CropScience Report No. RARVP046, amended version including 18-month data (KIIA 6.1.1/01).

The total BYI 02960 residue data from sugar cane crops planted at 14 days following application of BYI 02960 200 SL to soil are shown in Table 6.6.3.2.-6.

Table 6.6.3.2-6: Total BYI 02960 residue data from sugar cane crops planted at 14 days after soil application of BYI 02960 SL 200

Trial Number	Location (City, State, Region, and Year)	Plot Name	Crop Variety	Commodity	Total Rate Lb ai/A (kg ai/ha)	PBI (Plant Back Interval, days)[a]	BYI 02960 Residue (ppm)	DFA Residue (ppm) (parent equivalents)	DFEAF Residue (ppm) (parent equivalents)	Total BYI 02960 Residue (ppm)[b]
RV286-10RA	[redacted], FL, Region 3, 2010	TRTD1	Saccharum spp.	Sugar cane	0.369 (0.414)	14	<0.010	<0.050	<0.010	<0.070
RV287-10RB	[redacted], FL, Region 3, 2011	TRTD1	2143	Sugar cane	0.356 (0.399)	14	<0.010	<0.050	<0.010	<0.070
RV001-11RA	[redacted], FL, Region 3, 2011	TRTD1	1446	Sugar cane	0.366 (0.411)	14	<0.010	<0.050	<0.010	<0.070
RV002-11RA	[redacted], FL, Region 3, 2010	TRTD1	CP52-48	Sugar cane	0.373 (0.418)	13	<0.010	<0.050	<0.010	<0.070

a Plant Back Interval (PBI) is the interval between the application and the planting of the sugar cane.

b Total BYI 02960 residue is the sum of BYI 02960, DFA, and DFEAF residue in parent equivalents. Residue measurements below the analyte LOQ were summed into the total BYI 02960 residue value as the analyte LOQ value. These totals represent the upper limit of what the residue levels might be.

Conclusion:

Four rotational crop field trials were conducted to measure the magnitude of total BYI 02960 residue in/on sugar cane following one application of BYI 02960 200 SL to bare ground, followed by planting of sugar cane 13 to 14 days later.

The total BYI 02960 residue in sugar cane was less than the limit of quantification.

The residue data provided in this report support the NAFTA registration of a 14-day plant-back interval for sugar cane as a rotational crop following the approved label uses of BYI 02960 200 SL in NAFTA Crop Region 3.

IIA 6.7 Proposed residue definition and maximum residue levels

IIA 6.7.1 Proposed residue definition

► PLANT MATRICES

– Data collection, risk assessment

For BYI 02960 residues in *target plants* (primary crops) and *rotational crops* (succeeding crops), the proposed residue definition for **data collection** and **risk assessment** is the sum of parent compound BYI 02960 and its metabolites DFA and BYI 02960-difluoroethyl-amino-furanone (DFEAF), expressed in BYI 02960 equivalents.

Metabolism studies have been conducted in five diverse crops (tomato, apple, potato, cotton, and rice) for foliar and soil applications and in confined rotational crops (Swiss chard, turnip, and wheat) after application of BYI 02960 onto bare soil and cultivating of succeeding crops at three plant-back intervals. The plant metabolism studies have shown a reasonably consistent metabolic profile across both foliar and soil application.

The only residues of BYI 02960 that were consistently observed at significant levels across all primary and succeeding crops were the parent compound BYI 02960 and DFA, both of which are specific to BYI 02960 use. In primary crops, all other major metabolites were detected in individual RACs only, and generally at low concentrations. Only the natural class of compounds glucose/carbohydrates, which was formed from the degradation of the furanone moiety and incorporation of ^{14}C into natural plant constituents, was detected in relatively high concentrations.

In confined rotational crops, nine major metabolites were detected besides the parent compound and DFA. However, all of them were detected in individual RACs only, mainly in feed commodities. The major metabolites detected in food commodities were generally at low concentrations, except for glucose/carbohydrates, which are natural compounds, and the metabolites BYI 02960-OH and BYI 02960-OH-glyc, which were also observed in the rat. The metabolite BYI 02960-difluoroethyl-amino-furanone (=DFEAF) was also a major metabolite found in Swiss chard RACs in all rotations. Since it was not observed in the rat and the metabolism studies indicated that no other appropriate marker compound was present, BCS included this metabolite in the residue definition for the data collection method.

BYI 02960-difluoroethyl-amino-furanone appeared to be a suitable marker compound for estimating residue levels of other metabolites, if deemed necessary. For the sake of consistency, BCS analysed the samples of all supervised residue trials on target plants and rotational crops for these three compounds. Thus the residue definition for risk assessment for target plants and rotational crops has three constituents: BYI 02960 (parent compound), DFA, and BYI 02960-difluoroethyl-amino-furanone (DFEAF).

No other metabolite need be included in the residue definition for risk assessment, since it has been shown that none of the metabolites present a risk for the consumer (cf KIIA 5.10/03). All metabolites identified in the metabolism studies show either no consumer exposure under realistic conditions or a consumer exposure below the agreed Threshold level of Toxicological Concern (TTC; <1.5 µg/kg bw), or it has been shown that the metabolites are covered by the endpoints derived for the parent compound BYI 02960 (either via additional toxicity testing or their presence in the rat ADME studies).

– Enforcement

Results from supervised residue trials show that BYI 02960 and DFA are, by far, the most prominent components of the residues in target plants and rotational crops. The residues of metabolite BYI 02960-difluoroethyl-amino-furanone (DFEAF) were below the LOQ of 0.01 mg/kg in virtually all samples.

Considering these results as well as those from the metabolism studies, parent compound BYI 02960 and DFA are the proposed constituents (expressed as their sum, in BYI 02960 equivalents) for the residue definition for **enforcement** for *target plants* and *rotational crops*.

► **ANIMAL MATRICES**

– Data collection

For *animal matrices* the sum of BYI 02960, DFA, BYI 02960-OH, and BYI 02960-acetyl-AMCP, expressed as BYI 02960 equivalents, is proposed as residue definition for **data collection**.

The proposal is based on the results of the livestock metabolism studies (cf KIIA 6.2). In these studies, parent compound BYI 02960 is a significant, if not the dominant constituent of the residue in milk, eggs, and edible tissues of both tested species. Other metabolites determined in comparable concentrations are the natural compound lactose in goat's milk after administration of [furanone-4-^{14}C]BYI 02960, BYI 02960-acetyl-AMCP in eggs and tissues of laying hens after administration of [pyridinylmethyl-^{14}C]BYI 02960, and BYI 02960-OH in eggs.

DFA was determined in selected livestock samples by high-resolution LC-MS subsequent to the metabolism studies, since rat studies conducted with [ethyl-1-^{14}C]BYI 02960 showed major amounts of this metabolite in organs and tissues. Extrapolation of rat data suggested high DFA levels in livestock tissues as well, which was confirmed by the non-radioactive LC-MS analyses. Based on these findings, it was concluded that difluoroacetic acid is a major livestock metabolite and should be a constituent of the residue definition for data collection.

– Risk assessment, enforcement

On the basis of the results of the feeding studies conducted in poultry and cattle (cf KIIA 6.4.1 and KIIA 6.4.2), it has been shown that parent BYI 02960 and metabolite DFA were by far the predominant compounds detected. The residues of the metabolite BYI 02960-acetyl-AMCP were well below the LOQ of 0.01 mg/kg in all animal matrices at the corresponding 1X dose levels; the metabolite BYI 02960-OH was detected in cattle liver and kidney, only (0.011-0.019 mg/kg). However, this metabolite is also a major rat metabolite and therefore its toxicity is covered by the endpoints derived for the parent compound.

Considering these results in combination with those from livestock metabolism, BYI 02960 parent compound and its metabolite DFA (expressed as their sum, in BYI 02960 equivalents) are the proposed constituents for the residue definitions for **risk assessment** and **enforcement** in *animal matrices*.

No other metabolite need be included in the residue definition for risk assessment, since it has been shown that none of the metabolites pose a risk for the consumer (cf KIIA 5.10/03). All metabolites identified in the metabolism studies show either no consumer exposure under realistic conditions or a consumer exposure below the agreed Threshold level of Toxicological Concern (TTC; <1.5 µg/kg bw), or it has been shown that the metabolites are covered by the endpoints derived for the parent compound BYI 02960 (either via additional toxicity testing or their presence in the rat ADME studies).

IIA 6.7.2 Proposed maximum residue levels (MRLs) and justification

General remark:

In this summary section (KIIA 6.7.2), the name DFEAF will be used for the metabolite BYI 02960-difluoroethyl-amino-furanone, which is relevant to the tested residue definition:

Name	*Metab. No.*	*Standard "dossier name"*
DFEAF	M34	BYI 02960-difluoroethyl-amino-furanone

Based on the proposed residue definition for risk assessment in plant materials — the calculated total residues of BYI 02960, consisting of the sum of the residues of the parent compound and its metabolites DFA and DFEAF — and on the studies presented in this dossier, MRL proposals are presented below for the primary use of BYI 02960 in the EU, as well as in crops grown around the world (primarily in countries addressed by the Global Joint Review) which are exported from there to the EU. In addition, the effect of crop rotation was evaluated in this dossier; appropriate MRLs are proposed for these cases as well.

The proposed residue definition for enforcement is slightly different than the one for risk assessment, as it does not include DFEAF. However, DFEAF did not play a major role in any of the trials and thus its effect on the MRL calculation is negligible. The total residue values are valid for MRL calculations.

IIA 6.7.2.1 MRL Proposals in Plant Matrices Based on EUROPEAN Residue Data

Based on the proposed residue definition for risk assessment in plant materials — the calculated total residues of BYI 02960, consisting of the sum of the residues of the parent compound and its metabolites DFA and DFEAF — and on the studies presented in this dossier, MRL proposals are presented below for the primary use of BYI 02960 in lettuce and hops, as well as in apple (pome fruit), grape, tomato (incl. eggplant), peppers, cucumber (including gherkins and zucchini), and watermelon.

Besides primary uses, residues in following crops were also tested, based on data circulating in 2010 re. considerations for draft guidance in rotational crops in the EU. In addition to a "main" study, i.e. covering multiple rotations and 3 rotational crop groups (root, leafy, and cereal crops), further data from 1-crop, 1-rotation studies for root and tuber, stem, fruiting, bulb, and legume vegetables, as well as for pulses reflect the situation in which the original crop failed, and the field was used again shortly thereafter, in the same season, to grow a subsequent crop. MRL proposals are also presented below for these "rotational" uses of BYI 02960; additional data from a study on oilseeds (rape) will be submitted later.

Calculations were made according to the statistical methods described in EU guideline 7039/VI/95 and the German BBA-Guideline, Part IV, 3-6 (1990), using methods I (including elimination of outliers) and II; and to the OECD calculator.

► PRIMARY USES

The EU studies described in this dossier reflect the "safe uses", i.e. in lettuce and hops, as well as further scheduled uses – both agricultural and for "home & garden" use – in apples and pears, grapes, tomatoes and eggplants, peppers, cucumbers (incl. gherkins) and zucchini, and watermelons.

● Lettuce

Complete sets of field residue trials were conducted in lettuce in both the northern and southern European field residue regions, as well as in greenhouses. When comparing the results, it is evident that final residue levels are generally highest in the greenhouse, with the highest HR value of any trial set and considerably higher median residues. Total residue levels of BYI 02960 in all lettuce head samples taken at 3 days after the final application (3 days represents the envisaged PHI for this crop, in the field "home & garden use" as well as in the "agricultural use" in greenhouses) were 0.14-3.0 mg/kg in the north (median 0.71 mg/kg), 0.39-3.2 mg/kg in the south (median 1.2 mg/kg), and 0.80-6.0 mg/kg in the greenhouse (median 2.2 mg/kg). Residues for the outdoor "agricultural use" (1 application, 10-day PHI) were markedly lower.

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of 0.01-0.09 mg/kg in each residue result reported [0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

Thus, the greenhouse use can be defined as critical "region" for the calculation of the MRL. A summary of the calculation is shown below in table 6.7.2-1. (More details of the calculations are shown in table 6.7.2-6, later in this chapter.)

Table 6.7.2-1: Total residues of BYI 02960/ lettuce — maximum residue values for a pre-harvest interval of 3 days (from greenhouse trials)

EU Method I (all values)	7.12 mg/kg
EU Method II (75% quantile)	6.20 mg/kg
OECD Unrounded MRL Estimate	8.58 mg/kg

0.80; 1.4; 1.8; 2.0; 2.2; 2.5; 2.7; 3.5; 6.0 mg/kg
STMR: 2.2 mg/kg
HR: 6.0 mg/kg

Based on the actual trial results, in which the highest residue levels were 6.0 mg/kg, combined with the calculated results using the EU system, the proposed EU MRL for BYI 02960 in lettuce is 7.0 mg/kg.

Remark 1:
If based on the OECD calculator, the proposal would be 9.0 mg/kg.

Remark 2:
The residue behaviour was similar in both open and closed-headed varieties of lettuce. In the greenhouse trials with closed-head varieties, total residues on day 3 ranged from 1.8-3.5 mg/kg (n=4). In trials with open-headed (leafy) varieties, the range was 0.80-6.0 mg/kg (n=5). In the field trials in section 6.3.1, residues in closed-head varieties ranged from 0.40-2.7 mg/kg (n=6) while those in open-head varieties ranged from 0.14-3.2 mg/kg (n=12).

Thus, these trials also provide valid data for the establishment of MRLs, despite the stipulation in the new guidance, soon to be effective (2013/14), that only open-headed varieties should be used.)

● Hops

Eight field residue trials were conducted in hops in the northern European field residue region. Total residue levels of BYI 02960 in all green cone samples taken at 21 days after the final application (representing the envisaged PHI for this crop) were <0.40-0.87 mg/kg, with a median value of 0.47 mg/kg.

In general, MRLs in Europe are set on the dried hop cones. In the kiln-dried commodity, total residue levels of BYI 02960 21 days after the final application were 0.56-2.4 mg/kg, with a median value of 1.1 mg/kg. However, in three trials, residues were higher on day 28 than on day 21; when taking these higher values into consideration, residues ranged from 0.61-2.4 mg/kg, with a median value of 1.2 mg/kg.

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF were below its LOQ [0.1 mg/kg in BYI 02960 equivalents] in each residue result reported, and, as such, it is a very minor contributor to the total residue levels calculated and reported in these trials. Its effect on the MRL calculation is negligible.)

A summary of the calculation is shown below in table 6.7.2-2. (More details of the calculations are shown in table 6.7.2-7, later in this chapter.)

Table 6.7.2-2: Total residues of BYI 02960/ dried hop cones — maximum residue values for a pre-harvest interval of 21 days

EU Method I (all values)	3.56 mg/kg
EU Method II (75% quantile)	4.25 mg/kg
OECD Unrounded MRL Estimate	4.13 mg/kg

0.61; 0.73; 0.78; 1.1; 1.2; 1.6; 2.3; 2.4
STMR: 1.2 mg/kg
HR: 2.4 mg/kg

Based on the actual trial results and using both the EU and the OECD calculation systems, the proposed EU MRL for BYI 02960 in hop (dried cone) is 4.0 mg/kg.

● Pome fruit

Ten field residue trials were conducted in apples in both the northern and southern European field residue regions. When comparing the results, the most critical residue levels at or after the envisaged PHI of 14 days were observed in the northern European trials, in which peak total residue values were 0.09-0.37 mg/kg (median 0.13 mg/kg). In the southern European trials, the total residue values were found at 0.04-0.12 mg/kg (median 0.07 mg/kg).

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of <0.01 mg/kg in each residue result reported [0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

Thus, the northern European field data can be defined as the critical "region" for the calculation of the MRL. A summary of the calculations is shown below in table 6.7.2-3a. (More details of the calculations are shown in table 6.7.2-20a, later in this chapter.)

Table 6.7.2-3a: Total residues of BYI 02960/ apple — maximum residue values for a pre-harvest interval of 14 days (northern European residue region)

EU Method I (all values)	0.393 mg/kg
EU Method II (75% quantile)	0.345 mg/kg
OECD Unrounded MRL Estimate	0.484 mg/kg

0.09; 0.094; 0.10; 0.10; 0.12; 0.13; 0.15; 0.17; 0.18; 0.37 mg/kg
STMR: 0.125 mg/kg
HR: 0.37 mg/kg

As expected, the southern European field data are less critical, leading to lower MRL suggestions, as shown below in table 6.7.2-3b. (More details of the calculations are shown in table 6.7.2-20b.)

Table 6.7.2-3b: Total residues of BYI 02960/ apple — maximum residue values for a pre-harvest interval of 14 days (southern European residue region)

EU Method I (all values)	0.153 mg/kg
EU Method II (75% quantile)	0.187 mg/kg
OECD Unrounded MRL Estimate	0.199 mg/kg

<0.04; 0.04; 0.05; 0.058; 0.06; 0.06; 0.083; 0.088; 0.11; 0.12 mg/kg
STMR: 0.06 mg/kg
HR: 0.12 mg/kg

Based on the actual trial results, in which the highest residue levels were 0.37 mg/kg, combined with the calculated results using the EU system, the proposed EU MRL for BYI 02960 in pome fruit based on European trial data alone would be 0.4 mg/kg.

Remark 1:
If based on the OECD calculator, the proposal would be 0.5 mg/kg.

However, for this crop group, uses are planned outside of the EU which are import-relevant. The data from NAFTA trials is presented in chapter 6.3.2. An additional MRL calculation for those trials is presented below in section 6.7.2.2.

● Grape

Nine field residue trials were conducted in grape in the northern European field residue region, and eight in the south. When comparing the results, it is evident that final residue levels are higher in the northern European trials, with the higher HR value and considerably higher median residues. Peak total residue levels of BYI 02960 in all grape bunch samples taken at or after the envisaged PHI (14 days after the final application) ranged from 0.18-0.50 mg/kg in the northern European residue region (median 0.26 mg/kg), and 0.08-0.33 mg/kg in southern trials (median 0.18 mg/kg). Residue levels determined in bunches and in the grapes themselves were virtually identical, thus either data set can be used for MRL calculation.

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of <0.01 mg/kg in each residue result reported [0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

Thus, the northern European use can be defined as critical "region" for the calculation of the MRL. A summary of the calculations is shown below in table 6.7.2-4a. (More details of the calculations are shown in table 6.7.2-21a, later in this chapter.)

Table 6.7.2-4a: Total residues of BYI 02960/ grape — maximum residue values for a pre-harvest interval of 14 days (northern European residue region)

EU Method I (all values)	0.711 mg/kg
EU Method II (75% quantile)	0.940 mg/kg
OECD Unrounded MRL Estimate	0.987 mg/kg

0.18; 0.23; 0.23; 0.24; 0.26; 0.38; 0.45; 0.49; 0.50 mg/kg
STMR: 0.26 mg/kg
HR: 0.50 mg/kg

As explained above, the southern European field data are less critical. This is confirmed in the results shown below in table 6.7.2-4b. (More details of the calculations are shown in table 6.7.2-21b.)

Table 6.7.2-4b: Total residues of BYI 02960/grape — maximum residue values for a pre-harvest interval of 14 days (southern European residue region)

EU Method I (all values)	0.452 mg/kg
EU Method II (75% quantile)	0.520 mg/kg
OECD Unrounded MRL Estimate	0.566 mg/kg

0.08; 0.11; 0.16; 0.17; 0.18; 0.20; 0.28; 0.33 mg/kg
STMR: 0.18 mg/kg
HR: 0.33 mg/kg

Based on the actual trial results, in which the highest residue levels were 0.50 mg/kg, combined with the calculated results using the EU system, the proposed EU MRL for BYI 02960 in grapes based on EU data along would be 0.9 mg/kg.

Remark 1:
If based on the OECD calculator, the proposal would be 1.0 mg/kg.

However, for this crop, uses are planned outside of the EU which are import-relevant. The data from NAFTA trials is presented in chapter 6.3.2. An additional MRL calculation for those trials is presented below in section 6.7.2.2.

● Tomatoes and eggplant

Complete sets of field residue trials were conducted in tomato in the southern European field residue region, as well as in greenhouses. When comparing the results, it is evident that final residue levels are generally highest in the greenhouse, with the higher HR value and considerably higher median residues. Peak total residue levels of BYI 02960 in all tomato fruit samples taken at or after the designated PHI of 3 days were <0.04-0.11 mg/kg in the southern European residue region (median 0.08 mg/kg), and 0.09-0.50 mg/kg in the greenhouse (median 0.14 mg/kg).

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of 0.01-0.029 mg/kg in each residue result reported

[0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

Thus, the greenhouse use can be defined as critical "region" for the calculation of the MRL. A summary of the calculations is shown below in table 6.7.2-5a. (More details of the calculations are shown in table 6.7.2-22a, later in this chapter.)

Table 6.7.2-5a: Total residues of BYI 02960/ tomato — maximum residue values for a pre-harvest interval of 3 days (from greenhouse trials)

EU Method I (all values)	0.706 mg/kg
EU Method II (75% quantile)	0.705 mg/kg
OECD Unrounded MRL Estimate	0.830 mg/kg

0.09; 0.10; 0.11; 0.13; 0.15; 0.30; 0.37; 0.50 mg/kg
STMR: 0.14 mg/kg
HR: 0.50 mg/kg

As explained above, the southern European field data are less critical. This is confirmed below in table 6.7.2-5b. (More details of the calculations are shown in table 6.7.2-22b.)

Table 6.7.2-5b: Total residues of BYI 02960/ tomato — maximum residue values for a pre-harvest interval of 3 days (southern European residue region)

EU Method I (all values)	0.149 mg/kg
EU Method II (75% quantile)	0.192 mg/kg
OECD Unrounded MRL Estimate	0.217 mg/kg

<0.04; 0.063; 0.067; 0.08; 0.08; 0.095; 0.096; 0.11 mg/kg
STMR: 0.08 mg/kg
HR: 0.11 mg/kg

Based on the actual trial results, in which the highest residue levels were 0.50 mg/kg, combined with the calculated results using the EU system, the proposed EU MRL for BYI 02960 in tomatoes and eggplants based on European trial data alone would be <u>0.7 mg/kg</u>.

Remark 1:
If based on the OECD calculator, the proposal would be 0.9 mg/kg.

Remark 2:
The HR in these trials, 0.50 mg/kg, was determined in a case of increasing residues on the final day of sampling. Most trials in this program showed plateau behavior, and there is little reason to believe that residues would continue to climb appreciably in the trial in question. The calculated MRL (0.7 or 0.9 mg/kg) also allows enough "space", so that even a higher HR would be "covered".

However, for this crop group, uses are planned outside of the EU which are import-relevant. The data from NAFTA trials is presented in chapter 6.3.2. An additional MRL calculation for those trials is presented below in section 6.7.2.2.

● Sweet (bell) peppers

Eight field residue trials were conducted in peppers in the southern European field residue region as well as 8 in greenhouses. When comparing the results, it is evident that final residue levels are generally highest in the greenhouse, with the higher HR value of the two trial sets and considerably higher median residues. Peak total residue levels of BYI 02960 in all pepper fruit samples taken at or after the designated PHI of 3 days were 0.05-0.25 mg/kg in the south (median 0.17 mg/kg), and 0.12-0.63 mg/kg in the greenhouse (median 0.27 mg/kg).

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of <0.01-0.022 mg/kg in each residue result reported [0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

Thus, the greenhouse use can be defined as critical "region" for the calculation of the MRL. A summary of the calculations is shown below in table 6.7.2-6a. (More details of the calculations are shown in table 6.7.2-23a, later in this chapter.)

Table 6.7.2-6a: Total residues of BYI 02960/sweet peppers — maximum residue values for a pre-harvest interval of 3 days (from greenhouse trials)

EU Method I (all values)	0.801 mg/kg
EU Method II (75% quantile)	0.740 mg/kg
OECD Unrounded MRL Estimate	0.931 mg/kg

0.12; 0.18; 0.20; 0.26; 0.27; 0.28; 0.40; 0.63 mg/kg
STMR: 0.27 mg/kg
HR: 0.63 mg/kg

As explained above, the southern European field data are less critical. This is confirmed below in table 6.7.2-6b. (More details of the calculations are shown in table 6.7.2-23b.)

Table 6.7.2-6b: Total residues of BYI 02960/sweet peppers — maximum residue values for a pre-harvest interval of 3 days (southern European residue region)

EU Method I (all values)	0.393 mg/kg
EU Method II (75% quantile)	0.470 mg/kg
OECD Unrounded MRL Estimate	0.503 mg/kg

0.05; 0.12; 0.12; 0.14; 0.20; 0.22; 0.24; 0.25 mg/kg
STMR: 0.17 mg/kg
HR: 0.25 mg/kg

Based on the actual trial results, in which the highest residue levels were 0.63 mg/kg, combined with the calculated results using the EU system, the proposed EU MRL for BYI 02960 in peppers is 0.8 mg/kg.

Remark 1:
If based on the OECD calculator, the proposal would be 1.0 mg/kg.

Remark 2:
In some trials in the pepper program, increasing residues were seen, even up to the final sampling interval, both in field and greenhouse studies. The residues in the field were considerably lower than those in the greenhouse, thus this issue is of less importance in the field; nevertheless, the "erratic" nature of the residues over the sampling period and the fact that the measured peaks were reached at various intervals – with the designated PHI being the most frequent point – would seem to indicate that the residue values from the field are very suitable for evaluation.

With regard to the greenhouse, the HR in these trials, 0.63 mg/kg, was determined in a case of "erratic" residue levels which appeared to be part of a "plateau" behavior seen in most trials. (The trend towards peak residues being determined at late intervals was also seen in several other trials, but the values in question were not particularly close to the HR, so there is little reason to believe they could affect the HR of these trials.) The calculated MRL (0.8 or 1.0 mg/kg) would seem to allow enough "space", so that even a higher HR would be "covered".

● Cucumbers, gherkins, and zucchini

Complete sets of field residue trials were conducted on cucumbers/gherkins in both the southern European field residue region as well as in greenhouses. When comparing the results, it is evident that final residue levels are similar in both trials settings. Maximum total residue levels of BYI 02960 in all cucumber fruit samples taken at or after the envisaged PHI of 3 days after the final application ranged from 0.09-0.74 mg/kg in the southern field trials (median 0.21 mg/kg) and 0.18-0.52 mg/kg in greenhouses (median 0.31 mg/kg).

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of <0.01 mg/kg in each residue result reported [0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

Thus, the southern European field and greenhouse were compared to define a critical "region" for the calculation of the MRL. A summary of the calculations is shown below in table 6.7.2-7a&b. (More details of the calculations are shown in table 6.7.2-24a&b, later in this chapter.)

Table 6.7.2-7a: Total residues of BYI 02960/ cucumber and related crops — maximum residue values for a pre-harvest interval of 3 days (southern European field residue region)

EU Method I (all values)	0.937 mg/kg
EU Method II (75% quantile)	0.690 mg/kg
OECD Unrounded MRL Estimate	1.107 mg/kg

0.09; 0.12; 0.16; 0.19; 0.22; 0.27; 0.37; 0.74 mg/kg
STMR: 0.21 mg/kg
HR: 0.74 mg/kg

Table 6.7.2-7b: Total residues of BYI 02960/ cucumber and related crops — maximum residue values for a pre-harvest interval of 3 days (from greenhouse trials)

EU Method I (all values)	0.666 mg/kg
EU Method II (75% quantile)	0.810 mg/kg
OECD Unrounded MRL Estimate	0.971 mg/kg

0.18; 0.24; 0.28; 0.29; 0.32; 0.33; 0.43; 0.52 mg/kg
STMR: 0.31 mg/kg
HR: 0.52 mg/kg

Based on the actual trial results, in which the highest residue levels were 0.74 mg/kg, combined with the calculated results using the EU system, the field use will be the "driver" of the MRL, as the calculated values are somewhat higher. Thus, the proposed EU MRL for BYI 02960 in cucumber, zucchini, and gherkins is 0.9 mg/kg.

Remark 1:
If based on the OECD calculator, the proposal would be 1.5 mg/kg.

● Watermelon

Nine field residue trials were conducted in melons watermelons in the southern European field residue region, and nine more in greenhouses. When comparing the results, it is evident that final residue levels are somewhat higher in the greenhouse trials, with the higher HR value and considerably higher median residues. Peak total residue levels of BYI 02960 in all melon samples taken at or after the designated PHI of 3 days after the final application were in the range of 0.05-0.25 mg/kg in the southern European residue region (median 0.13 mg/kg), and 0.10-0.30 mg/kg in the greenhouse trials (median 0.17 mg/kg).

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of <0.01 mg/kg in each residue result reported [0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

Thus, the greenhouse use seems to be the critical "region" for the calculation of the MRL. A summary of the calculations is shown below in table 6.7.2-8a. (More details of the calculations are shown in table 6.7.2-25a, later in this chapter.)

Table 6.7.2-8a: Total residues of BYI 02960/ watermelons — maximum residue values for a pre-harvest interval of 3 days (from greenhouses)

EU Method I (all values)	0.425 mg/kg
EU Method II (75% quantile)	0.570 mg/kg
OECD Unrounded MRL Estimate	0.587 mg/kg

0.10; 0.13; 0.14; 0.16; 0.17 0.19; 0.27; 0.30; 0.30 mg/kg
STMR: 0.17 mg/kg
HR: 0.30 mg/kg

As explained above, the data from the field trials are less critical. This is confirmed below in table 6.7.2-8b. (More details of the calculations are shown in table 6.7.2-25b.)

Table 6.7.2-8b: Total residues of BYI 02960/ watermelon — maximum residue values for a pre-harvest interval of 3 days (southern European field residue region)

EU Method I (all values)	0.326 mg/kg
EU Method II (75% quantile)	0.340 mg/kg
OECD Unrounded MRL Estimate	0.403 mg/kg

0.05; 0.05; 0.11; 0.12; 0.13; 0.16; 0.16; 0.18; 0.25 mg/kg
STMR: 0.13 mg/kg
HR: 0.25 mg/kg

Based on the actual trial results, in which the highest residue levels were 0.30 mg/kg, combined with the calculated results using the EU system, the proposed EU MRL for BYI 02960 in watermelon is 0.6 mg/kg.

Remark 1:
If based on the OECD calculator, the proposal would also be 0.6 mg/kg.

Remark 2:
In some trials in the watermelon program, increasing residues were seen, even up to the final sampling interval, both in field and greenhouse studies. The residues in the field were less critical than those in the greenhouse. However, the HR in the field, 0.25 mg/kg, while measured on the final day of sampling, was quite evidently part of a "plateau" and thus is valid for MRL evaluation. Further cases of "increasing residues" in the field also exhibited plateau behavior, as evidenced by the fact that residues peaked at various sampling points across the entire package.

With regard to the greenhouse, the HR in these trials, 0.30 mg/kg, was determined in a case of slow, steady increase in residue levels seen in many trials. The calculated MRL (0.6 mg/kg) allows considerable "space", so that even a higher HR could be "covered", but the trend in the greenhouse trials is difficult to evaluate conclusively.

► ROTATIONAL CROPS (based on earlier uses on a plot)

The field rotational crop data described in this dossier reflect the "main"study, i.e. covering multiple rotations and 3 rotational crop groups (root, leafy, and cereal crops). Further data from limited rotational crop studies for root, tuber, stem, fruiting, bulb, and legume vegetables, as well as for pulses reflect the situation in which the original crop failed, and the field was used again shortly thereafter, in the same season, to grow a subsequent crop. (Additional data from limited rotational crop studies for oilseeds [rapeseed] will be submitted later.)

● Cereals (based on crop rotation)

In rotational crop trials, levels of the total residues of BYI 02960 in grain were highest in the first rotation, i.e. after the shortest plant-back interval of 25-33 days, representing field re-use after crop failure. Residue levels were 0.11-0.65 mg/kg, with a median value of 0.35 mg/kg.

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of <0.01 mg/kg in each residue result reported [0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

A summary of the calculation is shown below in table 6.7.2-9. (More details of the calculations are shown in table 6.7.2-26, later in this chapter.)

Table 6.7.2-9: Total residues of BYI 02960/ **rotational** cereal crops — maximum residue values for a plant-back interval of 25-33 days

EU Method I (all values)	2.44 mg/kg
EU Method II (75% quantile)	1.30 mg/kg
OECD Unrounded MRL Estimate	1.45 mg/kg

0.11; 0.35; 0.65 mg/kg
STMR: 0.35 mg/kg
HR: 0.65 mg/kg

Based on the actual trial results, in which the highest residue levels were 0.65 mg/kg, combined with the calculated results using both the EU and OECD calculation systems, the proposed EU MRL for BYI 02960 in cereal grain as following crops (i.e. as a result of field re-use) would be 1.5 mg/kg.

However, as stated in section 6.6.3.1.1 of this dossier, the values from the European trials will be extrapolated by the Australian authority to account for differences in the use pattern (tested seasonal rate in the EU: 200 g a.s/ha; max. seasonal rate in Australia: 450 g a.s./ha), as well as associated steady-state peak concentration due to use over consecutive seasons (a factor of 1.2 is applied; for details of how this factor is derived, cf. KIIA 6.10/02) in order to establish an MRL there for rotated cereal crops.

Cereals are one of the most important export commodities in Australia. As cereals are also considered to be a commodity traded in significant quantities from GJR countries to the EU, a harmonized EU MRL should reflect the values established in relevant exporting countries. Based on assumptions relevant to Australia, using the new values obtained after re-assessment of the EU rotational crop study with barley, the revised MRL calculation is summarized below:

Table 6.7.2-9a: Total residues of BYI 02960/ **rotational** cereal crops — maximum residue values for a plant-back interval of 25-33 days
FOLLOWING RE-CALCULATION TO ACCOUNT FOR AUSTRALIAN CONDITIONS

OECD Unrounded MRL Estimate	3.921 mg/kg

0.297; 0.945; 1.755 mg/kg (recalculated for Australian use pattern and soil uptake)
STMR: *0.945* mg/kg
HR: *1.755* mg/kg

Based on the these re-calculated results and using the OECD MRL calculation, the proposed EU MRL for BYI 02960 cereal crops as following crops (i.e. as a result of worldwide field re-use, and importation of such crops) would be 4.0 mg/kg.

● Root vegetables (based on crop rotation)

No primary residue trials were conducted on root crops, but residues in these plants can arise by re-use of a particular field following a previous application of BYI 02960. In rotational crop trials, levels of the total residues of BYI 02960 in roots (carrot or turnip) were generally highest in the first rotation, i.e. after the shortest plant-back interval of 25-30 days, representing field re-use after crop failure. In one case, residues were higher in the third rotation (PBI 284 days). Highest total residue levels in "marketable" root vegetables ranged from 0.06-0.14 mg/kg, with a median value of 0.08 mg/kg.

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of <0.01 mg/kg in each residue result reported [0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

A summary of the calculation is shown below in table 6.7.2-10. (More details of the calculations are shown in table 6.7.2-27, later in this chapter.)

Table 6.7.2-10: Total residues of BYI 02960/ **rotational** root crops — maximum residue values for a plant-back interval of 25-30 days

EU Method I (all values)	0.27 mg/kg
EU Method II (75% quantile)	0.25 mg/kg
OECD Unrounded MRL Estimate	0.26 mg/kg

0.06; 0.07; 0.08; 0.14 mg/kg
STMR: 0.08 mg/kg
HR: 0.14 mg/kg

Based on the these trial results and using both the EU and OECD MRL calculations, the proposed EU MRL for BYI 02960 in root vegetable crops as following crops (i.e. as a result of field re-use) is 0.3 mg/kg.

● Leafy vegetables (based on crop rotation)

Although primary residue trials were conducted on lettuce, residues in other botanically related leafy vegetable plants can arise by re-use of a particular field following a previous application of BYI 02960. In rotational crop trials, levels of the total residues of BYI 02960 in lettuce were highest in the first rotation, i.e. after the shortest plant-back interval of 25-30 days, representing field re-use after crop failure. Total residue levels in "marketable" lettuce heads ranged from <0.04-0.16 mg/kg, with a median value of 0.08 mg/kg.

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of <0.01 mg/kg in each residue result reported [0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

A summary of the calculation is shown below in table 6.7.2-11. (More details of the calculations are shown in table 6.7.2-28, later in this chapter.)

Table 6.7.2-11: Total residues of BYI 02960/**rotational** leafy vegetable crops — maximum residue values for a plant-back interval of 25-30 days

EU Method I (all values)	0.35 mg/kg
EU Method II (75% quantile)	0.29 mg/kg
OECD Unrounded MRL Estimate	0.29 mg/kg

<0.04; 0.07; 0.09; 0.16 mg/kg
STMR: 0.08 mg/kg
HR: 0.16 mg/kg

Based on the these trial results and using the EU and OECD calculation systems, the proposed EU MRL for BYI 02960 in leafy vegetable crops as following crops (i.e. as a result of field re-use) is 0.3 mg/kg.

● Tuber vegetables (based on crop rotation)

No primary EU residue trials were conducted on potato tuber or similar vegetables, but residues in these plants can arise by re-use of a particular field following a previous application of BYI 02960. In rotational crop trials, levels of the total residues of BYI 02960 in mature potato tubers ranged from 0.048 mg/kg to 0.27 mg/kg after a plant-back interval of 25-33 days, representing field re-use after crop failure.

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of <0.01 mg/kg in each residue result reported [0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

A summary of the MRL calculation is shown below in table 6.7.2-12. (More details of the calculations are shown in table 6.7.2-29, later in this chapter.)

Table 6.7.2-12: Total residues of BYI 02960/ **rotational** tuber vegetable crops — maximum residue values for a plant-back interval of 25-33 days

EU Method I (all values)	0.719 mg/kg
EU Method II (75% quantile)	0.510 mg/kg
OECD Unrounded MRL Estimate	0.591 mg/kg

0.048; 0.056; 0.21; 0.27 mg/kg
STMR: 0.13 mg/kg
HR: 0.27 mg/kg

Based on the these trial results and using both the EU and OECD MRL calculations, the proposed EU MRL for BYI 02960 potato tuber and similar crops as following crops (i.e. as a result of field re-use) would be 0.7 mg/kg.

However, as stated in section 6.6.3.1.2 of this dossier, the values from the European trials will be extrapolated by the Australian authority to account for differences in the use pattern (tested seasonal rate in the EU: 250 g a.s/ha; max. seasonal rate in Australia: 450 g a.s./ha), as well as associated steady-state peak concentration due to use over consecutive seasons (a factor of 1.2 is applied; for details of how this factor is derived, cf. KIIA 6.10/02) in order to establish an MRL there for rotated tuber crops.

As potatoes are considered to be a commodity traded in significant quantities from GJR countries to the EU, a harmonized EU MRL should reflect the values established in relevant exporting countries. Based on assumptions relevant to Australia, using the new values obtained after re-assessment of the EU rotational crop study with potatoes, the revised MRL calculation is summarized below:

Table 6.7.2-12a: Total residues of BYI 02960/ **rotational** tuber vegetable crops — maximum residue values for a plant-back interval of 25-33 days
FOLLOWING RE-CALCULATION TO ACCOUNT FOR AUSTRALIAN CONDITIONS

OECD Unrounded MRL Estimate	1.277 mg/kg

0.104; 0.121; 0.454; 0.583 mg/kg (recalculated for Australian use pattern and soil uptake)
STMR: *0.287* mg/kg
HR: *0.583* mg/kg

Based on the these re-calculated results and using the OECD MRL calculation, the proposed EU MRL for BYI 02960 potato tuber and similar crops as following crops (i.e. as a result of worldwide field re-use, and importation of such crops) would be 1.5 mg/kg.

● Stem vegetables (based on crop rotation)

No primary residue trials were conducted on leek or similar stem vegetables in the EU, but residues in these plants can arise by re-use of a particular field following a previous application of BYI 02960. In rotational crop trials, levels of the total residues of BYI 02960 in leek sampled at harvest maturity ranged from 0.040 mg/kg to 0.25 mg/kg after a plant-back interval of 26-33 days, representing field re-use after crop failure.

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of <0.01 mg/kg in each residue result reported [0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

A summary of the MRL calculation is shown below in table 6.7.2-13. (More details of the calculations are shown in table 6.7.2-30, later in this chapter.)

Table 6.7.2-13: Total residues of BYI 02960/ **rotational** stem vegetable crops — maximum residue values for a plant-back interval of 26-33 days

EU Method I (all values)	0.603 mg/kg
EU Method II (75% quantile)	0.430 mg/kg
OECD Unrounded MRL Estimate	0.494 mg/kg

0.040; 0.059; 0.11; 0.25 mg/kg
STMR: 0.08 mg/kg
HR: 0.25 mg/kg

Based on the actual trial results combined with the calculated results using both the EU and OECD calculation systems, the proposed EU MRL for BYI 02960 in stem vegetables as following crops (i.e. as a result of field re-use) is <u>0.6 mg/kg</u>.

● Fruiting vegetables (based on crop rotation)

Although primary residue trials were conducted on cucumbers and gherkins as well as in tomatoes and peppers in the EU, residues in other botanically related fruiting vegetable plants can arise by re-use of a particular field following a previous application of BYI 02960. In limited rotational crop trials, levels of the total residues of BYI 02960 in cucumber fruit sampled at harvest ripeness ranged from 0.067 mg/kg to 0.43 mg/kg after a plant-back interval of 25-30 days, representing field re-use after crop failure.

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of <0.01 mg/kg in each residue result reported [0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

A summary of the MRL calculation is shown below in table 6.7.2-14. (More details of the calculations are shown in table 6.7.2-31, later in this chapter.)

Table 6.7.2-14: Total residues of BYI 02960/ **rotational** fruiting vegetable crops — maximum residue values for a plant-back interval of 25-30 days

EU Method I (all values)	1.08 mg/kg
EU Method II (75% quantile)	0.815 mg/kg
OECD Unrounded MRL Estimate	0.903 mg/kg

0.067; 0.30; 0.34; 0.43 mg/kg
STMR: 0.32 mg/kg
HR: 0.43 mg/kg

Based on the these trial results and using the EU and OECD calculation systems, the proposed EU MRL for BYI 02960 in fruiting vegetable crops as following crops (i.e. as a result of field re-use) is 1 mg/kg.

● Bulb vegetables (based on crop rotation)

No primary residue trials were conducted in the EU on bulb vegetable crops, but residues in these plants can arise by re-use of a particular field following a previous application of BYI 02960. In rotational crop trials, levels of the total residues of BYI 02960 in onion bulb ranged from <0.04 mg/kg to 0.18 mg/kg after a plant-back interval of 25-33 days, representing field re-use after crop failure.

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of <0.01 mg/kg in each residue result reported [0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

A summary of the MRL calculation is shown below in table 6.7.2-15. (More details of the calculations are shown in table 6.7.2-32, later in this chapter.)

Table 6.7.2-15: Total residues of BYI 02960/ **rotational** bulb vegetable crops — maximum residue values for a plant-back interval of 25-33 days

EU Method I (all values)	0.402 mg/kg
EU Method II (75% quantile)	0.316 mg/kg
OECD Unrounded MRL Estimate	0.334 mg/kg

<0.04; 0.078; 0.091; 0.18 mg/kg
STMR: 0.08 mg/kg
HR: 0.18 mg/kg

Based on the these trial results and using both the EU and OECD MRL calculations, the proposed EU MRL for BYI 02960 in bulb vegetable crops as following crops (i.e. as a result of field re-use) would be 0.4 mg/kg.

However, as stated in section 6.6.3.1.5 of this dossier, the values from the European trials will be extrapolated by the Australian authority to account for differences in the use pattern (tested seasonal rate in the EU: 250 g a.s/ha; max. seasonal rate in Australia: 450 g a.s./ha), as well as associated steady-state peak concentration due to use over consecutive seasons (a factor of 1.2 is applied; for details of how this factor is derived, cf. KIIA 6.10/02) in order to establish an MRL there for rotated bulb vegetables.

As onions are considered to be a commodity traded in significant quantities from GJR countries to the EU, a harmonized EU MRL should reflect the values established in relevant exporting countries. Based on assumptions relevant to Australia, using the new values obtained after re-assessment of the EU rotational crop study with onions, the revised MRL calculation is summarized below:

Table 6.7.2-15a: Total residues of BYI 02960/ **rotational** bulb vegetable crops — maximum residue values for a plant-back interval of 25-33 days
FOLLOWING RE-CALCULATION TO ACCOUNT FOR AUSTRALIAN CONDITIONS

OECD Unrounded MRL Estimate	0.722 mg/kg

0.086; 0.168; 0.197; 0.389 mg/kg (recalculated for Australian use pattern and soil uptake)
STMR: *0.183* mg/kg
HR: *0.389* mg/kg

Based on the these re-calculated results and using the OECD MRL calculation, the proposed EU MRL for BYI 02960 onions and similar crops as following crops (i.e. as a result of worldwide field re-use, and importation of such crops) would be 0.8 mg/kg.

● **Legume vegetables (based on crop rotation)**

No primary residue trials were conducted on legume vegetable crops in the EU, but residues in these plants can arise by re-use of a particular field following a previous application of BYI 02960. In rotational crop trials, levels of the total residues of BYI 02960 in French bean pods ranged from 0.28 mg/kg to 1.1 mg/kg after a plant-back interval of 25-30 days, representing field re-use after crop failure.

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of <0.01 mg/kg in each residue result reported [0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

A summary of the MRL calculation is shown below in table 6.7.2-16. (More details of the calculations are shown in table 6.7.2-33, later in this chapter.)

Table 6.7.2-16: Total residues of BYI 02960/ **rotational** legume vegetable crops — maximum residue values for a plant-back interval of 25-30 days

EU Method I (all values)	2.45 mg/kg
EU Method II (75% quantile)	1.95 mg/kg
OECD Unrounded MRL Estimate	2.04 mg/kg

0.28; 0.40; 0.59; 1.1 mg/kg
STMR: 0.50 mg/kg
HR: 1.1 mg/kg

Based on the these trial results and using both the EU and OECD MRL calculations, the proposed EU MRL for BYI 02960 in legume vegetable crops as following crops (i.e. as a result of field re-use) is 2 mg/kg.

● Pulses (based on crop rotation)

No primary EU residue trials were conducted on pulses, but residues in these plants can arise by re-use of a particular field following a previous application of BYI 02960. In rotational crop trials, levels of the total residues of BYI 02960 in dry pea seeds ranged from 0.67 mg/kg to 2.3 mg/kg after a plant-back interval of 25-35 days, representing field re-use after crop failure.

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of <0.01 mg/kg in each residue result reported [0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

A summary of the MRL calculation results is shown below in table 6.7.2-17. (More details of the calculations are shown in table 6.7.2-34, later in this chapter.)

Table 6.7.2-17: Total residues of BYI 02960/ **rotational** pulses — maximum residue values for a plant-back interval of 25-35 days

EU Method I (all values)	5.65 mg/kg
EU Method II (75% quantile)	4.50 mg/kg
OECD Unrounded MRL Estimate	4.73 mg/kg

0.67; 1.0; 2.1; 2.3 mg/kg
STMR: 1.6 mg/kg
HR: 2.3 mg/kg

Based on the these trial results and using both the EU and OECD MRL calculations, the proposed EU MRL for BYI 02960 in pulses as following crops (i.e. as a result of field re-use) would be 6 mg/kg.

However, as stated in section 6.6.3.1.7 of this dossier, the values from the European trials will be extrapolated by the Australian authority to account for differences in the use pattern (tested seasonal rate in the EU: 250 g a.s/ha; max. seasonal rate in Australia: 450 g a.s./ha), as well as associated steady-state peak concentration due to use over consecutive seasons (a factor of 1.2 is applied; for details of how this factor is derived, cf. KIIA 6.10/02) in order to establish an MRL there for rotated pulses.

Pulses are one of the most important export commodities in Australia. As pulses are also considered to be a commodity traded in significant quantities from GJR countries to the EU, a harmonized EU MRL should reflect the values established in relevant exporting countries. Based on assumptions relevant to Australia, using the new values obtained after re-assessment of the EU rotational crop study with field peas, the revised MRL calculation is summarized below:

Table 6.7.2-17a: Total residues of BYI 02960/ **rotational** pulses — maximum residue values for a plant-back interval of 25-35 days
FOLLOWING RE-CALCULATION TO ACCOUNT FOR AUSTRALIAN CONDITIONS

OECD Unrounded MRL Estimate	10.222 mg/kg

1.45; 2.16; 4.54; 4.97 mg/kg (recalculated for Australian use pattern and soil uptake)
STMR: *3.35* mg/kg
HR: *4.97* mg/kg

Based on the these re-calculated results and using the OECD MRL calculation, the proposed EU MRL for BYI 02960 field peas and similar pulse crops as following crops (i.e. as a result of worldwide field re-use, and importation of such crops) would be 10 mg/kg.

• Oilseeds (based on crop rotation)

No primary residue trials were conducted on oilseed crops, but residues in these plants can arise by re-use of a particular field following a previous application of BYI 02960. In rotational crop trials, levels of the total residues of BYI 02960 in oilseed rape, seeds ranged from 0.070 to 0.17 mg/kg after a plant-back interval of 27-41 days, representing field re-use after crop failure.

(The total residue values include the metabolite DFEAF, which is not proposed to be a constituent of the enforcement residue definition. However, residues of DFEAF did not play a major role in any of the trials, having been determined at levels of <0.01 mg/kg in each residue result reported [0.01 mg/kg is the LOQ for the analyte, expressed in parent compound equivalents]. As such, it is a very minor contributor to the total residue levels determined in these trials; its effect on the MRL calculation is negligible.)

A summary of the calculation is shown below in table 6.7.2-35. (More details of the calculations are shown in table 6.7.2-36, later in this chapter.)

Table 6.7.2-35: Total residues of BYI 02960/ **rotational** oilseed crops — maximum residue values for a plant-back interval of 27-41 days

EU Method I (all values)	0.33 mg/kg
EU Method II (75% quantile)	0.31 mg/kg
OECD Unrounded MRL Estimate	0.33 mg/kg

0.070; 0.092; 0.11; 0.17 mg/kg
STMR: 0.101 mg/kg
HR: 0.17 mg/kg

Based on the these trial results and using both the EU and OECD MRL calculations, the proposed EU MRL for BYI 02960 in oilseeds as following crops (i.e. as a result of field re-use) would be 0.4 mg/kg.

However, as stated in section 6.6.3.1.8 of this dossier, the values from the European trials will be extrapolated by the Australian authority to account for differences in the use pattern (tested seasonal rate in the EU: 250 g a.s/ha; max. seasonal rate in Australia: 450 g a.s./ha), as well as associated steady-state peak concentration due to use over consecutive seasons (a factor of 1.2 is applied; for details of how this factor is derived, cf. KIIA 6.10/02) in order to establish an MRL there for rotated oilseed crops.

Oilseeds are one of the most important export commodities in Australia. As oilseed commodities are also considered to be traded in significant quantities from GIR countries to the EU, a harmonized EU MRL should reflect the values established in relevant exporting countries. Based on assumptions relevant to Australia, using the new values obtained after re-assessment of the EU rotational crop study with oilseed rape, the revised MRL calculation is summarized below:

Table 6.7.2-35a: Total residues of BYI 02960/ **rotational** oilseed crops — maximum residue values for a plant-back interval of 27-41 days
FOLLOWING RE-CALCULATION TO ACCOUNT FOR AUSTRALIAN CONDITIONS

OECD Unrounded MRL Estimate	0.716 mg/kg

0.151; 0.199; 0.238; 0.367 mg/kg (recalculated for Australian use pattern and soil uptake)
STMR: *0.218* mg/kg
HR: *0.367* mg/kg

Based on the these trial results and using the OECD MRL calculation, the proposed EU MRL for BYI 02960 oilseed rape and similar crops as following crops (i.e. as a result of worldwide field re-use, and importation of such crops) would be 0.8 mg/kg.

Table 6.7.2-18: Calculation of MRL proposals for lettuce according to EU and OECD guidelines

BASIC DATA

Residue :	**total residue of BYI 02960 calc.**	Crop group :	**leaf and stem vegetables**
Portion analyzed :	**head**	Commodity :	**lettuce (greenhouse)**
Target value :	**MRL**	PHI :	**3 d**

No.	Crop	Days after appli-cation	Residue value (mg/kg)	Trial No./ Study No.	No. of appl.	FL-Type	Product	Country	Area of appl.
1	lettuce	7[2]	1.4	10-2212-01/10-2212	2	SL 200	BYI 02960 SL 200	France	G
2	lettuce	3	2.0	10-2212-02/10-2212	2	SL 200	BYI 02960 SL 200	Germany	G
3	lettuce, head	3	3.5	10-2212-03/10-2212	2	SL 200	BYI 02960 SL 200	Germany	G
4	lettuce, head	3	2.5	10-2212-04/10-2212	2	SL 200	BYI 02960 SL 200	Netherlands	G
5	lettuce, head	3	1.8	10-2212-05/10-2212	2	SL 200	BYI 02960 SL 200	Italy	G
6	lettuce	3	2.2	11-2070-01/11-2070	2	SL 200	BYI 02960 SL 200	France	G
7	lettuce	3	0.80	11-2070-02/11-2070	2	SL 200	BYI 02960 SL 200	Italy	G
8	lettuce	3	6.0	11-2070-03/11-2070	2	SL 200	BYI 02960 SL 200	Spain	G
9	lettuce, head	3	2.7	11-2070-04/11-2070	2	SL 200	BYI 02960 SL 200	Germany	G

* - this value was used as it was higher than the value at the PHI (3 days)

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Table 6.7.2-18 (cont'd): Calculation of MRL proposals for lettuce according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (lettuce)

Method I (Weinmann/Nolting) (all values)	R s k Rmax=R+k*s	2.544 1.508 3.032 7.118
Method II (Wilkening) (75 % quantile)	R (0.75) Rber=2*R(0.75)	3.100 6.200

Summary of results:
Maximum residue values for a pre-harvest interval of: 3 days

Method I (all values)	7.12 mg/kg
Method II (75% quantile)	6.20 mg/kg

● OECD Calculator

Results (lettuce)

Total number of data (n)	9	Standard deviation (SD)	1.508
Lowest residue	0.8	Percentage of censored data	0
Highest residue	6	Number of non-censored data	9
Median residue	2.200	Correction factor for censoring (CF)	1.000
Mean	2.544		

Proposed MRL estimate

Highest residue	6
Mean + 4 SD	8.578
CF × 3 mean	7.633
Unrounded MRL	8.578
Rounded MRL	9

Table 6.7.2-19: Calculation of MRL proposals for hops according to EU and OECD guidelines

BASIC DATA

Residue :	**total residue of BYI 02960 calc.**	Crop group :	**stimulant plants**
Portion analyzed :	**cone, kiln-dried**	Commodity :	**hop**
Target value :	**MRL**	PHI :	**21 d**

No.	Crop	Days after application	Residue value (mg/kg)	Trial No./ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	hop	28*	1.6	10-2225-01 / 10-2225	1	SL 200	BYI 02960 SL 200	Germany	F
2	hop	20	0.78	10-2225-02 / 10-2225	1	SL 200	BYI 02960 SL 200	Germany	F
3	hop	21	1.1	10-2225-03 / 10-2225	1	SL 200	BYI 02960 SL 200	Germany	F
4	hop	21	1.2	10-2225-04 / 10-2225	1	SL 200	BYI 02960 SL 200	Germany	F
5	hop	28*	2.3	11-2076-01 / 11-2076	1	SL 200	BYI 02960 SL 200	Germany	F
6	hop	28*	0.61	11-2076-02 / 11-2076	1	SL 200	BYI 02960 SL 200	Germany	F
7	hop	20	2.4	11-2076-03 / 11-2076	1	SL 200	BYI 02960 SL 200	Germany	F
8	hop	22	0.73	11-2076-04 / 11-2076	1	SL 200	BYI 02960 SL 200	Germany	F

* - this value was used as it was higher than the value at the PHI (21 days)

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Table 6.7.2-19 (cont'd): Calculation of MRL proposals for hops according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (hop)

Method I (Weinmann/Nolting)	R	1.340
(all values)	s	0.698
	k	3.188
	Rmax=R+k*s	3.565
Method II (Wilkening)	R (0.75)	2.125
(75 % quantile)	Rber=2*R(0.75)	4.250

Summary of results:

Maximum residue values for a pre-harvest interval of: 21 days

Method I (all values)	3.56 mg/kg
Method II (75% quantile)	4.25 mg/kg

● OECD Calculator

Results (hop)

Total number of data (n)	8	Standard deviation (SD)	0.698
Lowest residue	0.61	Percentage of censored data	0
Highest residue	2.4	Number of non-censored data	8
Median residue	1.150	Correction factor for censoring (CF)	1.000
Mean	1.340		

Proposed MRL estimate

Highest residue	2.4
Mean + 4 SD	4.131
CF × 3 mean	4.020
Unrounded MRL	4.131
Rounded MRL	5

Table 6.7.2-20a: Calculation of MRL proposals for pome fruit in the northern European residue region according to EU and OECD guidelines

BASIC DATA

Residue :	**total residue of BYI 02960 calc.**	Crop group :	**pome fruits**
Portion analyzed :	**fruit**	Commodity :	**apple (northern Europe)**
Target value :	**MRL**	PHI :	**14 d**

No.	Crop	Days after appli-cation	Residue value (mg/kg)	Trial No./ Study No.	No. of appl.	FL-Type	Product	Country	Area of appl.
1	apple	14	0.10	10-2171-01/ 10-2171	2	SL 200	BYI 02960 SL 200	Germany	F
2	apple	14	0.18	10-2171-02/ 10-2171	2	SL 200	BYI 02960 SL 200	Germany	F
3	apple	14	0.10	10-2171-03/ 10-2171	2	SL 200	BYI 02960 SL 200	Germany	F
4	apple	14	0.09	10-2171-04/ 10-2171	2	SL 200	BYI 02960 SL 200	Northern France	F
5	apple	21*	0.17	10-2171-05/ 10-2171	2	SL 200	BYI 02960 SL 200	Netherlands	F
6	apple	14	0.12	10-2171-06/ 10-2171	2	SL 200	BYI 02960 SL 200	Belgium	F
7	apple	36*	0.13	11-2077-01/ 10-2077	2	SL 200	BYI 02960 SL 200	Germany	F
8	apple	14	0.094	11-2077-02/ 10-2077	2	SL 200	BYI 02960 SL 200	Northern France	F
9	apple	28*	0.37	11-2077-03/ 10-2077	2	SL 200	BYI 02960 SL 200	Germany	F
10	apple	21*	0.15	11-2077-04/ 10-2077	2	SL 200	BYI 02960 SL 200	United Kingdom	F

* - this value was used as it was higher than the value at the PHI (14 days)

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Table 6.7.2-20a (cont'd): Calculation of MRL proposals for pome fruit in the northern European residue region according to EU and OECD guidelines

EVALUATION SUMMARIES

- EU guideline 7039/VI/95 of 22 July 1997

Results (apple)

Method I (Weinmann/Nolting)	R	0.150
(all values)	s	0.083
	k	2.911
	Rmax=R+k*s	0.393
Method II (Wilkening)	R (0.75)	0.173
(75 % quantile)	Rber=2*R(0.75)	0.345

Summary of results:
Maximum residue values for a pre-harvest interval of: 14 days

Method I (all values)	0.393 mg/kg
Method II (75% quantile)	0.345 mg/kg

- OECD Calculator

Results (apple)

Total number of data (n)	10	Standard deviation (SD)	0.083
Lowest residue	0.09	Percentage of censored data	0
Highest residue	0.37	Number of non-censored data	10
Median residue	0.125	Correction factor for censoring (CF)	1.000
Mean	0.15		

Proposed MRL estimate

Highest residue	0.37
Mean + 4 SD	0.484
CF × 3 mean	0.451
Unrounded MRL	0.484
Rounded MRL	0.5

Table 6.7.2-20b: Calculation of MRL proposals for pome fruit in the southern European residue region according to EU and OECD guidelines

BASIC DATA

Residue :	**total residue of BYI 02960 calc.**	Crop group :	**pome fruits**
Portion analyzed :	**fruit**	Commodity :	**apple (southern Europe)**
Target value :	**MRL**	PHI :	**14 d**

No.	Crop	Days after appli-cation	Residue value (mg/kg)	Trial No./ Study No.	No. of appl.	FL-Type	Product	Country	Area of appl.
1	apple	14*	0.06	10-2172-01/ 10-2172	2	SL 200	BYI 02960 SL 200	Southern France	F
2	apple	14*	0.04	10-2172-02/ 10-2172	2	SL 200	BYI 02960 SL 200	Southern France	F
3	apple	14*	0.05	10-2172-03/ 10-2172	2	SL 200	BYI 02960 SL 200	Italy	F
4	apple	14*	0.06	10-2172-04/ 10-2172	2	SL 200	BYI 02960 SL 200	Italy	F
5	apple	14*	0.12	10-2172-05/ 10-2172	2	SL 200	BYI 02960 SL 200	Spain	F
6	apple	14*	<0.04	10-2172-06/ 10-2172	2	SL 200	BYI 02960 SL 200	Spain	F
7	apple	35**	0.058	11-2078-01/ 11-2078	1	SL 200	BYI 02960 SL 200	Southern France	F
8	apple	14	0.11	11-2078-02/ 11-2078	1	SL 200	BYI 02960 SL 200	Spain	F
9	apple	14	0.088	11-2078-03/ 11-2078	1	SL 200	BYI 02960 SL 200	Italy	F
10	apple	21**	0.083	11-2078-04/ 11-2078	1	SL 200	BYI 02960 SL 200	Portugal	F

* 14 days after the first application = immediately before the second application in 2010-trials

** this value was used as it was higher than the value at the PHI (14 days)

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Table 6.7.2-20b (cont'd): Calculation of MRL proposals for pome fruit in the southern European residue region according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (apple)

Method I (Weinmann/Nolting) (all values)	R s k Rmax=R+k*s	0.071 0.028 2.911 0.153
Method II (Wilkening) (75 % quantile)	R (0.75) Rber=2*R(0.75)	0.094 0.187

Summary of results:
Maximum residue values for a pre-harvest interval of: 14 days

Method I (all values)	0.153 mg/kg
Method II (75% quantile)	0.187 mg/kg

● OECD Calculator

Results (apple)

Total number of data (n)	10	Standard deviation (SD)	0.028
Lowest residue	0.04	Percentage of censored data	10
Highest residue	0.12	Number of non-censored data	9
Median residue	0.06	Correction factor for censoring (CF)	0.933
Mean	0.071		

Proposed MRL estimate

Highest residue	0.120
Mean + 4 SD	0.183
CF × 3 mean	0.199
Unrounded MRL	0.199
Rounded MRL	0.2

Table 6.7.2-21a: Calculation of MRL proposals for grape in the northern European residue region according to EU and OECD guidelines

BASIC DATA

Residue :	**total residue of BYI 02960 calc.**	Crop group :	**berries and small fruit**
Portion analyzed :	**fruit**	Commodity :	**grape (northern Europe)**
Target value :	**MRL**	PHI :	**14 d**

No.	Crop	Days after appli-cation	Residue value (mg/kg)	Trial No./ Study No.	No. of appl.	FL-Type	Product	Country	Area of appl.
1	grape	21*	0.49	10-2218-01 / 10-2218	2	SL 200	BYI 02960 SL 200	Germany	F
2	grape	28*	0.45	10-2218-02 / 10-2218	2	SL 200	BYI 02960 SL 200	Germany	F
3	grape	28*	0.26	10-2218-03 / 10-2218	2	SL 200	BYI 02960 SL 200	Northern France	F
4	grape	21*	0.18	10-2218-04 / 10-2218	2	SL 200	BYI 02960 SL 200	Northern France	F
5	grape	21*	0.23	10-2218-05 / 10-2218	2	SL 200	BYI 02960 SL 200	Belgium	F
6	grape	42*	0.38	11-2089-01 / 11-2089	2	SL 200	BYI 02960 SL 200	Germany	F
7	grape	21*	0.50	11-2089-02 / 11-2089	2	SL 200	BYI 02960 SL 200	Germany	F
8	grape	21*	0.23	11-2089-03 / 11-2089	2	SL 200	BYI 02960 SL 200	Northern France	F
9	grape	14	0.24	11-2089-04 / 11-2089	2	SL 200	BYI 02960 SL 200	Northern France	F

* this value was used as it was higher than the value at the PHI (14 days)

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Table 6.7.2-21a (cont'd): Calculation of MRL proposals for grape in the northern European residue region according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (grape)

Method I (Weinmann/Nolting) (all values)	R	0.329
	s	0.126
	k	3.032
	Rmax=R+k*s	0.711
Method II (Wilkening) (75 % quantile)	R (0.75)	0.470
	Rber=2*R(0.75)	0.940

Summary of results:
Maximum residue values for a pre-harvest interval of: 14 days

Method I (all values)	0.711 mg/kg
Method II (75% quantile)	0.940 mg/kg

● OECD Calculator

Results (grape)

Total number of data (n)	9	Standard deviation (SD)	0.126
Lowest residue	0.18	Percentage of censored data	0
Highest residue	0.50	Number of non-censored data	9
Median residue	0.26	Correction factor for censoring (CF)	1.000
Mean	0.329		

Proposed MRL estimate

Highest residue	0.50
Mean + 4 SD	0.833
CF × 3 mean	0.987
Unrounded MRL	0.987
Rounded MRL	1

Table 6.7.2-21b: Calculation of MRL proposals for grape in the southern European residue region according to EU and OECD guidelines

BASIC DATA

Residue :	**total residue of BYI 02960 calc.**	Crop group :	**berries and small fruit**
Portion analyzed :	**fruit**	Commodity :	**grape (southern Europe)**
Target value :	**MRL**	PHI :	**14 d**

No.	Crop	Days after appli-cation	Residue value (mg/kg)	Trial No./ Study No.	No. of appl.	FL-Type	Product	Country	Area of appl.
1	grape	21*	0.28	10-2219-01/ 10-2219	2	SL 200	BYI 02960 SL 200	Southern France	F
2	grape	28*	0.20	10-2219-02/ 10-2219	2	SL 200	BYI 02960 SL 200	Spain	F
3	grape	21*	0.16	10-2219-03/ 10-2219	2	SL 200	BYI 02960 SL 200	Italy	F
4	grape	14	0.08	10-2219-04/ 10-2219	2	SL 200	BYI 02960 SL 200	Spain	F
5	grape	42*	0.33	11-2090-01-T/ 11-2090	2	SL 200	BYI 02960 SL 200	Southern France	F
6	grape	21*	0.11	11-2090-02-T / 11-2090	2	SL 200	BYI 02960 SL 200	Spain	F
7	grape	21*	0.18	11-2090-03-T / 11-2090	2	SL 200	BYI 02960 SL 200	Spain	F
8	grape	14	0.17	11-2090-04-T / 11-2090	2	SL 200	BYI 02960 SL 200	Italy	F

* this value was used as it was higher than the value at the PHI (14 days)

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Table 6.7.2-21b (cont'd): Calculation of MRL proposals for grape in the southern European residue region according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (grape)

Method I (Weinmann/Nolting)	R	0.189
(all values)	s	0.083
	k	3.188
	Rmax=R+k*s	0.452
Method II (Wilkening)	R (0.75)	0.260
(75 % quantile)	Rber=2*R(0.75)	0.520

Summary of results:
Maximum residue values for a pre-harvest interval of: 14 days

Method I (all values)	0.452 mg/kg
Method II (75% quantile)	0.520 mg/kg

● OECD Calculator

Results (grape)

Total number of data (n)	8	Standard deviation (SD)	0.083
Lowest residue	0.08	Percentage of censored data	0
Highest residue	0.33	Number of non-censored data	8
Median residue	0.175	Correction factor for censoring (CF)	1.000
Mean	0.189		

Proposed MRL estimate

Highest residue	0.33
Mean + 4 SD	0.519
CF × 3 mean	0.566
Unrounded MRL	0.566
Rounded MRL	0.6

Table 6.7.2-22a: Calculation of MRL proposals for tomato/eggplant in the field according to EU and OECD guidelines

BASIC DATA

Residue :	**total residue of BYI 02960 calc.**	Crop group :	**fruiting vegetables**
Portion analyzed :	**fruit**	Commodity :	**tomato (southern Europe)**
Target value :	**MRL**	PHI :	**3 d**

No.	Crop	Days after appli-cation	Residue value (mg/kg)	Trial No./ Study No.	No. of appl.	FL-Type	Product	Country	Area of appl.
1	tomato	3	< 0.04	10-2186-01/ 10-2186	2	SL 200	BYI 02960 SL 200	Southern France	F
2	tomato	3	0.08	10-2186-02/ 10-2186	2	SL 200	BYI 02960 SL 200	Italy	F
3	tomato	3	0.11	10-2186-03/ 10-2186	2	SL 200	BYI 02960 SL 200	Spain	F
4	tomato	5*	0.08	10-2186-04/ 10-2186	2	SL 200	BYI 02960 SL 200	Portugal	F
5	tomato	10*	0.096	11-2087-01/ 11-2087	2	SL 200	BYI 02960 SL 200	Spain	F
6	tomato	7*	0.095	11-2087-02/ 11-2087	2	SL 200	BYI 02960 SL 200	Italy	F
7	tomato	3	0.063	11-2087-03/ 11-2087	2	SL 200	BYI 02960 SL 200	Portugal	F
8	tomato	10*	0.067	11-2087-04/ 11-2087	2	SL 200	BYI 02960 SL 200	Greece	F

* this value was used as it was higher than the value at the PHI (3 days)

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Table 6.7.2-22a (cont'd): Calculation of MRL proposals for tomato/eggplant in the field according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (tomato)

Method I (Weinmann/Nolting)	R	0.079
(all values)	s	0.022
	k	3.188
	Rmax=R+k*s	0.149
Method II (Wilkening)	R (0.75)	0.096
(75 % quantile)	Rber=2*R(0.75)	0.192

Summary of results:
Maximum residue values for a pre-harvest interval of: 3 days

Method I (all values)	0.149 mg/kg
Method II (75% quantile)	0.192 mg/kg

● OECD Calculator

Results (tomato)

Total number of data (n)	8	Standard deviation (SD)	0.022
Lowest residue	0.04	Percentage of censored data	13
Highest residue	0.11	Number of non-censored data	7
Median residue	0.080	Correction factor for censoring (CF)	0.917
Mean	0.079		

Proposed MRL estimate

Highest residue	0.11
Mean + 4 SD	0.167
CF × 3 mean	0.217
Unrounded MRL	0.217
Rounded MRL	0.3

Table 6.7.2-22b: Calculation of MRL proposals for tomato/eggplant in greenhouses according to EU and OECD guidelines

BASIC DATA

Residue :	**total residue of BYI 02960 calc.**	Crop group :	**fruiting vegetables**
Portion analyzed :	**fruit**	Commodity :	**tomato (greenhouse)**
Target value :	**MRL**	PHI :	**3 d**

No.	Crop	Days after appli-cation	Residue value (mg/kg)	Trial No./ Study No.	No. of appl.	FL-Type	Product	Country	Area of appl.
1	tomato	3	0.09	10-2190-01/ 10-2190	2	SL 200	BYI 02960 SL 200	Germany	G
2	tomato	7*	0.15	10-2190-02/ 10-2190	2	SL 200	BYI 02960 SL 200	Netherlands	G
3	tomato	5*	0.11	10-2190-03/ 10-2190	2	SL 200	BYI 02960 SL 200	France	G
4	tomato	5*	0.10	10-2190-04/ 10-2190	2	SL 200	BYI 02960 SL 200	Belgium	G
5	tomato	4	0.30	11-2085-01/ 11-2085	2	SL 200	BYI 02960 SL 200	Germany	G
6	tomato	3	0.13	11-2085-02/ 11-2085	2	SL 200	BYI 02960 SL 200	Netherlands	G
7	tomato	3	0.37	11-2085-03/ 11-2085	2	SL 200	BYI 02960 SL 200	Italy	G
8	tomato	10*	0.50	11-2085-04/ 11-2085	2	SL 200	BYI 02960 SL 200	Spain	G

* this value was used as it was higher than the value at the PHI (3 days)

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Table 6.7.2-22b (cont'd): Calculation of MRL proposals for tomato/eggplant in greenhouses according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (tomato)

Method I (Weinmann/Nolting)	R	0.219
(all values)	s	0.153
	k	3.188
	Rmax=R+k*s	0.706
Method II (Wilkening)	R (0.75)	0.353
(75 % quantile)	Rber=2*R(0.75)	0.705

Summary of results:
Maximum residue values for a pre-harvest interval of: 3 days

Method I (all values)	0.706 mg/kg
Method II (75% quantile)	0.705 mg/kg

● OECD Calculator

Results (tomato)

Total number of data (n)	8	Standard deviation (SD)	0.153
Lowest residue	0.09	Percentage of censored data	0
Highest residue	0.50	Number of non-censored data	8
Median residue	0.140	Correction factor for censoring (CF)	1.000
Mean	0.219		

Proposed MRL estimate

Highest residue	0.50
Mean + 4 SD	0.830
CF × 3 mean	0.656
Unrounded MRL	0.830
Rounded MRL	0.9

Table 6.7.2-23a: Calculation of MRL proposals for sweet (bell) pepper in the field according to EU and OECD guidelines

BASIC DATA

Residue :	**total residue of BYI 02960 calc.**	Crop group :	**fruiting vegetables**
Portion analyzed :	**fruit**	Commodity :	**sweet pepper (southern Europe)**
Target value :	**MRL**	PHI :	**3 d**

No.	Crop	Days after application	Residue value (mg/kg)	Trial No./ Study No.	No. of appl.	FL-Type	Product	Country	Area of appl.
1	pepper, sweet	3	0.12	10-2187-01/ 10-2187	2	SL 200	BYI 02960 SL 200	Southern France	F
2	pepper, sweet	3	0.05	10-2187-02/ 10-2187	2	SL 200	BYI 02960 SL 200	Italy	F
3	pepper, sweet	3	0.24	10-2187-03/ 10-2187	2	SL 200	BYI 02960 SL 200	Spain	F
4	pepper, sweet	6*	0.12	10-2187-04/ 10-2187	2	SL 200	BYI 02960 SL 200	Portugal	F
5	pepper, sweet	14*	0.22	11-2083-01/ 11-2083	2	SL 200	BYI 02960 SL 200	Southern France	F
6	pepper, sweet	14*	0.20	11-2083-02/ 11-2083	2	SL 200	BYI 02960 SL 200	Spain	F
7	pepper, sweet	3	0.25	11-2083-03/ 11-2083	2	SL 200	BYI 02960 SL 200	Italy	F
8	pepper, sweet	14*	0.14	11-2083-04/ 11-2083	2	SL 200	BYI 02960 SL 200	Italy	F

* this value was used as it was higher than the value at the PHI (3 days)

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Table 6.7.2-23a (cont'd): Calculation of MRL proposals for sweet (bell) pepper in the field according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (sweet pepper)

Method I (Weinmann/Nolting) (all values)	R s k Rmax=R+k*s	0.168 0.071 3.188 0.393
Method II (Wilkening) (75 % quantile)	R (0.75) Rber=2*R(0.75)	0.235 0.470

Summary of results:
Maximum residue values for a pre-harvest interval of: 3 days

Method I (all values)	0.393 mg/kg
Method II (75% quantile)	0.470 mg/kg

● OECD Calculator

Results (sweet pepper)

Total number of data (n)	8	Standard deviation (SD)	0.071
Lowest residue	0.05	Percentage of censored data	0
Highest residue	0.25	Number of non-censored data	8
Median residue	0.170	Correction factor for censoring (CF)	1.000
Mean	0.168		

Proposed MRL estimate

Highest residue	0.25
Mean + 4 SD	0.450
CF × 3 mean	0.503
Unrounded MRL	0.503
Rounded MRL	0.5

Table 6.7.2-23b: Calculation of MRL proposals for sweet (bell) pepper in greenhouses according to EU and OECD guidelines

BASIC DATA

Residue :	**total residue of BYI 02960 calc.**	Crop group :	**fruiting vegetables**
Portion analyzed :	**fruit**	Commodity :	**sweet pepper (greenhouse)**
Target value :	**MRL**	PHI :	**3 d**

No.	Crop	Days after appli-cation	Residue value (mg/kg)	Trial No./ Study No.	No. of appl.	FL-Type	Product	Country	Area of appl.
1	pepper, sweet	10*	0.27	11-2081-01/ 11-2081	2	SL 200	BYI 02960 SL 200	France	G
2	pepper, sweet	14*	0.20	11-2081-02/ 11-2081	2	SL 200	BYI 02960 SL 200	France	G
3	pepper, sweet	3	0.28	11-2081-03/ 11-2081	2	SL 200	BYI 02960 SL 200	Spain	G
4	pepper, sweet	3	0.12	11-2081-04/ 11-2081	2	SL 200	BYI 02960 SL 200	Spain	G
5	pepper, sweet	14*	0.40	11-2081-05/ 11-2081	2	SL 200	BYI 02960 SL 200	Italy	G
6	pepper, sweet	14*	0.63	11-2081-06/ 11-2081	2	SL 200	BYI 02960 SL 200	Italy	G
7	pepper, sweet	14*	0.26	11-2081-07/ 11-2081	2	SL 200	BYI 02960 SL 200	Greece	G
8	pepper, sweet	14*	0.18	11-2081-08/ 11-2081	2	SL 200	BYI 02960 SL 200	Greece	G

* this value was used as it was higher than the value at the PHI (3 days)

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Table 6.7.2-23b (cont'd): Calculation of MRL proposals for sweet (bell) pepper in greenhouses according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (sweet pepper)

Method I (Weinmann/Nolting)	R	0.293
(all values)	s	0.160
	k	3.188
	Rmax=R+k*s	0.801
Method II (Wilkening)	R (0.75)	0.370
(75 % quantile)	Rber=2*R(0.75)	0.740

Summary of results:
Maximum residue values for a pre-harvest interval of: 3 days

Method I (all values)	0.801 mg/kg
Method II (75% quantile)	0.740 mg/kg

● OECD Calculator

Results (sweet pepper)

Total number of data (n)	8	Standard deviation (SD)	0.160
Lowest residue	0.12	Percentage of censored data	0
Highest residue	0.63	Number of non-censored data	8
Median residue	0.265	Correction factor for censoring (CF)	1.000
Mean	0.293		

Proposed MRL estimate

Highest residue	0.63
Mean + 4 SD	0.931
CF × 3 mean	0.878
Unrounded MRL	0.931
Rounded MRL	1

Table 6.7.2-24a: Calculation of MRL proposals for cucumber (incl. zucchini and gherkin) in the field according to EU and OECD guidelines

BASIC DATA

Residue :	**total residue of BYI 02960 calc.**	Crop group :	**fruiting vegetables**
Portion analyzed :	**fruit**	Commodity :	**cucumber (southern Europe)**
Target value :	**MRL**	PHI :	**3 d**

No.	Crop	Days after appli-cation	Residue value (mg/kg)	Trial No./ Study No.	No. of appl.	Fl.-Type	Product	Country	Area of appl.
1	cucumber	5*	0.19	10-2184-01/ 10-2184	2	SL 200	BYI 02960 SL 200	Southern France	F
2	cucumber	4*	0.27	10-2184-02/ 10-2184	2	SL 200	BYI 02960 SL 200	Spain	F
3	cucumber	7*	0.09	10-2184-03/ 10-2184	2	SL 200	BYI 02960 SL 200	Italy	F
4	cucumber	7*	0.22	10-2184-04/ 10-2184	2	SL 200	BYI 02960 SL 200	Southern France	F
5	gherkin	14*	0.16	11-2066-01/ 11-2066	2	SL 200	BYI 02960 SL 200	Southern France	F
6	gherkin	3	0.37	11-2066-02/ 11-2066	2	SL 200	BYI 02960 SL 200	Spain	F
7	gherkin	9*	0.74	11-2066-03/ 11-2066	2	SL 200	BYI 02960 SL 200	Spain	F
8	gherkin	9*	0.12	11-2066-04/ 11-2066	2	SL 200	BYI 02960 SL 200	Italy	F

* this value was used as it was higher than the value at the PHI (3 days)

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Table 6.7.2-24a (cont'd): Calculation of MRL proposals for cucumber (incl. zucchini and gherkin) in the field according to EU and OECD guidelines

EVALUATION SUMMARIES

- EU guideline 7039/VI/95 of 22 July 1997

Results (cucumber)

Method I (Weinmann/Nolting) (all values)	R s k Rmax=R+k*s	0.270 0.209 3.188 0.937
Method II (Wilkening) (75 % quantile)	R (0.75) Rber=2*R(0.75)	0.345 0.690

Summary of results:
Maximum residue values for a pre-harvest interval of: 3 days

Method I (all values)	0.937 mg/kg
Method II (75% quantile)	0.690 mg/kg

- OECD Calculator

Results (cucumber)

Total number of data (n)	8	Standard deviation (SD)	0.209
Lowest residue	0.09	Percentage of censored data	0
Highest residue	0.74	Number of non-censored data	8
Median residue	0.205	Correction factor for censoring (CF)	1.000
Mean	0.270		

Proposed MRL estimate

Highest residue	0.74
Mean + 4 SD	1.107
CF × 3 mean	0.810
Unrounded MRL	1.107
Rounded MRL	1.5

Table 6.7.2-24b: Calculation of MRL proposals for cucumber (incl. zucchini and gherkin) in greenhouses according to EU and OECD guidelines

BASIC DATA

Residue :	**total residue of BYI 02960 calc.**	Crop group :	**fruiting vegetables**
Portion analyzed :	**fruit**	Commodity :	**cucumber (greenhouse)**
Target value :	**MRL**	PHI :	**3 d**

No.	Crop	Days after appli-cation	Residue value (mg/kg)	Trial No./ Study No.	No. of appl.	FL-Type	Product	Country	Area of appl.
1	cucumber	3	0.24	10-2189-01/ 10-2189	2	SL 200	BYI 02960 SL 200	Southern France	G
2	cucumber	3	0.32	10-2189-02/ 10-2189	2	SL 200	BYI 02960 SL 200	Netherlands	G
3	cucumber	7*	0.52	10-2189-03/ 10-2189	2	SL 200	BYI 02960 SL 200	Germany	G
4	cucumber	3	0.28	10-2189-04/ 10-2189	2	SL 200	BYI 02960 SL 200	Italy	G
5	cucumber	10*	0.18	11-2067-01/ 11-2067	2	SL 200	BYI 02960 SL 200	Greece	G
6	cucumber	3	0.33	11-2067-02/ 11-2067	2	SL 200	BYI 02960 SL 200	Italy	G
7	cucumber	3	0.29	11-2067-03/ 11-2067	2	SL 200	BYI 02960 SL 200	Portugal	G
8	cucumber	10*	0.43	11-2067-04/ 11-2067	2	SL 200	BYI 02960 SL 200	Portugal	G

* this value was used as it was higher than the value at the PHI (3 days)

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Table 6.7.2-24b (cont'd): Calculation of MRL proposals for cucumber (incl. zucchini and gherkin) in greenhouses according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (cucumber)

Method I (Weinmann/Nolting)	R	0.324
(all values)	s	0.107
	k	3.188
	Rmax=R+k*s	0.666
Method II (Wilkening)	R (0.75)	0.405
(75 % quantile)	Rber=2*R(0.75)	0.810

Summary of results:
Maximum residue values for a pre-harvest interval of: 3 days

Method I (all values)	0.67 mg/kg
Method II (75% quantile)	0.81 mg/kg

● OECD Calculator

Results (cucumber)

Total number of data (n)	8	Standard deviation (SD)	0.107
Lowest residue	0.18	Percentage of censored data	0
Highest residue	0.52	Number of non-censored data	8
Median residue	0.305	Correction factor for censoring (CF)	1.000
Mean	0.324		

Proposed MRL estimate

Highest residue	0.52
Mean + 4 SD	0.753
CF × 3 mean	0.971
Unrounded MRL	0.971
Rounded MRL	1

Table 6.7.2-25a: Calculation of MRL proposals for watermelon (in the field) according to EU and OECD guidelines

BASIC DATA

Residue :	**total residue of BYI 02960 calc.**	Crop group :	**fruiting vegetables**
Portion analyzed :	**fruit**	Commodity :	**watermelon (southern Europe)**
Target value :	**MRL**	PHI :	**3 d**

No.	Crop	Days after appli-cation	Residue value (mg/kg)	Trial No./ Study No.	No. of appl.	FL-Type	Product	Country	Area of appl.
1	melon	4*	0.05	10-2185-01/ 10-2185	2	SL 200	BYI 02960 SL 200	Spain	F
2	melon	5*	0.18	10-2185-02/ 10-2185	2	SL 200	BYI 02960 SL 200	Italy	F
3	melon	5*	0.12	10-2185-03/ 10-2185	2	SL 200	BYI 02960 SL 200	Southern France	F
4	melon	3	0.05	10-2185-04/ 10-2185	2	SL 200	BYI 02960 SL 200	Portugal	F
5	watermelon	10*	0.13	11-2074-01 11-2074	2	SL 200	BYI 02960 SL 200	Portugal	F
6	watermelon	14*	0.25	11-2074-02 11-2074	2	SL 200	BYI 02960 SL 200	Italy	F
7	watermelon	14*	0.16	11-2074-03 11-2074	2	SL 200	BYI 02960 SL 200	Spain	F
8	watermelon	14*	0.16	11-2074-04 11-2074	2	SL 200	BYI 02960 SL 200	Italy	F
9	watermelon	10*	0.11	11-2074-05 11-2074	2	SL 200	BYI 02960 SL 200	Spain	F

* this value was used as it was higher than the value at the PHI (3 days)

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Table 6.7.2-25a (cont'd): Calculation of MRL proposals for watermelon (in the field) according to EU and OECD guidelines

EVALUATION SUMMARIES

- EU guideline 7039/VI/95 of 22 July 1997

Results (watermelon)

Method I (Weinmann/Nolting) (all values)	R	0.134
	s	0.063
	k	3.032
	Rmax=R+k*s	0.326
Method II (Wilkening) (75 % quantile)	R (0.75)	0.170
	Rber=2*R(0.75)	0.340

Summary of results:
Maximum residue values for a pre-harvest interval of 3 days

Method I (all values)	0.326 mg/kg
Method II (75% quantile)	0.340 mg/kg

- OECD Calculator

Results (watermelon)

Total number of data (n)	9	Standard deviation (SD)	0.063
Lowest residue	0.05	Percentage of censored data	0
Highest residue	0.25	Number of non-censored data	9
Median residue	0.13	Correction factor for censoring (CF)	1.000
Mean	0.134		

Proposed MRL estimate

Highest residue	0.25
Mean + 4 SD	0.387
CF × 3 mean	0.403
Unrounded MRL	0.403
Rounded MRL	0.4

Table 6.7.2-25b: Calculation of MRL proposals for watermelon in greenhouses according to EU and OECD guidelines

BASIC DATA

Residue :	**total residue of BYI 02960 calc.**	Crop group :	**fruiting vegetables**
Portion analyzed :	**fruit**	Commodity :	**watermelon (greenhouse)**
Target value :	**MRL**	PHI :	**3 d**

No.	Crop	Days after appli-cation	Residue value (mg/kg)	Trial No./ Study No.	No. of appl.	FL-Type	Product	Country	Area of appl.
1	melon	3	0.17	10-2188-01/ 10-2188	2	SL 200	BYI 02960 SL 200	Netherlands	G
2	melon	7*	0.30	10-2188-02/ 10-2188	2	SL 200	BYI 02960 SL 200	Italy	G
3	melon	7*	0.19	10-2188-03/ 10-2188	2	SL 200	BYI 02960 SL 200	Spain	G
4	watermelon	14*	0.13	11-2075-01/ 11-2075	2	SL 200	BYI 02960 SL 200	Spain	G
5	watermelon	14*	0.14	11-2075-02/ 11-2075	2	SL 200	BYI 02960 SL 200	Italy	G
6	watermelon	14*	0.10	11-2075-03/ 11-2075	2	SL 200	BYI 02960 SL 200	Spain	G
7	watermelon	14*	0.27	11-2075-04/ 11-2075	2	SL 200	BYI 02960 SL 200	Italy	G
8	watermelon	14*	0.30	11-2075-05/ 11-2075	2	SL 200	BYI 02960 SL 200	Italy	G
9	watermelon	14*	0.16	11-2075-06/ 11-2075	2	SL 200	BYI 02960 SL 200	Italy	G

* this value was used as it was higher than the value at the PHI (3 days)

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Table 6.7.2-25b (cont'd): Calculation of MRL proposals for watermelon in greenhouses according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (watermelon)

Method I (Weinmann/Nolting)	R	0.196
(all values)	s	0.076
	k	3.032
	Rmax=R+k*s	0.425
Method II (Wilkening)	R (0.75)	0.285
(75 % quantile)	Rber=2*R(0.75)	0.570

Summary of results:
Maximum residue values for a pre-harvest interval of: 3 days

Method I (all values)	0.425 mg/kg
Method II (75% quantile)	0.570 mg/kg

● OECD Calculator

Results (watermelon)

Total number of data (n)	9	Standard deviation (SD)	0.076
Lowest residue	0.10	Percentage of censored data	0
Highest residue	0.30	Number of non-censored data	9
Median residue	0.170	Correction factor for censoring (CF)	1.000
Mean	0.196		

Proposed MRL estimate

Highest residue	0.300
Mean + 4 SD	0.498
CF × 3 mean	0.587
Unrounded MRL	0.587
Rounded MRL	0.6

Table 6.7.2-26: Calculation of MRL proposals for rotational cereal crops according to EU and OECD guidelines

BASIC DATA

Residue:	**total residue of BYI 02960 calc.**	Crop group :	**rotational cereals**
Portion analyzed :	**grain**	Commodity :	**barley**
Target value :	**MRL**	PBI :	**25-33 days**

No.	Crop	Days after application*	Residue value (mg/kg)	Plot No./ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	barley	116	0.35	10-2503-01-T-1C / 10-2503	1	SL 200	BYI 02960 SL 200	Germany	F
2	barley	218	0.65	10-2503-03-T-1C / 10-2503	1	SL 200	BYI 02960 SL 200	France	F
3	barley	233	0.11	10-2503-04-T-1C / 10-2503	1	SL 200	BYI 02960 SL 200	Spain	F

* - PBI (plant-back interval) for these, relevant trials: 25-33 days

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Table 6.7.2-26 (cont'd): Calculation of MRL proposals for rotational cereal crops according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (rotational cereal crops, represented by barley)

Method I (Weinmann/Nolting) (all values)	R	0.370
	s	0.271
	k	7.656
	Rmax=R+k*s	2.441
Method II (Wilkening) (75 % quantile)	R (0.75)	0.650
	Rber=2*R(0.75)	1.300

Summary of results:

Maximum residue values for a plant-back interval of: 25-33 days

Method I (all values)	2.44 mg/kg
Method II (75% quantile)	1.30 mg/kg

● OECD Calculator

Results (rotational cereal crops, represented by barley)

Total number of data (n)	3	Standard deviation (SD)	0.271
Lowest residue	0.11	Percentage of censored data	0
Highest residue	0.65	Number of non-censored data	3
Median residue	0.350	Correction factor for censoring (CF)	1.000
Mean	0.370		

Proposed MRL estimate

Highest residue	0.65
Mean + 4 SD	1.452
CF × 3 mean	1.110
Unrounded MRL	1.452
Rounded MRL	1.5

Table 6.7.2-27: Calculation of MRL proposals for rotational root crops according to EU and OECD guidelines

BASIC DATA

Residue:	**total residue of BYI 02960 calc.**	Crop group :	**rotational root vegetables**
Portion analyzed :	**root (=body)**	Commodity :	**carrot, turnip**
Target value :	**MRL**	PBI :	**25-30 days**

No.	Crop	Days after application*	Residue value (mg/kg)	Plot No./ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	carrot	410	0.06	10-2503-01-T-3A / 10-2503	1	SL 200	BYI 02960 SL 200	Germany	F
2	carrot	106	0.07	10-2503-02-T-1A / 10-2503	1	SL 200	BYI 02960 SL 200	Nether-lands	F
3	turnip, edible	82	0.14	10-2503-03-T-1A / 10-2503	1	SL 200	BYI 02960 SL 200	France	F
4	carrot	114	0.08	10-2503-04-T-1A / 10-2503	1	SL 200	BYI 02960 SL 200	Spain	F

* - PBI (plant-back interval) for these, relevant trials: 25-30 days

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Table 6.7.2-27 (cont'd): Calculation of MRL proposals for rotational root crops according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (rotational root crops, represented by carrot/turnip)

Method I (Weinmann/Nolting) (all values)	R s k Rmax=R+k*s	0.088 0.036 5.144 0.272
Method II (Wilkening) (75 % quantile)	R (0.75) Rber=2*R(0.75)	0.125 0.250

Summary of results:

Maximum residue values for a plant-back interval of: 25-30 days

Method I (all values)	0.27 mg/kg
Method II (75% quantile)	0.25 mg/kg

● OECD Calculator

Results (rotational root crops, represented by carrot/turnip)

Total number of data (n)	4	Standard deviation (SD)	0.036
Lowest residue	0.06	Percentage of censored data	0
Highest residue	0.14	Number of non-censored data	4
Median residue	0.075	Correction factor for censoring (CF)	1.000
Mean	0.088		

Proposed MRL estimate

Highest residue	0.14
Mean + 4 SD	0.231
CF × 3 mean	0.263
Unrounded MRL	0.263
Rounded MRL	0.3

Table 6.7.2-28: Calculation of MRL proposals for rotational leafy vegetable crops according to EU and OECD guidelines

BASIC DATA

Residue :	**total residue of BYI 02960 calc.**	Crop group :	**rotational leafy vegetables**
Portion analyzed :	**head**	Commodity :	**lettuce**
Target value :	**MRL**	PBI :	**25-30 days**

No.	Crop	Days after application*	Residue value (mg/kg)	Plot No./ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	lettuce	63	0.09	10-2503-01-T-1B / 10-2503	1	SL 200	BYI 02960 SL 200	Germany	F
2	lettuce	60	<0.04	10-2503-02-T-1B / 10-2503	1	SL 200	BYI 02960 SL 200	Nether-lands	F
3	lettuce	69	0.16	10-2503-03-T-1B / 10-2503	1	SL 200	BYI 02960 SL 200	France	F
4	lettuce	72	0.07	10-2503-04-T-1B / 10-2503	1	SL 200	BYI 02960 SL 200	Spain	F

* - PBI (plant-back interval) for these, relevant trials: 25-30 days

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Table 6.7.2-28 (cont'd): Calculation of MRL proposals for rotational leafy vegetable crops according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (rotational leafy crops, represented by lettuce)

Method I (Weinmann/Nolting) (all values)	R s k Rmax=R+k*s	0.090 0.051 5.144 0.352
Method II (Wilkening) (75 % quantile)	R (0.75) Rber=2*R(0.75)	0.143 0.285

Summary of results:

Maximum residue values for a plant-back interval of: 25-30 days

Method I (all values)	0.35 mg/kg
Method II (75% quantile)	0.29 mg/kg

● OECD Calculator

Results (rotational leafy crops, represented by lettuce)

Total number of data (n)	4	Standard deviation (SD)	0.051
Lowest residue	0.04	Percentage of censored data	25
Highest residue	0.16	Number of non-censored data	3
Median residue	0.080	Correction factor for censoring (CF)	0.833
Mean	0.090		

Proposed MRL estimate

Highest residue	0.16
Mean + 4 SD	0.294
CF × 3 mean	0.225
Unrounded MRL	0.294
Rounded MRL	0.3

Table 6.7.2-29: Calculation of MRL proposals for rotational tuber vegetables according to EU and OECD guidelines

BASIC DATA

Residue:	**total residue of BYI 02960 calc.**	Crop group :	**tuber vegetables**
Portion analyzed :	**tuber**	Commodity :	**potato**
Target value :	**MRL**	PBI :	**25-33 days**

No.	Crop	Days after application*	Residue value (mg/kg)	Plot No./ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	potato	122	0.21	11-2550-01/ 11-2550	2	SL 200	BYI 02960 SL 200	Northern France	F
2	potato	98	0.048	11-2550-02/ 11-2550	2	SL 200	BYI 02960 SL 200	Netherlands	F
3	potato	126	0.27	11-2550-03/ 11-2550	2	SL 200	BYI 02960 SL 200	Spain	F
4	potato	137	0.056	11-2550-04/ 11-2550	2	SL 200	BYI 02960 SL 200	Italy	F

* - PBI (plant-back interval) for these, relevant trials: 25-33 days
Remark: application interval: 9-10 days

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Table 6.7.2-29 (cont'd): Calculation of MRL proposals for tuber vegetables according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (rotational tuber vegetable crops, represented by potato)

Method I (Weinmann/Nolting)	R	0.146
(all values)	s	0.111
	k	5.144
	Rmax=R+k*s	0.719
Method II (Wilkening)	R (0.75)	0.255
(75 % quantile)	Rber=2*R(0.75)	0.510

Summary of results:

Maximum residue values for a plant-back interval of: 25-33 days

Method I (all values)	0.719 mg/kg
Method II (75% quantile)	0.510 mg/kg

● OECD Calculator

Results (rotational root and tuber vegetable crops, represented by potato)

Total number of data (n)	4	Standard deviation (SD)	0.111
Lowest residue	0.048	Percentage of censored data	0
Highest residue	0.27	Number of non-censored data	4
Median residue	0.133	Correction factor for censoring (CF)	1.000
Mean	0.146		

Proposed MRL estimate

Highest residue	0.27
Mean + 4 SD	0.591
CF × 3 mean	0.438
Unrounded MRL	0.591
Rounded MRL	0.6

Table 6.7.2-30: Calculation of MRL proposals for rotational stem vegetables according to EU and OECD guidelines

BASIC DATA

Residue:	**total residue of BYI 02960 calc.**	Crop group :	**stem vegetables**
Portion analyzed :	**Whole plant without root**	Commodity :	**leek**
Target value :	**MRL**	PBI :	**26-33 days**

No.	Crop	Days after application*	Residue value (mg/kg)	Plot No./ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	leek	103	0.25	11-2551-01/ 11-2551	2	SL 200	BYI 02960 SL 200	Northern France	F
2	leek	130	0.11	11-2551-02/ 11-2551	2	SL 200	BYI 02960 SL 200	Germany	F
3	leek	97	0.040	11-2551-03/ 11-2551	2	SL 200	BYI 02960 SL 200	Spain	F
4	leek	112	0.059	11-2551-04/ 11-2551	2	SL 200	BYI 02960 SL 200	Italy	F

* - PBI (plant-back interval) for these relevant trials: 25-33 days

Remark: application interval: 10-13 days

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Table 6.7.2-30 (cont'd): Calculation of MRL proposals for rotational stem vegetables according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (rotational stem vegetable crops, represented by leek)

Method I (Weinmann/Nolting)	R	0.115
(all values)	s	0.095
	k	5.144
	Rmax=R+k*s	0.603
Method II (Wilkening)	R (0.75)	0.215
(75 % quantile)	Rber=2*R(0.75)	0.430

Summary of results:

Maximum residue values for a plant-back interval of: 25-33 days

Method I (all values)	0.603 mg/kg
Method II (75% quantile)	0.430 mg/kg

● OECD Calculator

Results (rotational stem vegetable crops, represented by leek)

Total number of data (n)	4	Standard deviation (SD)	0.095
Lowest residue	0.040	Percentage of censored data	0
Highest residue	0.25	Number of non-censored data	4
Median residue	0.085	Correction factor for censoring (CF)	1.000
Mean	0.115		

Proposed MRL estimate

Highest residue	0.25
Mean + 4 SD	0.494
CF × 3 mean	0.344
Unrounded MRL	0.494
Rounded MRL	0.5

Table 6.7.2-31: Calculation of MRL proposals for rotational fruiting vegetable crops according to EU and OECD guidelines

BASIC DATA

Residue:	**total residue of BYI 02960 calc.**	Crop group :	**rotational fruiting vegetables**
Portion analyzed :	**fruit**	Commodity :	**cucumber**
Target value :	**MRL**	PBI :	**25-30 days**

No.	Crop	Days after application*	Residue value (mg/kg)	Plot No./ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	cucumber	79	0.30	11-2552-01/ 11-2552	2	SL 200	BYI 02960 SL 200	France	F
2	cucumber	73	0.34	11-2552-02/ 11-2552	2	SL 200	BYI 02960 SL 200	Germany	F
3	cucumber	83	0.067	11-2552-03/ 11-2552	2	SL 200	BYI 02960 SL 200	Spain	F
4	cucumber	69	0.43	11-2552-04/ 11-2552	2	SL 200	BYI 02960 SL 200	Italy	F

* - PBI (plant-back interval) for these, relevant trials: 25-30 days
Remark: application interval: 10 days

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Table 6.7.2-31 (cont'd): Calculation of MRL proposals for rotational fruiting vegetable crops according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (rotational fruiting vegetable crops represented by cucumber)

Method I (Weinmann/Nolting) (all values)	R s k Rmax=R+k*s	0.284 0.155 5.144 1.080
Method II (Wilkening) (75 % quantile)	R (0.75) Rber=2*R(0.75)	0.408 0.815

Summary of results:

Maximum residue values for a plant-back interval of: 25-30 days

Method I (all values)	1.08 mg/kg
Method II (75% quantile)	0.815 mg/kg

● OECD Calculator

Results (rotational fruiting vegetable crops represented by cucumber)

Total number of data (n)	4	Standard deviation (SD)	0.155
Lowest residue	0.07	Percentage of censored data	0
Highest residue	0.43	Number of non-censored data	4
Median residue	0.320	Correction factor for censoring (CF)	1.000
Mean	0.284		

Proposed MRL estimate

Highest residue	0.430
Mean + 4 SD	0.903
CF × 3 mean	0.853
Unrounded MRL	0.903
Rounded MRL	0.9

Table 6.7.2-32: Calculation of MRL proposals for rotational bulb vegetable crops according to EU and OECD guidelines

BASIC DATA

Residue:	**total residue of BYI 02960 calc.**	Crop group :	**rotational bulb vegetables**
Portion analyzed :	**bulb**	Commodity :	**onion, bulb**
Target value :	**MRL**	PBI :	**25-33 days**

No.	Crop	Days after application*	Residue value (mg/kg)	Plot No./ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	onion	175	0.18	11-2553-01/ 11-2553	2	SL 200	BYI 02960 SL 200	Northern France	F
2	onion	133	0.091	11-2553-02/ 11-2553	2	SL 200	BYI 02960 SL 200	Germany	F
3	onion	116	0.078	11-2553-03/ 11-2553	2	SL 200	BYI 02960 SL 200	Italy	F
4	onion	118	<0.04	11-2553-04/ 11-2553	2	SL 200	BYI 02960 SL 200	Spain	F

* - PBI (plant-back interval) for these, relevant trials: 25-33 days
Remark: application interval: 10-11 days

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Table 6.7.2-32 (cont'd): Calculation of MRL proposals for rotational bulb vegetable crops according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (rotational bulb vegetable crops, represented by onion)

Method I (Weinmann/Nolting) (all values)	R s k Rmax=R+k*s	0.097 0.059 5.144 0.402
Method II (Wilkening) (75 % quantile)	R (0.75) Rber=2*R(0.75)	0.158 0.316

Summary of results:

Maximum residue values for a plant-back interval of: 25-33 days

Method I (all values)	0.402 mg/kg
Method II (75% quantile)	0.316 mg/kg

● OECD Calculator

Results (rotational bulb vegetable crops, represented by onion)

Total number of data (n)	4	Standard deviation (SD)	0.059
Lowest residue	<0.04	Percentage of censored data	0
Highest residue	0.18	Number of non-censored data	4
Median residue	0.085	Correction factor for censoring (CF)	1.000
Mean	0.097		

Proposed MRL estimate

Highest residue	0.180
Mean + 4 SD	0.334
CF × 3 mean	0.243
Unrounded MRL	0.334
Rounded MRL	0.4

Table 6.7.2-33: Calculation of MRL proposals for rotational legume vegetable crops according to EU and OECD guidelines

BASIC DATA

Residue:	**total residue of BYI 02960 calc.**	Crop group :	**legume vegetables**
Portion analyzed :	**pod**	Commodity :	**bean, pod**
Target value :	**MRL**	PBI :	**25-30 days**

No.	Crop	Days after application*	Residue value (mg/kg)	Plot No./ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	bean	93	1.1	11-2555-01/ 11-2555	2	SL 200	BYI 02960 SL 200	Northern France	F
2	bean	105	0.59	11-2555-02/ 11-2555	2	SL 200	BYI 02960 SL 200	Germany	F
3	bean	85	0.40	11-2555-03/ 11-2555	2	SL 200	BYI 02960 SL 200	Italy	F
4	bean	90	0.28	11-2555-04/ 11-2555	2	SL 200	BYI 02960 SL 200	Spain	F

* - PBI (plant-back interval) for these, relevant trials: 25-30 days
Remark: application interval: 10 days

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Table 6.7.2-33 (cont'd): Calculation of MRL proposals for rotational legume vegetable crops according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (rotational legume vegetable crops, represented by bean)

Method I (Weinmann/Nolting) (all values)	R s k Rmax=R+k*s	0.593 0.362 5.144 2.453
Method II (Wilkening) (75 % quantile)	R (0.75) Rber=2*R(0.75)	0.973 1.945

Summary of results:

Maximum residue values for a plant-back interval of: 25-30 days

Method I (all values)	2.45 mg/kg
Method II (75% quantile)	1.95 mg/kg

● OECD Calculator

Results (rotational legume vegetable crops, represented by bean)

Total number of data (n)	4	Standard deviation (SD)	0.362
Lowest residue	0.28	Percentage of censored data	0
Highest residue	1.1	Number of non-censored data	4
Median residue	0.495	Correction factor for censoring (CF)	1.000
Mean	0.593		

Proposed MRL estimate

Highest residue	1.1
Mean + 4 SD	2.039
CF × 3 mean	1.778
Unrounded MRL	2.039
Rounded MRL	2

Table 6.7.2-34: Calculation of MRL proposals for rotational pulses according to EU and OECD guidelines

BASIC DATA

Residue:	**total residue of BYI 02960 calc.**	Crop group :	**pulses**
Portion analyzed :	**Dry seeds**	Commodity :	**pea**
Target value :	**MRL**	PBI :	**25-35 days**

No.	Crop	Days after application*	Residue value (mg/kg)	Plot No./ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	pea	136	2.3	11-2556-01/ 11-2556	2	SL 200	BYI 02960 SL 200	Northern France	F
2	pea	144	1.0	11-2556-02/ 11-2556	2	SL 200	BYI 02960 SL 200	Germany	F
3	pea	100	0.67	11-2556-03/ 11-2556	2	SL 200	BYI 02960 SL 200	Italy	F
4	pea	132	2.1	11-2556-04/ 11-2556	2	SL 200	BYI 02960 SL 200	Spain	F

* - PBI (plant-back interval) for these, relevant trials: 25-35 days

Remark: application interval: 10 days

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Table 6.7.2-34 (cont'd): Calculation of MRL proposals for rotational pulses according to EU and OECD guidelines

EVALUATION SUMMARIES

● EU guideline 7039/VI/95 of 22 July 1997

Results (rotational pulses crops, represented by pea)

Method I (Weinmann/Nolting)	R	1.518
(all values)	s	0.804
	k	5.144
	Rmax=R+k*s	5.652
Method II (Wilkening)	R (0.75)	2.250
(75 % quantile)	Rber=2*R(0.75)	4.500

Summary of results:

Maximum residue values for a plant-back interval of: 25-35 days

Method I (all values)	5.65 mg/kg
Method II (75% quantile)	4.50 mg/kg

● OECD Calculator

Results (rotational pulses crops, represented by pea)

Total number of data (n)	4	Standard deviation (SD)	0.804
Lowest residue	0.67	Percentage of censored data	0
Highest residue	2.3	Number of non-censored data	4
Median residue	1.55	Correction factor for censoring (CF)	1.000
Mean	1.518		

Proposed MRL estimate

Highest residue	2.3
Mean + 4 SD	4.732
CF × 3 mean	4.553
Unrounded MRL	4.732
Rounded MRL	5

Table 6.7.2-36: Calculation of MRL proposals for rotational oilseed crops according to EU and OECD guidelines

BASIC DATA

Residue:	**total residue of BYI 02960 calc.**	Crop group :	**oilseeds**
Portion analyzed :	**seed**	Commodity :	**oilseed rape**
Target value :	**MRL**	PBI :	**27-41 days**

No.	Crop	Days after application*	Residue value (mg/kg)	Plot No./ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	rape, winter	369	0.11	11-2554-01/ 11-2554	2	SL 200	BYI 02960 SL 200	Northern France	F
2	rape, winter	361	0.17	11-2554-02/ 11-2554	2	SL 200	BYI 02960 SL 200	Germany	F
3	rape, winter	307	0.070	11-2554-03/ 11-2554	2	SL 200	BYI 02960 SL 200	Italy	F
4	rape, winter	290	0.092	11-2554-04/ 11-2554	2	SL 200	BYI 02960 SL 200	Spain	F

*-PBI (plant-back interval) for these, relevant trials: 27-41 days
Remark: application interval: 9-10 days

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Table 6.7.2-36 (cont'd): Calculation of MRL proposals for rotational oilseed crops according to EU and OECD guidelines

EVALUATION SUMMARIES

- EU guideline 7039/VI/95 of 22 July 1997

Results (rotational oilseed crops, represented by winter rape)

Method I (Weinmann/Nolting) (all values)	R s k Rmax=R+k*s	0.111 0.043 5.144 0.331
Method II (Wilkening) (75% quantile)	R (0.75) Rber=2*R(0.75)	0.155 0.310

Summary of results:

Maximum residue values for a plant-back interval of: 27-41 days

Method I (all values)	0.33 mg/kg
Method II (75% quantile)	0.31 mg/kg

- OECD Calculator

Results (rotational oilseed crops, represented by winter rape)

Total number of data (n)	4	Standard deviation (SD)	0.043
Lowest residue	0.07	Percentage of censored data	0
Highest residue	0.17	Number of non-censored data	4
Median residue	0.101	Correction factor for censoring (CF)	1.000
Mean	0.111		

Proposed MRL estimate

Highest residue	0.17
Mean + 4 SD	0.282
CF x 3 mean	0.332
Unrounded MRL	0.332
Rounded MRL	0.4

IIA 6.7.2.2 MRL Proposals in Plant Matrices Based on GLOBAL Residue Data

In addition to uses in Europe, the MRL calculations presented below also reflect global uses of plant commodities which are exported from the GJR countries to the EU.

► ***Background:*** **GLOBAL JOINT REVIEW**

As part of the Global Joint Review submission in the USA, Canada, Mexico, Brazil, and Australia, crop residue data from trials conducted in and/or for those countries was summarized in the "GJR dossier", submitted in October 2012.

As in the European dossier, the combined residues of BYI 02960 and its metabolite DFA, calculated as BYI 02960 parent equivalents, were proposed in the GJR for *enforcement* of MRLs as the relevant BYI 02960 residues in crop commodities. The proposed residue definition for *data collection* and *risk assessment* is, however, slightly different than the the one for enforcement, as it also includes DFEAF. Therefore, the total BYI 02960 residue data presented in Section 6.3.2 of this dossier include all three compounds. However, DFEAF did not play a major role – if detected at all – in most trials and thus its effect on the MRL calculation is negligible. The total residue values are therefore valid for MRL calculations.

The OECD calculator was used to calculate the MRLs for total BYI 02960 residues in crop commodities. The total residue values are also presented in Section KIIA 6.3 of this summary document. For example, the residue data in table 6.3.2.3-7 from KIIA 6.3.2.3 were used to calculate an MRL value for pome fruit. (The total BYI 02960 residue values used for the calculation of MRLs are in Table 8 of the respective NAFTA residue reports.) As stated in the previous paragraph, the total BYI 02960 residue is the sum of BYI 02960, DFA, and DFEAF residues in parent equivalents. Residue measurements below the analyte LOQ were summed into the total BYI 02960 residue value as being <u>*at*</u> the analyte LOQ value.

For all crops (except tree crops), average residue values from the desired pre-harvest intervals (PHIs) were used in the calculations. For tree crops where dilute and concentrated spray applications were used, single treated samples were collected from each plot and data from each application type/plot were used to calculate separate MRL values for each scenario. The higher of the two MRL values was selected as the value for that crop commodity.

For a crop group, individual MRLs were calculated for each representative crop and matrix. The highest MRL value from the individual crop/matrices within the crop group was selected as the MRL value for that commodity for the entire crop group. For example, separate MRLs were calculated for orange, lemon, grapefruit, and mandarin, and the highest value was selected for citrus from the respective NAFTA Crop Group. (Crop grouping for the GJR was based on the standard NAFTA system.)

The full list of calculated MRLs sumbmitted with the GJR dossier is presented below in Table

6.7.2.2-1. As indicated above, residue values from the desired PHIs were used in calculating the MRL values. However, in some crops, higher total BYI 02960 residues were observed in samples collected *after* the PHI interval in decline trials. If the calculated MRL was lower than the highest residue observed for a given crop or crop group, then the MRL was proposed based on the MRL class for the highest total residue. For example, an MRL of 1.5 mg/kg was calculated for citrus from samples collected at the desired 1-day PHI. However, the highest total BYI 02960 residue (2.2 mg/kg) was found in a sample collected at 10 days after the final treatment. Therefore, an MRL of 3.0 mg/kg was proposed for citrus fruit in the GJR dossier.

Table 6.7.2.2-1: MRLs calculated for BYI 02960 residues using the OECD Calculator for uses in the USA, Canada, Mexico, Brazil, and Australia ***as presented in the 2012 Global Joint Review dossier***

Representative Crop(s)	Commodity	**Imported to EU?***	Mode of Appl.	PHI (days)	HR (mg/kg) at PHI or later	MRL (mg/kg) Crop/ Commodity	MRL (mg/kg) Crop Group/ Subgroup**
Carrot	Root	no	Foliar	7	1.1 (12 d)	1.5	1.5
Radish	Root	no	Foliar	7	0.28 (7 d)	0.5	
Potato	Tuber	?	Foliar	7	0.1	0.15	0.15
Bulb Onion	Bulb	no	Foliar	14	0.17 (35 d)	0.3	0.3 (CG 3A)
Green Onion	Whole plant w/o root	no	Foliar	14	1.6 (14 d)	3	3 (CG 3B)
Leaf Lettuce	Leaf	no	Foliar	1	8.0 (1 d)	15	40
Head Lettuce	Leaf	no	Foliar	1	2.1 (1 d)	4	
Celery	Leaf Stalk	minor	Foliar	1	6.8 (1 d)	10	
Spinach	Leaf	no	Foliar	1	19 (1 d)	40	
Broccoli	Flower head & stem	no	Foliar	1	3.2 (1 d)	6	6
Cabbage	Leaf	no	Foliar	1	1.3 (1 d)	2	
Cauliflower	Flower head & stem	no	Foliar	1	2.6 (1 d)	6	
Mustard Greens	Leaf	no	Foliar	1	25.0	40	40
				3	19.0	30	
Snap Bean	Seed	no	Foliar	7	2.1 (26 d)	3	5
Snow Pea	Seed	no	Foliar	7	2.9 (26 d)	5	
Garden Pea	Seed	no	Foliar	7	3.1 (33 d)	3	4
Lima Bean	Seed	no	Foliar	7	0.81 (21 d)	0.90	
Dry Bean	Forage	no	Foliar	7	7.08 (7 d)	10	15
	Hay	no		7	14.3 (7 d)	30	40
	Seed	**yes**		7	0.57 (7 d)	0.8	0.8

n.a. = not applicable
* commodity imported from NAFTA, Brazil, or Australia into the EU in significant quantities
** crop grouping references and conventions according to NAFTA system

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Table 6.7.2.2-1 (continued)

Representative Crop(s)	Commodity	**Imported to EU?***	Mode of Appl.	PHI (days)	HR (mg/kg) at PHI or later	MRL (mg/kg) Crop/ Commodity	MRL (mg/kg) Crop Group/ Subgroup**
Dry Pea	Green Vines	no		7	8.27 (28 d)	15	15
	Hay	no		7	21.0 (7 d)	40	40
	Seed	**yes**		7	4.46 (7 d)	6	6
Soybean	Forage	no	Foliar	7	11.6	20	20
	Hay	no	Foliar	7	31.6	50	50
	Seed	**yes**	Foliar	21	3.6	4	4
	Aspirated Grains Fractions	no	Foliar	21	n.a	40	40
Tomato	Fruit	**yes**	Foliar	1	2.0 (60 d; soil app.)	0.9	3
		yes	Soil	45		2	
Pepper, Bell	Fruit	no	Foliar	1	0.7 (45 d; soil)	0.8	
		no	Soil	45		3	
Pepper, Chili	Fruit	minor	Foliar	1	0.98 (70 d; soil app.)	1.5	
		minor	Soil	45		1	
Cucumber	Fruit	no	Foliar	1	1.1 (28 d)	0.7	2.0 (higher than recommended 1.5 ppm to cover highest residues occuring after PHI events)
			Soil	21	1.5 (42 d)	1.5	
Melon	Fruit	no	Foliar	1	1.2 (34 d; soil)	0.6	
			Soil	21		0.9	
Squash	Fruit	no	Foliar	1	1.3 (28 d)	0.7	
			Soil	21	1.6 (42 d)	1.0	
Orange (Dil. Spray)	Fruit			1	2.2 (10 d; ULV)	1.5	3.0 (based on highest residue of 2.2 ppm on day 10)
Orange (ULV)		**yes**		1		1.5	
Lemon (Dil. Spray)				1	0.74 (1 d; ULV)	0.9	
Lemon (ULV)		**yes**		1		1.5	
Grapefruit (Dil. Spray)				1	0.32 (1 d; ULV)	0.6	
Grapefruit (ULV)		**yes**		1		0.6	
Mandarin (Dil. Spray)				1	1.0 (10 d; ULV)	0.9	
Mandarin (ULV)		**yes**	Foliar	1		1.0	

n.a. = not applicable
* commodity imported from NAFTA, Brazil, or Australia into the EU in significant quantities
** crop grouping references and conventions according to NAFTA system

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Table 6.7.2.2-1 (continued)

Representative Crop(s)	Commodity	**Imported to EU?***	Mode of Appl.	PHI (days)	HR (mg/kg) at PHI or later	MRL (mg/kg) Crop/ Commodity	MRL (mg/kg) Crop Group/ Subgroup**
Apple (Dil. Spray)	Fruit	**yes**	Foliar	14	0.63 (28 d)	0.6	1.5
Apple (Conc. Spray)			Foliar	14		0.6	
Pear (Dil. Spray)		**yes**	Foliar	14	0.7 (14 d)	1.0	
Pear (Conc. Spray)			Foliar	14		1.5	
Pear (Dil. + Conc. Spray)			Foliar	14		1.5	
Blueberry	Fruit	**yes**	Foliar	3	2.61	4.0	4.0
Grapes	Fruit	**yes**	Foliar and Soil	0	2.34 (0 d)	3.0	3.0
				3		2.0	
				7		2.0	
Strawberry	Fruit	no	Foliar	0	0.95 (21 d)	1.5	1.5
				3		1.5	
Almond	Hulls	no	Foliar, Dil	7	6.30	15.0	15
			Foliar, Conc	7		10.0	
	Nutmeat	**yes**	Foliar, Dil	7	0.08	0.10	0.15
			Foliar, Conc	7		0.15	
Pecan	Nutmeat	**yes**	Foliar, Dil	7	0.07	0.1	
			Foliar, Conc	7		0.07	
Barley	Hay	no	Foliar	7	28	40	40
	Straw	no	Foliar	21	5.95	9	30
	Grain	**yes**	Foliar	21	2.49	3	4
Sweet Corn	Sweet Corn Forage	no	Foliar	7	10	15	20
	K + CWHR	**yes**	Foliar	7	0.27	0.4	0.4
	Sweet CornStover	no	Foliar	7	9.70	15	15

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** crop grouping references and conventions according to NAFTA system

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Table 6.7.2.2-1 (continued)

Representative Crop(s)	Commodity	**Imported to EU?***	Mode of Appl.	PHI (days)	HR (mg/kg) at PHI or later	MRL (mg/kg) Crop/ Commodity	MRL (mg/kg) Crop Group/ Subgroup**
Field Corn	Field Corn Forage	no	Foliar	7	4.2	7	Combined Field Corn and Sweet Corn Forage Data = 10 ppm)
	Field Corn Stover	no	Foliar	7	6.3	8	15
	Field Corn Grain	**yes**	Foliar	21	0.21	0.15	0.5 (combined Foliar + ST = 0.2 ppm)
	Field Corn Grain	no	Seed treatment	ECH	0.19	0.5	
	Aspirated Grains Fractions	no	Foliar	21	n.a	1.5	40
Sorghum	Forage	no	Foliar	7	5	10	20
	Stover	no	Foliar	21	6.1	8	15
	Grain	**yes**	Foliar	21	1.9	3	4
Wheat	Forage	no	Foliar	7	16	20	20
	Hay	no	Foliar	7	24	30	40
	Straw	no	Foliar	21	20	30	30
	Grain	**yes**	Foliar	21	2.8	4	4
	Aspirated Grains Fractions	no	Foliar	21	n.a	30	40
Cotton	Undelinted Seed	**yes**	Foliar	14	0.69 (14 d)	0.7	0.9
	Undelinted Seed	**yes**	Seed Treatment	ECH	0.41 (ECH)	0.9	
	Gin By-products	no	Foliar	14	23 (14 d)	40	40
Alfalfa	Forage	no	Foliar	7	11	15	15
	Hay	no	Foliar	7	32	40	40
Clover	Forage	no	Foliar (410 g a.s./ha)	7	6.8	20	20
	Hay	no		11 - 17	13.6	40	40
	Forage	no	Foliar (205 g a.s./ha)	7	4	9	20
	Hay	no		11 - 17	7	20	40

n.a. = not applicable
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** crop grouping references and conventions according to NAFTA system

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Table 6.7.2.2-1 (continued)

Representative Crop(s)	Commodity	**Imported to EU?***	Mode of Appl.	PHI (days)	HR (mg/kg) at PHI or later	MRL (mg/kg) Crop/ Commodity	MRL (mg/kg) Crop Group/ Subgroup**
Coffee	Bean	yes	Soil + Foliar	0	0.87	1.5	2
				7	0.93	2	
				14	0.61	1.5	
				21	0.66	2	
				28	0.98	1.5	
Hops	Dried Cones	yes	Foliar (Conc.)	21		20	20
	Dried Cones	yes	Foliar (Dil.)	21	7.98	15	
Peanut	Hay	no	Foliar	7	19 (7 d)	30	30
	Nutmeat	yes	Foliar	7	0.097 (14 d)	0.1	0.15
Prickly Pear Cactus	Fruit	yes	Foliar	21	0.21	0.5	0.5
	Pads	no	Foliar	21	0.35	0.9	0.9
	Fruit + Pads (combined data)	no	Foliar	21	0.35	0.7	0.7

n.a. = not applicable
* commodity imported from NAFTA, Brazil, or Australia into the EU in significant quantities
** crop grouping references and conventions according to NAFTA system

In addition, residue values from rotational crops were considered. Residue data obtained in European field rotational crop studies were used as the basis to estimate worst-case "global" residues in succeeding crops. Assuming linearity of residues incurred relative to the application rate, a factor of 1.8 or 2.25 is required to account for the rate applied in the European rotational crop studies (dosed at 250 or 200 g a.s./ha) compared to the global worst-case use rate (up to a total of 450 g a.s./ha per crop, as used in Australia).

The estimated residue values from succeeding crops were used to calculate rotational-crop MRLs. These MRLs were compared to the MRLs proposed for the primary crops as summarized in Table 6.7.2.2-67. With few exceptions, the MRLs resulting from the use of BYI 02960 on primary crops were higher and were therefore critical for MRL-setting.

► Proposed EU import tolerances

Some of the crops submitted to the GJR are of relevance in international trade from GJR countries to the EU. For crops indicated in the third column of the table above as being of import relevance in the EU, data from the GJR are being submitted with this EU dossier (section 6.3.2) in order to establish harmonized tolerances (MRLs) in the EU, thus allowing free trade of the affected commodities.

As described above, for the GJR, calculations were made according to the OECD Calculator. Details of the results are presented below.

● Citrus fruits (orange, grapefruit; lemon, mandarin)

Complete sets of field residue trials were conducted in the NAFTA zone in various citrus fruits based on NAFTA guidance. The set included a major study covering two relevant application scenarios, each with 12 trials in oranges, 8 in lemons, and 6 in grapefruits. Two further studies were submitted as well, one with 4 additional trials in oranges, the other with 8 trials in mandarins. The trials were presented above in section 6.3.2.1 .

As shown in tables 6.7.2.2-2 and -3, the residue values in those trials led to individual crop MRL calculations of 0.6-1.5 mg/kg, and an initial NAFTA group tolerance calculation of 1.5 mg/kg. The final proposal in the GJR dossier was 3.0 mg/kg, taking higher residue levels than those at the PHI of 1 day into account.

Taking the relevant *peak* residue levels into account (i.e. highest residues at or after the designated PHI of 1 day), the following re-calculated results are achieved for large citrus fruits (oranges and grapefruits):

Table 6.7.2.2-2: Total residues of BYI 02960/large citrus – OECD maximum residue level calculation results for a pre-harvest interval of 1 day (Trials in the NAFTA region)

Commodity	unrounded value
Orange, dilute spray (incl. comparative trials)	1.75 mg/kg
0.08;0.097;0.13;0.15;*0.15;*0.17;*0.18;*0.21;0.22;0.28;0.30;0.30;0.32;*0.54;* 0.73;*1.5* mg/kg STMR: 0.22 mg/kg HR: 1.5 mg/kg	
Orange, conc. spray	3.09 mg/kg
0.05;0.10;0.22;0.24;0.26;0.26;0.26;*0.37;*0.66;*0.92;1.3;2.2* mg/kg STMR: 0.26 mg/kg HR: 2.2 mg/kg	
Grapefruit, dilute spray	0.60 mg/kg
0.15;*0.18;*0.19;0.22;0.22;0.23 mg/kg STMR: 0.21 mg/kg HR: 0.23 mg/kg	
Grapefruit, conc. spray	0.66 mg/kg
0.092;0.19;0.20;0.22;*0.30;*0.32 mg/kg STMR: 0.21 mg/kg HR: 0.32 mg/kg	
Large citrus (orange, grapefruit): dilute + conc. spray, plus comparative trials	2.2 mg/kg
0.05;0.08;0.092;0.097;0.1;0.13;0.15;0.15;0.15;0.17;0.18;0.18;0.19;0.19;0.2; 0.21;0.22;0.22;0.22;0.22;0.22;0.23;0.24;0.26;0.26;0.26;0.28;0.3;0.3;0.3;0.32; 0.32;0.37;0.54;0.66;0.73;0.92;1.3;1.5;2.2 mg/kg STMR: 0.22 mg/kg HR: 2.2 mg/kg	

Taking the relevant *peak* residue levels into account (i.e. highest residues at or after the designated PHI of 1 day), the following re-calculated results are achieved for small citrus fruits (lemons and mandarins):

Table 6.7.2.2-3: Total residues of BYI 02960/small citrus – OECD maximum residue level calculation results for a pre-harvest interval of 1 day
(Trials in the NAFTA region)

Commodity	unrounded value
Lemon, dilute spray	0.91 mg/kg
0.15;0.21;0.26;0.26;0.31;*0.33;0.36;0.55* mg/kg STMR: 0.29 mg/kg HR: 0.55 mg/kg	
Lemon, conc. spray	1.42 mg/kg
0.067;0.082;0.084;*0.13*;0.24;0.38;0.70;0.74 mg/kg STMR: 0.19 mg/kg HR: 0.74 mg/kg	
Mandarin, dilute spray	0.93 mg/kg
0.22;0.41;*0.22;0.42*;0.21;*0.42;0.34*;0.25 mg/kg STMR: 0.29 mg/kg HR: 0.42 mg/kg	
Mandarin, conc. spray	1.70 mg/kg
0.085;0.12;*0.27;0.45;0.57;0.61;0.67;1.0* mg/kg STMR: 0.51 mg/kg HR: 1.0 mg/kg	
Small citrus (lemon, mandarin): dilute + conc. spray	1.2 mg/kg
0.067;0.082;0.084;0.085;0.12;*0.13*;0.15;0.21;0.21;0.22;*0.22*;0.24;0.25;0.26;0.26;*0.27*;0.31;*0.33;0.34;0.36*;0.38;0.41;*0.42;0.42;0.45;0.55;0.57;0.61;0.67*;0.70;0.74;*1.0* mg/kg STMR: 0.29 mg/kg HR: 1.0 mg/kg	

In addition to the studies in the NAFTA region, trials were also conducted in Brazil on oranges. Two use patterns were compared, one with two foliar sprays and another also incorporating a soil drench treatment well prior to the foliar sprays, each with 5 trials. The trials were presented above in section 6.3.2.1.

Taking the relevant *peak* residue levels into account (i.e. highest residues at or after the designated PHI of 0 days), the following re-calculated results are achieved for large citrus fruits (oranges and grapefruits):

Table 6.7.2.2-4: Total residues of BYI 02960/orange – OECD maximum residue level calculation results for a pre-harvest interval of 0 days
(Trials in Brazil)

Commodity	unrounded value
Orange, 1 soil drench + 2 foliar	1.2 mg/kg
0.21;*0.36;0.41;0.49;0.53* mg/kg STMR: 0.41 mg/kg HR: 0.53 mg/kg	
Orange, 2 foliar	0.82 mg/kg
0.16;0.23;*0.28;0.29*;0.40 mg/kg STMR: 0.28 mg/kg HR: 0.40 mg/kg	

<u>*Summary of citrus calculations*</u>

Based on peak residue values and using the OECD calculator, the unrounded result for each of the individual crop/application scheme combination ranged from 0.6 mg/kg to 3.1 mg/kg. When grouped according to EU principles, the unrounded values for large and small citrus are 2.2 and 1.2 mg/kg, respectively. The GJR proposal based on the same data, but using different evaluation criteria, was 3.0 mg/kg for all citrus crops.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL of <u>3.0 mg/kg</u> is proposed for citrus fruit.

● Tree nuts (almonds, pecans, etc.)

Based on the NAFTA guidance, a complete set of field residue trials was conducted on almonds and pecans, representing the "tree nuts" crop group. Two different application scenarios were tested (concentrated and dilute spray); each scenario included 5 almond and 5 pecan trials. The results for the nutmeat of both nut varieties, as presented above in section 6.3.2.2, showed that both data sets were similar. The only clear difference was the HR in the set of trials with concentrated spray, which, at 0.12 mg/kg on day 14, was higher than any other result and thus will drive the MRL. Peak residues at or after the designated PHI of 7 days in this data set ranged from <0.07-0.12 mg/kg, with a median value of <0.07 mg/kg. (The corresponding values after dilute-spray treatment were <0.07-0.075 mg/kg, also with a median <LOQ.)

Table 6.7.2.2-5: Total residues of BYI 02960/tree nuts – OECD maximum residue level calculation results for a pre-harvest interval of 7 days
(concentrated-spray trials in the NAFTA region)

Commodity	unrounded value
Tree nuts (almonds, pecans)*	0.14 mg/kg
<0.070; <0.070; <0.070; <0.070; <0.070; <0.070; <0.070; <0.070; <0.070; *0.12* mg/kg STMR: <0.07 mg/kg HR**: 0.12 mg/kg	

* nutmeat
** HAFT, highest average field trial value

Based on peak residue values and using the OECD calculator, the unrounded result for combined data set of both crops for the concentrated application scheme combination was 0.14 mg/kg. The GJR proposal based on the same data, but using different evaluation criteria, was 0.15 mg/kg for all tree nut crops.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL of <u>0.15 mg/kg</u> is proposed for the nutmeat of tree nuts.

● Pome fruit (apples, pears)

Complete sets of field residue trials were conducted in the NAFTA zone on the two primary pome fruits, apples and pears, based on NAFTA guidance. Two different application scenarios were tested (concentrated and dilute spray). 14 apple and 9 pear trials were conducted with each of the scenarios. The results for the fruit, as presented above in section 6.3.2.3, showed that residues for the diluted spray were slightly more critical for apples, while those for the concentrated spray were slightly more critical for pears. The differences were evident at least in the MRL-critical HR value from the respective data sets and in the STMR for pears, although the STMR for apples was the same in both sets. Peak residues at or after the designated PHI of 14 days in the more critical apple and pear data set ranged from 0.12-0.63 mg/kg and 0.12-0.70 mg/kg, respectively, with respective median values of 0.18 and 0.43 mg/kg. (Residues in the less critical sets ranged from 0.08-0.52 mg/kg [apples] and 0.22-0.50 mg/kg [pears], with respective medians of 0.18 and 0.32 mg/kg.)

Table 6.7.2.2-6: Total residues of BYI 02960/pome fruit – OECD maximum residue level calculation results for a pre-harvest interval of 14 days
(trials in the NAFTA region)

Commodity	unrounded value
Apples (dilute spray)	0.73 mg/kg
0.12; 0.14; 0.15; 0.16; 0.17; 0.17; 0.18; 0.18; *0.19;* 0.20; 0.22; 0.28; 0.29; *0.63* mg/kg STMR: 0.18 mg/kg HR: 0.63 mg/kg	
Pears (concentrated spray)	1.29 mg/kg
0.12; 0.23; *0.33;* 0.38; 0.43; 0.45; 0.59; 0.64; 0.70 mg/kg STMR: 0.43 mg/kg HR: 0.70 mg/kg	

Based on peak residue values and using the OECD calculator, the unrounded result for the relevant data sets for apples and pears were 0.73 and 1.29 mg/kg, respectively. The GJR proposal based on the same data, but using different evaluation criteria, was 1.5 mg/kg for the pome fruit group.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL of 1.5 mg/kg is proposed for pome fruit.

● Grapes

Based on NAFTA guidance, a complete set of field residue trials was conducted on grapes. Two different application scenarios were tested, with either 2 foliar or a single soil application; each scenario included 16 trials. The results for the bunches (reported as "fresh fruit"), as presented above in section 6.3.2.4, showed that the residue levels were clearly more critical following the foliar application, as reflected in considerably higher HR and STMR values. Peak residues in grapes at or after the designated PHI of 0 days in this data set ranged from 0.37-2.0 mg/kg, with a median value of 0.57 mg/kg. (The corresponding values after soil application ranged from <0.07-0.10 mg/kg; the median was <0.07 mg/kg.)

Table 6.7.2.2-7: Total residues of BYI 02960/ grapes – OECD maximum residue level calculation results for a pre-harvest interval of 0 days
(foliar-spray trials in the NAFTA region)

Commodity	unrounded value
Grapes	2.43 mg/kg
0.37; 0.37; 0.38; 0.44; 0.48; *0.49;* 0.51; 0.55; 0.58; *0.63; 0.64; 0.75;* 0.84; *1.2;* 1.2; 2.0 mg/kg STMR: 0.57 mg/kg HR*: 2.0 mg/kg	

* HAFT, highest average field trial value

Based on peak residue values and using the OECD calculator, the unrounded result for grapes based on the foliar spray application scheme was 2.43 mg/kg. The GJR proposal based on the same data, but using different evaluation criteria, was 3.0 mg/kg for this commodity.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL of 3.0 mg/kg is proposed for grapes.

● Blueberries

In an IR-4 program, an extensive set of field residue trials was conducted worldwide in major blueberry-producing countries in North and South America, Australasia, and Europe. The use pattern called for 2 foliar spray applications and was the same in all countries/regions. 26 trials were conducted in total. As presented above in section 6.3.2.5, peak residues in the berries at or after the designated PHI of 3 days ranged from 0.19-2.6 mg/kg, with a median value of 0.87 mg/kg.

Table 6.7.2.2-8: Total residues of BYI 02960/blueberry – OECD maximum residue level calculation results for a pre-harvest interval of 3 days
(IR-4 program)

Commodity	unrounded value
Blueberries	3.58 mg/kg
0.193; *0.280;* 0.290; 0.327; 0.407; 0.454; 0.479; 0.506; 0.621; 0.626; 0.731; 0.834; 0.843; 0.891; 0.960; 1.007; 1.04; 1.079; 1.21; 1.31; *1.60;* 1.64; 1.79; *1.80;* 2.39; 2.60 mg/kg STMR: 0.87 mg/kg HR*: 2.6 mg/kg	

* HAFT, highest average field trial value

Based on peak residue values and using the OECD calculator, the unrounded result for blueberries based on the foliar spray application scheme was 3.58 mg/kg. The GJR proposal based on the same data, but using different evaluation criteria, was 4.0 mg/kg for this commodity.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL of 4.0 mg/kg is proposed for blueberries.

● Tomatoes

Based on NAFTA guidance, a complete set of field residue trials was conducted on tomatoes. Two different application scenarios were tested, with either 2 foliar treatments or a single soil application; each scenario included 19 trials. Residue levels in the fruit, as presented above in section 6.3.2.8, were clearly more critical following the soil application, as reflected in the considerably higher HR value, which is crucial to the MRL calculations. Peak residues at or after the designated PHI of 45 days in this data set ranged from <0.07-1.9 mg/kg, with a median value of 0.20 mg/kg. (In the foliar-application data set, residues ranged from 0.12-0.90 mg/kg, with a median value of 0.21 mg/kg.)

Table 6.7.2.2-9: Total residues of BYI 02960/tomatoes – OECD maximum residue level calculation results for a pre-harvest interval of 45 days
(soil-application trials in the NAFTA region)

Commodity	unrounded value
Tomatoes	2.36 mg/kg
<0.070; <0.070; 0.08; 0.08; 0.09; *0.11; 0.14;* 0.16; 0.16; 0.20; 0.20; 0.23; 0.33; *0.63; 0.81; 0.82;* 0.83; *1.1; 1.9* mg/kg STMR: 0.20 mg/kg HR*: 1.9 mg/kg	

* HAFT, highest average field trial value

Based on peak residue values and using the OECD calculator, the unrounded result for tomatoes based on the soil application scheme was 2.36 mg/kg. The GJR proposal based on the same data, but using different evaluation criteria, was 3.0 mg/kg for non-cucurbit fruit vegetables.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL of 3.0 mg/kg is proposed for tomatoes.

● Chili (non-bell) peppers

Based on NAFTA guidance, a complete set of field residue trials was conducted on various solanacaea, including chili peppers (=non-bell peppers). Two different application scenarios were tested, with either 2 foliar treatments or a single soil application; each scenario included 4 trials. Residue levels in chili pepper fruit, as presented above in section 6.3.2.8, are relatively similar following both application schemes – due in part to the small data sets – but the HR and STMR values were higher following the soil application scheme. Peak residues at or after the designated PHI of 45 days in this data set ranged from 0.18-0.91 mg/kg, with a median value of 0.55 mg/kg. (The corresponding residue values after foliar treatment were 0.13-0.72 mg/kg, median 0.42 mg/kg)

Table 6.7.2.2-10: Total residues of BYI 02960/ chili peppers – OECD maximum residue level calculation results for a pre-harvest interval of 45 days
(soil-application trials in the NAFTA region)

Commodity	unrounded value
Chili peppers	1.88 mg/kg
0.18; 0.37; *0.73; 0.91* mg/kg STMR: 0.55 mg/kg HR*: 0.91 mg/kg	

* HAFT, highest average field trial value

Based on peak residue values and using the OECD calculator, the unrounded result for chili peppers based on the soil application scheme was 1.88 mg/kg. The GJR proposal based on the same data, but using different evaluation criteria, was 3.0 mg/kg for non-cucurbit fruit vegetables.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL of 3.0 mg/kg is proposed for chili peppers.

● Sweet corn

Based on NAFTA guidance, a complete set of field residue trials was conducted on various cereal crops, including sweet corn/maize. Two different application scenarios were tested, with either 2 foliar treatments or a single seed treatment application; the former scenario included 13 trials, the latter 3. Residue levels in ears without husks (reported as "kernel + cob with husk removed"), as presented above in section 6.3.2.15, were more critical following the foliar application, as reflected in a considerably higher HR, as well as a higher STMR value. Peak residues at or after the designated PHI of 7 days in this data set ranged from <0.07-0.26 mg/kg, with a median value of 0.14 mg/kg. (The corresponding residue values at harvest after seed treatment were 0.08-0.13 mg/kg; median 0.13 mg/kg.)

Table 6.7.2.2-11: Total residues of BYI 02960/sweet corn – OECD maximum residue level calculation results for a pre-harvest interval of 7 days
(foliar-application trials in the NAFTA region)

Commodity	unrounded value
Sweet corn (maize)	0.42 mg/kg
<0.070; <0.070; <0.070; 0.078; 0.11; 0.13; 0.14; 0.14; 0.16; 0.19; *0.21; 0.26;* 0.26 mg/kg STMR: 0.14 mg/kg HR*: 0.26 mg/kg	

* HAFT, highest average field trial value

Based on peak residue values and using the OECD calculator, the unrounded result for sweet corn based on the foliar application scheme was 0.42 mg/kg. The GJR proposal based on the same data, but using different evaluation criteria, was 0.40 mg/kg for this commodity.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL of <u>0.40 mg/kg</u> is proposed for sweet corn.

● Celery

Based on NAFTA guidance, a complete set of field residue trials was conducted on celery. The tested application scenario called for two foliar sprays; 10 trials were conducted. As presented above in section 6.3.2.9, peak residues at the designated PHI of 1 day in untrimmed stalks ranged from 0.28-6.1 mg/kg, with a median value of 2.2 mg/kg.

Table 6.7.2.2-12: Total residues of BYI 02960/celery – OECD maximum residue level calculation results for a pre-harvest interval of 1 day
(trials in the NAFTA region)

Commodity	unrounded value
Celery	9.1 mg/kg
0.28; 0.61; 1.1; 2.0; 2.2; 2.2; 2.4; 3.2; 3.6; 6.1 mg/kg STMR: 2.2 mg/kg HR*: 6.1 mg/kg	

* HAFT, highest average field trial value

Based on peak residue values and using the OECD calculator, the unrounded result for untrimmed celery stalks was 9.1 mg/kg. The GJR proposal based on the same data, but using different evaluation criteria, was 40 mg/kg for the NAFTA crop group of leaf & stem vegetables.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL of <u>40 mg/kg</u> is proposed for celery.

● Pulses – dry beans, dry peas

Complete sets of field residue trials were conducted in the NAFTA zone on two important pulses, dry beans and peas, based on NAFTA guidance. The tested application scenario called for two foliar sprays; 9 bean and 10 pea trials were conducted. As presented above in section 6.3.2.10, peak residues at or after the designated PHI of 7 days for beans and peas ranged from <0.07-0.53 mg/kg and 0.077-5.3 mg/kg, respectively, with respective median values of 0.17 and 0.80 mg/kg.

Table 6.7.2.2-13: Total residues of BYI 02960/ pulses (dry) – OECD maximum residue level calculation results for a pre-harvest interval of 7 days
(trials in the NAFTA region)

Commodity	unrounded value
Beans (dry)	0.87 mg/kg
<0.070; 0.074; 0.081; 0.136; 0.165; 0.219; *0.304; 0.417;* 0.525 mg/kg STMR: 0.17 mg/kg HR: 0.53 mg/kg	
Peas (dry)	7.34 mg/kg
0.077; 0.257; *0.512;* 0.598; 0.629; 0.960; *1.27; 1.56;* 1.74; 5.31 mg/kg STMR: 0.80 mg/kg HR: 5.3 mg/kg	

Based on peak residue values and using the OECD calculator, the unrounded result for dry beans and peas were 0.87 and 7.34 mg/kg, respectively. The GJR proposals based on the same data, but using different evaluation criteria, was 0.8 and 6.0 mg/kg for the two pulses, as the differences in residue levels were too great to allow a common MRL for the entire group.

Based on this evaluation, the proposal for the MRL in the GJR dossier is, possibly, too low. Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL 8.0 mg/kg is proposed for dry peas, higher than the proposal in the GJR dossier.

For dry beans, the calculation would lead to a proposal of 0.9 mg/kg, which is also higher than the original GJR proposal. However, using EU residue data, a group MRL of 6.0 mg/kg is proposed in section 6.7.2.1 above, based on the field rotational crop studies.

● Peanuts

Based on NAFTA guidance, a complete set of field residue trials was conducted on peanuts. The tested application scenario called for two foliar sprays; 12 trials were conducted. As presented above in section 6.3.2.11, peak residues at or after the designated PHI of 7 days in the nutmeat ranged from <0.07-0.092 mg/kg, with a median value of <0.07 mg/kg.

Table 6.7.2.2-14: Total residues of BYI 02960/ p e a n u t s – OECD maximum residue level calculation results for a pre-harvest interval of 7 days
(trials in the NAFTA region)

Commodity	unrounded value
Peanuts*	0.12 mg/kg
<0.070; <0.070; <0.070; <0.070; <0.070; <0.070; <0.070; <0.070; *0.075; 0.077;* 0.087; *0.092* mg/kg STMR: <0.07 mg/kg HR**: 0.092 mg/kg	

* nutmeat
** HAFT, highest average field trial value

Based on peak residue values and using the OECD calculator, the unrounded result for peanut nutmeat was 0.12 mg/kg. The GJR proposal based on the same data, but using different evaluation criteria, was 0.15 mg/kg for this commodity.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL of 0.15 mg/kg is proposed for the nutmeat of peanuts.

● Potatoes

Based on NAFTA guidance, a complete set of field residue trials was conducted on potatoes. The tested application scenario called for two foliar sprays; 26 trials were conducted. As presented above in section 6.3.2.7, peak residues in tubers at or after the designated PHI of 7 days ranged from <0.07-0.12 mg/kg, with a median value of <0.07 mg/kg.

Table 6.7.2.2-15: Total residues of BYI 02960/ p o t a t o e s – OECD maximum residue level calculation results for a pre-harvest interval of 7 days
(trials in the NAFTA region)

Commodity	unrounded value
Potatoes	0.14 mg/kg
<0.070; <0.070; <0.070; <0.070; <0.070; <0.070; <0.070; <0.070; <0.070; <0.070; <0.070; <0.070; <0.070; <0.070; <0.070; <0.070; *0.072;* 0.074; 0.079; 0.081; 0.094; *0.098;* 0.10; 0.11; 0.11; 0.12 mg/kg STMR: <0.07 mg/kg HR*: 0.12 mg/kg	

* HAFT, highest average field trial value

Based on peak residue values and using the OECD calculator, the unrounded result for tubers was 0.14 mg/kg. The GJR proposal based on the same data, but using different evaluation criteria, was 0.15 mg/kg for this commodity.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL of 0.15 mg/kg is proposed for potatoes.

● Hops

Based on NAFTA guidance, a complete set of field residue trials was conducted on hops. Two different application scenarios were tested (concentrated and dilute spray). 3 trials were conducted with each of the scenarios. As presented above in section 6.3.2.19, peak residues in dried cones at the designated PHI of 21 days were very similar following both application schemes, ranging from 3.1-8.0 mg/kg in the "concentrated" trials, and from 3.1-7.8 mg/kg in the "diluted" trials. As each of the trial sets contained only 3 entities (the required data set for NAFTA use), the median values are not of particular substantiality, but they were also similar, at approx. 3.3 and 3.4 mg/kg, respectively.

Table 6.7.2.2-16: Total residues of BYI 02960/ hops – OECD maximum residue level calculation results for a pre-harvest interval of 21 days
(trials in the NAFTA region)

Commodity	unrounded value
Hop cones, dry (concentrated spray)	15.9 mg/kg
3.07; 3.32; 7.98 mg/kg STMR: 3.3 mg/kg HR: 8.0 mg/kg	
Hop cones, dry (diluted spray)	15.2 mg/kg
3.14; 3.35; 7.76 mg/kg STMR: 3.4 mg/kg HR: 7.8 mg/kg	
Hops: dilute + conc. spray	14.4 mg/kg
3.07; 3.14; 3.32; 3.35; 7.76; 7.98 mg/kg STMR: 3.3 mg/kg HR: 8.0 mg/kg	

Based on peak residue values and using the OECD calculator, the unrounded results for dried hop cones were 15.9 and 15.2 mg/kg for the concentrated and dilute-spray scenarios, respectively. Given the similarity of the populations, a 3rd calculation combined all values; the result was similar, at 14.4 mg/kg. The GJR proposal based on the same data, but using different evaluation criteria, was 20 mg/kg for this commodity.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL of <u>20 mg/kg</u> is proposed for dried hop cones.

● Coffee

Complete sets of field residue trials were conducted for the NAFTA zone and in Brazil on coffee. The set included two studies covering the same application scenario (one soil drench followed by 3 foliar applications), each with 4 trials. The trials in the "US" study took place in Guatemala and Mexico; 4 further trials in Brazil were reported in the Brazilian study. The trials were presented above in section 6.3.2.18.

Peak residues at or after the designated PHI of 0 days for green coffee beans ranged from 0.21-0.94 mg/kg and 0.08-0.19 mg/kg in the "US" and Brazilian studies, respectively, with respective median values of 0.58 and 0.11 mg/kg.

Table 6.7.2.2-17: Total residues of BYI 02960/ coffee – OECD maximum residue level calculation results for a pre-harvest interval of 0 days

Commodity	unrounded value
Coffee ("US" study)	2.13 mg/kg
0.206; 0.273; *0.879; 0.939* mg/kg STMR: 0.58 mg/kg HR*: 0.94 mg/kg	
Coffee (Brazilian trials)	0.36 mg/kg
0.08; 0.10; *0.11; 0.19* mg/kg STMR: 0.11 mg/kg HR*: 0.19 mg/kg	
Coffee: "US" + Brazilian data	1.76 mg/kg
0.08; 0.10; *0.11; 0.19; 0.206;* 0.273; *0.879; 0.939* mg/kg STMR: 0.20 mg/kg HR: 0.94 mg/kg	

* HAFT, highest average field trial value

Based on peak residue values and using the OECD calculator, the unrounded result for green coffee beans were 2.13 and 0.36 mg/kg in the "US" and Brazilian studies, respectively. However, the two packages reflect a common use pattern, and thus should be combined for calculation; the result for all data points is 1.76 mg/kg. The GJR proposal based on the same data, but using different evaluation criteria, was 2.0 mg/kg for this commodity.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL of <u>2.0 mg/kg</u> is proposed for green coffee beans.

● Cereals (barley, corn/maize, sorghum, wheat)

Complete sets of field residue trials were conducted in the NAFTA zone in various cereals based on NAFTA guidance. The program included studies in barley, corn/maize, sorghum, and wheat, each covering two relevant application scenarios (seed treatment or two foliar treatments). The trials were presented above in sections 6.3.2.14 - 6.3.2.17. For barley, sorghum, and wheat, the residues following the foliar applications were significantly more critical than those after seed treatment. The differences were evident in both the HR and STMR values from the respective data sets.

20 trials were conducted on barley; peak residues in grain at or after the designated PHI of 21 days after foliar treatment ranged from 0.52-2.4 mg/kg, with a median value of 0.93 mg/kg. In sorghum, peak values of 0.43-1.6 mg/kg were measured in grain samples from 9 trials, with a median value of 0.69 mg/kg. Finally, in wheat, 28 trials were conducted, yielding peak residues of 0.093-2.7 mg/kg in grain samples taken at or after day 21; the median was 0.71 mg/kg. (Following seed treatment, both the HR and STMR values in grain of all three crops were lower. In 3 trials each, residues ranged from

0.25-0.71 mg/kg in barley and 0.089-0.61 mg/kg in wheat, with medians of 0.52 and 0.29 mg/kg, respectively. All values in sorghum grain were below the LOQ, at <0.07 mg/kg.)

In corn, the data were not conclusive with regard to the "critical case". In 20 corn/maize trials with foliar application, peak residues in grain at or after day 21 were <0.07-0.14 mg/kg (median <0.07 mg/kg). In three further trials with seed treatment, residues at harvest ranged from 0.09-0.19 mg/kg.

Table 6.7.2.2-18: Total residues of BYI 02960/ c e r e a l s – OECD maximum residue level calculation results for a pre-harvest interval of 21 days
(trials in the NAFTA region)

Commodity	unrounded value
Barley (foliar treatment)	3.10 mg/kg
0.516; 0.575; 0.577; 0.703; 0.725; 0.761; 0.778; 0.814; 0.816; *0.926;* 0.926; 0.943; 1.10; *1.19;* 1.24; 1.25; 1.30; 1.33; 1.81; 2.38 mg/kg STMR: 0.93 mg/kg HR*: 2.4 mg/kg	
Sorghum (foliar treatment)	2.55 mg/kg
0.43; 0.52; 0.56; 0.65; 0.69; 0.89; 0.91; 1.4; *1.6* mg/kg STMR: 0.69 mg/kg HR*: 1.6 mg/kg	
Wheat (foliar treatment)	3.46 mg/kg
0.093; 0.102; 0.11; 0.22; 0.25; 0.27; 0.30; 0.31; 0.38; 0.57; 0.60; *0.66;* 0.66; 0.69; 0.72; 0.75; *0.76;* 0.78; 0.79; 0.82; 0.88; 0.91; 1.1; 1.3; 1.5; *1.8;* 2.6; 2.7 mg/kg STMR: 0.71 mg/kg HR*: 2.7 mg/kg	
Corn/maize (foliar treatment)	0.14 mg/kg
<0.07; <0.07; <0.07; <0.07; <0.07; <0.07; <0.07; <0.07; <0.07; <0.07; <0.07; <0.07; <0.07; <0.07; <0.07; <0.07; <0.07; <0.07; 0.07; 0.14 mg/kg STMR: <0.07 mg/kg HR*: 0.14 mg/kg	
Corn/maize (seed treatment**)	0.41 mg/kg
0.09; 0.13; 0.19 mg/kg STMR: 0.13 mg/kg HR*: 0.19 mg/kg	

* HAFT, highest average field trial value
** no PHI specified for seed-treatment use

Based on peak residue values and using the OECD calculator, the unrounded results for barley, sorghum, and wheat were 3.10, 2.55, and 3.46 mg/kg, respectively. The GJR proposal based on the same data, but using different evaluation criteria, was 4.0 mg/kg for this group of crops.

Corn/maize was evaluated separately, as the differences in residue levels were too great to allow a common MRL for the entire group. The unrounded results for foliar and seed treatment were 0.20 and 0.41 mg/kg, respectively. In the GJR dossier, an MRL of 0.5 mg/kg was proposed for corn, based on this data.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL 4.0 mg/kg is proposed for cereal crops except corn/maize.

As stated previously, for corn/maize, 0.5 mg/kg was proposed as the MRL in the GJR dossier. However, using EU residue data, a group MRL of 1.5 mg/kg is proposed in section 6.7.2 above, based on the field rotational crop studies.

● Cotton

Based on NAFTA guidance, a complete set of field residue trials was conducted on cotton. Two different application scenarios were tested (2 foliar sprays or seed treatment). 12 trials were conducted with the former scenario, 3 with the latter. As presented above in section 6.3.2.13, the data were not conclusive with regard to the "critical case". In 12 trials with foliar application, peak residues in undelinted seed at or after the designated PHI of 14 days ranged between <0.07-0.55 mg/kg (median 0.16 mg/kg). In the three seed-treatment trials, residues at harvest ranged from 0.07-0.36 mg/kg.

Table 6.7.2.2-19: Total residues of BYI 02960/ c o t t o n – OECD maximum residue level calculation results for a pre-harvest interval of 14 days
(trials in the NAFTA region)

Commodity	unrounded value
Cotton seed (foliar treatment)	0.82 mg/kg
<0.070; 0.078; 0.093; 0.122; 0.14; 0.14; *0.18*; 0.19; 0.24; 0.27; 0.46; *0.55* mg/kg STMR: 0.16 mg/kg HR*: 0.55 mg/kg	
Cotton seed (seed treatment**)	0.82 mg/kg
0.070; 0.087; 0.36 mg/kg STMR: 0.09 mg/kg HR: 0.36 mg/kg	

* HAFT, highest average field trial value
** no PHI specified for seed-treatment use

Based on peak residue values and using the OECD calculator, the unrounded results for undelinted cotton seeds were 0.82 mg/kg for both the foliar and seed-treatment scenarios. The GJR proposal based on the same data, but using different evaluation criteria, was 0.9 mg/kg for this commodity.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL of 0.9 mg/kg is proposed for cotton seed.

● Prickly pear

In an IR-4 program, an extensive set of field residue trials was conducted in the USA on prickly pear cactus. The use pattern called for 2 foliar spray applications. 4 trials were conducted in total, with plots for the collection of samples of each of the two edible commodities of this plant. As presented above in section 6.3.2.6, peak residues in the fruit and the pads sampled at the designated PHI of 21 days ranged from 0.13-0.18 mg/kg and 0.27-0.33 mg/kg, respectively, with respective median values of 0.17 and 0.28 mg/kg.

Table 6.7.2.2-20: Total residues of BYI 02960/ prickly pear – OECD maximum residue level calculation results for a pre-harvest interval of 21 days
(IR-4 program)

Commodity	unrounded value
Prickly pear (fruit)	0.49 mg/kg
0.128; 0.161; 0.178; 0.183 mg/kg STMR: 0.17 mg/kg HR*: 0.18 mg/kg	
Prickly pear (pads)	0.87 mg/kg
0.265; 0.266; 0.294; 0.329 mg/kg STMR: 0.28 mg/kg HR*: 0.33 mg/kg	
Prickly pear (fruit + pads)	0.68 mg/kg
0.128; 0.161; 0.178; 0.183; 0.265; 0.266; 0.294; 0.329 mg/kg STMR: 0.22 mg/kg HR*: 0.33 mg/kg	

* HAFT, highest average field trial value

Based on peak residue values and using the OECD calculator, the unrounded result for prickly pear fruit was 0.49 mg/kg, for pads 0.87 mg/kg, and 0.68 mg/kg for all edible commodities of the prickly pear plant. The GJR proposals based on the same data, but using different evaluation criteria, were 0.5 mg/kg for the fruit and 0.9 mg/kg for the pads.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), MRLs of <u>0.5 mg/kg</u> and <u>0.9 mg/kg</u> are proposed for prickly pear fruit and pads, respectively.

● Soybean

Based on NAFTA guidance, a complete set of field residue trials was conducted on soybeans. Two different application scenarios were tested (2 foliar sprays or seed treatment). 20 trials were conducted with the former scenario, 3 with the latter. As presented above in section 6.3.2.12, the residues following the foliar applications were significantly more critical than those after seed treatment. The differences were evident in the HR values of the data sets. (As the seed-treatment data set is small, the STMR in that set is not particularly substantial.) Peak residues in soybean seed at or after the designated PHI of 21 days following foliar treatment ranged between <0.07-3.6 mg/kg (median 0.26 mg/kg). (In the three seed-treatment trials, residues at harvest ranged from 0.15-0.82 mg/kg.)

Table 6.7.2.2-21: Total residues of BYI 02960/ soybean – OECD maximum residue level calculation results for a pre-harvest interval of 21 days
(foliar-application trials in the NAFTA region)

Commodity	unrounded value
Soybean (foliar treatment)	3.74 mg/kg
<0.070; <0.070; <0.070; <0.070; 0.08; 0.08; 0.08; 0.08; 0.20; 0.25; 0.27; 0.37; 0.38; 0.41; 0.50; 0.65; 0.73; *1.2;* 1.2; 3.6 mg/kg STMR: 0.26 mg/kg HR*: 3.6 mg/kg	
Soybean (seed treatment**)	1.83 mg/kg
0.15; 0.50; 0.82 mg/kg STMR: 0.50 mg/kg HR*: 0.82 mg/kg	

* HAFT, highest average field trial value
** no PHI specified for seed-treatment use

Based on peak residue values and using the OECD calculator, the unrounded result for soybean seeds were 3.74 mg/kg for the foliar-treatment scenario. The GJR proposal based on the same data, but using different evaluation criteria, was 4.0 mg/kg for this commodity.

Therefore, in order to facilitate international trade (including imports into the EU from GJR countries), an MRL of 4.0 mg/kg is proposed for soybean seed.

● Sugar cane

Based on NAFTA guidance, a complete set of field rotational crop residue trials was conducted on sugar cane. As presented above in section 6.6.3.2, the residues in the rotational cane were below the LOQ. Thus, for the NAFTA region, no specific MRL was requested in the GJR dossier. The EU MRL for sugar cane can thus be set at the LOQ.

Table 6.7.2.2-22: Calculation of import-based MRL proposals for orange according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Citrus fruit
Portion analysed :	fruit	Commodity :	**ORANGE** USA DILUTE
Target value :	MRL	PHI :	1 d

No.	Crop	Days after application	Residue value (mg/kg)	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Orange	1	0.08	2	SL 200	BYI 02960 SL 200	USA	F
2	Orange	1	0.097	2	SL 200	BYI 02960 SL 200	USA	F
3	Orange	1	0.13	2	SL 200	BYI 02960 SL 200	USA	F
4	Orange	1	0.15	2	SL 200	BYI 02960 SL 200	USA	F
5	Orange	**	0.15	2	SL 200	BYI 02960 SL 200	USA	F
6	Orange	1	0.17	2	SL 200	BYI 02960 SL 200	USA	F
7	Orange	**	0.18	2	SL 200	BYI 02960 SL 200	USA	F
8	Orange	1	0.21	2	SL 200	BYI 02960 SL 200	USA	F
9	Orange	1	0.22	2	SL 200	BYI 02960 SL 200	USA	F
10	Orange	1	0.28	2	SL 200	BYI 02960 SL 200	USA	F

** sample value from later interval than the nominal PHI

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Table 6.7.2.2-22 (cont'd): Calculation of import-based MRL proposals for orange according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	No. of applic.	FL-Type	Product	Country	Area of applic.
11	Orange	1	0.30	2	SL 200	BYI 02960 SL 200	USA	F
12	Orange	1	0.30	2	SL 200	BYI 02960 SL 200	USA	F
13	Orange	1	0.32	2	SL 200	BYI 02960 SL 200	USA	F
14	Orange	**	0.54	2	SL 200	BYI 02960 SL 200	USA	F
15	Orange	1	.73	2	SL 200	BYI 02960 SL 200	USA	F
16	Orange	**	1.5	2	SL 200	BYI 02960 SL 200	USA	F

value no. 16 is an outlier for tl
** sample value from later interval than the nominal PHI

Results (Orange USA dilute)

Total number of data (n)	16	Standard deviation (SD)	0.353
Lowest residue	0.08	Percentage of censored data	0
Highest residue	1.5	Number of non-censored data	16
Median residue	0.215	Correction factor for censoring (CF)	1.000
Mean	0.335		

Proposed MRL estimate

Highest residue	1.5
Mean + 4 SD	1.748
CF × 3 mean	1.004
Unrounded MRL	1.748
Rounded MRL	2

Table 6.7.2.2-23: Calculation of import-based MRL proposals for orange according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Citrus fruit
Portion analysed :	fruit	Commodity :	**ORANGE** USA CONC
Target value :	MRL	PHI :	1 d

No.	Crop	Days after application	Residue value (mg/kg)	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Orange	1	0.05	2	SL 200	BYI 02960 SL 200	USA	F
2	Orange	1	0.10	2	SL 200	BYI 02960 SL 200	USA	F
3	Orange	1	0.22	2	SL 200	BYI 02960 SL 200	USA	F
4	Orange	1	0.24	2	SL 200	BYI 02960 SL 200	USA	F
5	Orange	1	0.26	2	SL 200	BYI 02960 SL 200	USA	F
6	Orange	1	0.26	2	SL 200	BYI 02960 SL 200	USA	F
7	Orange	1	0.26	2	SL 200	BYI 02960 SL 200	USA	F
8	Orange	**	0.37	2	SL 200	BYI 02960 SL 200	USA	F

** sample value from later interval than the nominal PHI

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Table 6.7.2.2-23 (cont'd): Calculation of import-based MRL proposals for orange according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	No. of applic.	FL-Type	Product	Country	Area of applic.
9	Orange	1	0.66	2	SL 200	BYI 02960 SL 200	USA	F
10	Orange	**	0.92	2	SL 200	BYI 02960 SL 200	USA	F
11	Orange	**	1.3	2	SL 200	BYI 02960 SL 200	USA	F
12	Orange	**	2.2	2	SL 200	BYI 02960 SL 200	USA	F

** sample value from later interval than the nominal PHI

Results (Orange USA conc.)

Total number of data (n)	12	Standard deviation (SD)	0.630
Lowest residue	0.05	Percentage of censored data	0
Highest residue	2.2	Number of non-censored data	12
Median residue	0.260	Correction factor for censoring (CF)	1.000
Mean	0.570		

Proposed MRL estimate

Highest residue	2.2
Mean + 4 SD	3.092
CF × 3 mean	1.710
Unrounded MRL	3.092
Rounded MRL	3

Table 6.7.2.2-24: Calculation of import-based MRL proposals for grapefruit according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Citrus fruit
Portion analysed :	fruit	Commodity :	**GRAPEFRUIT** DILUTE
Target value :	MRL	PHI :	1 d

No.	Crop	Days after application	Residue value (mg/kg)	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Grapefruit	1	0.15	2	SL 200	BYI 02960 SL 200	USA	F
2	Grapefruit	**	0.18	2	SL 200	BYI 02960 SL 200	USA	F
3	Grapefruit	1	0.19	2	SL 200	BYI 02960 SL 200	USA	F
4	Grapefruit	1	0.22	2	SL 200	BYI 02960 SL 200	USA	F
5	Grapefruit	1	0.22	2	SL 200	BYI 02960 SL 200	USA	F
6	Grapefruit	1	0.23	2	SL 200	BYI 02960 SL 200	USA	F

** sample value from later interval than the nominal PHI

Results (Grapefruit dilute)

Total number of data (n)	6	Standard deviation (SD)	0.031
Lowest residue	0.15	Percentage of censored data	0
Highest residue	0.23	Number of non-censored data	6
Median residue	0.205	Correction factor for censoring (CF)	1.000
Mean	0.198		

Proposed MRL estimate

Highest residue	0.23
Mean + 4 SD	0.321
CF × 3 mean	0.595
Unrounded MRL	0.595
Rounded MRL	0.6

Table 6.7.2.2-25: Calculation of import-based MRL proposals for grapefruit according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Citrus fruit
Portion analysed :	fruit	Commodity :	**GRAPEFRUIT** CONC
Target value :	MRL	PHI :	1 d

No.	Crop	Days after application	Residue value (mg/kg)	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Grapefruit	1	0.092	2	SL 200	BYI 02960 SL 200	USA	F
2	Grapefruit	1	0.19	2	SL 200	BYI 02960 SL 200	USA	F
3	Grapefruit	1	0.20	2	SL 200	BYI 02960 SL 200	USA	F
4	Grapefruit	1	0.22	2	SL 200	BYI 02960 SL 200	USA	F
5	Grapefruit	**	0.30	2	SL 200	BYI 02960 SL 200	USA	F
6	Grapefruit	1	0.32	2	SL 200	BYI 02960 SL 200	USA	F

** sample value from later interval than the nominal PHI

Results (Grapefruit conc.)

Total number of data (n)	6	Standard deviation (SD)	0.083
Lowest residue	0.092	Percentage of censored data	0
Highest residue	0.32	Number of non-censored data	6
Median residue	0.210	Correction factor for censoring (CF)	1.000
Mean	0.220		

Proposed MRL estimate

Highest residue	0.32
Mean + 4 SD	0.551
CF × 3 mean	0.661
Unrounded MRL	0.661
Rounded MRL	0.7

Table 6.7.2.2-26: Calculation of import-based MRL proposals for lemon according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Citrus fruit
Portion analysed :	fruit	Commodity :	**LEMON** DILUTE
Target value :	MRL	PHI :	1 d

No.	Crop	Days after application	Residue value (mg/kg)	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Lemon	1	0.15	2	SL 200	BYI 02960 SL 200	USA	F
2	Lemon	1	0.21	2	SL 200	BYI 02960 SL 200	USA	F
3	Lemon	1	0.26	2	SL 200	BYI 02960 SL 200	USA	F
4	Lemon	1	0.26	2	SL 200	BYI 02960 SL 200	USA	F
5	Lemon	1	0.31	2	SL 200	BYI 02960 SL 200	USA	F
6	Lemon	**	0.33	2	SL 200	BYI 02960 SL 200	USA	F
7	Lemon	**	0.36	2	SL 200	BYI 02960 SL 200	USA	F
8	Lemon	**	0.55	2	SL 200	BYI 02960 SL 200	USA	F

** sample value from later interval than the nominal PHI

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Table 6.7.2.2-26 (cont'd): Calculation of import-based MRL proposals for lemon according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Results (Lemon dilute)

Total number of data (n)	8	Standard deviation (SD)	0.120
Lowest residue	0.15	Percentage of censored data	0
Highest residue	0.55	Number of non-censored data	8
Median residue	0.285	Correction factor for censoring (CF)	1.000
Mean	0.304		

Proposed MRL estimate

Highest residue	0.55
Mean + 4 SD	0.784
CF × 3 mean	0.911
Unrounded MRL	0.911
Rounded MRL	1

Table 6.7.2.2-27: Calculation of import-based MRL proposals for lemon according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Citrus fruit
Portion analysed :	fruit	Commodity :	**LEMON** CONC
Target value :	MRL	PHI :	1 d

No.	Crop	Days after application	Residue value (mg/kg)	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Lemon	1	0.067	2	SL 200	BYI 02960 SL 200	USA	F
2	Lemon	1	0.082	2	SL 200	BYI 02960 SL 200	USA	F
3	Lemon	1	0.084	2	SL 200	BYI 02960 SL 200	USA	F
4	Lemon	**	0.13	2	SL 200	BYI 02960 SL 200	USA	F
5	Lemon	1	0.24	2	SL 200	BYI 02960 SL 200	USA	F
6	Lemon	1	0.38	2	SL 200	BYI 02960 SL 200	USA	F
7	Lemon	1	0.70	2	SL 200	BYI 02960 SL 200	USA	F
8	Lemon	1	0.74	2	SL 200	BYI 02960 SL 200	USA	F

** sample value from later interval than the nominal PHI

Results (Lemon conc.)

Total number of data (n)	8	Standard deviation (SD)	0.278
Lowest residue	0.067	Percentage of censored data	0
Highest residue	0.74	Number of non-censored data	8
Median residue	0.185	Correction factor for censoring (CF)	1.000
Mean	0.303		

Proposed MRL estimate

Highest residue	0.74
Mean + 4 SD	1.415
CF × 3 mean	0.909
Unrounded MRL	1.415
Rounded MRL	1.5

Table 6.7.2.2-28: Calculation of import-based MRL proposals for mandarin orange according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Citrus fruit
Portion analysed :	fruit	Commodity :	**MANDARIN** DILUTE
Target value :	MRL	PHI :	1 d

No.	Crop	Days after application	Residue value (mg/kg)	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Mandarin	1	0.22	2	SL 200	BYI 02960 SL 200	USA	F
2	Mandarin	1	0.41	2	SL 200	BYI 02960 SL 200	USA	F
3	Mandarin	**	0.22	2	SL 200	BYI 02960 SL 200	USA	F
4	Mandarin	**	0.42	2	SL 200	BYI 02960 SL 200	USA	F
5	Mandarin	1	0.21	2	SL 200	BYI 02960 SL 200	USA	F
6	Mandarin	**	0.42	2	SL 200	BYI 02960 SL 200	USA	F
7	Mandarin	**	0.34	2	SL 200	BYI 02960 SL 200	USA	F
8	Mandarin	1	0.25	2	SL 200	BYI 02960 SL 200	USA	F

** sample value from later interval than the nominal PHI

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Table 6.7.2.2-28 (cont'd): Calculation of import-based MRL proposals for mandarin according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Results (Mandarin dilute)

Total number of data (n)	8	Standard deviation (SD)	0.096
Lowest residue	0.21	Percentage of censored data	0
Highest residue	0.42	Number of non-censored data	8
Median residue	0.295	Correction factor for censoring (CF)	1.000
Mean	0.311		

Proposed MRL estimate

Highest residue	0.42
Mean + 4 SD	0.696
CF × 3 mean	0.934
Unrounded MRL	0.934
Rounded MRL	1

Table 6.7.2.2-29: Calculation of import-based MRL proposals for mandarin orange according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Citrus fruit
Portion analysed :	fruit	Commodity :	**MANDARIN** CONC
Target value :	MRL	PHI :	1 d

No.	Crop	Days after application	Residue value (mg/kg)	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Mandarin	1	0.085	2	SL 200	BYI 02960 SL 200	USA	F
2	Mandarin	1	0.12	2	SL 200	BYI 02960 SL 200	USA	F
3	Mandarin	**	0.27	2	SL 200	BYI 02960 SL 200	USA	F
4	Mandarin	**	0.45	2	SL 200	BYI 02960 SL 200	USA	F
5	Mandarin	**	0.57	2	SL 200	BYI 02960 SL 200	USA	F
6	Mandarin	**	0.61	2	SL 200	BYI 02960 SL 200	USA	F
7	Mandarin	**	0.67	2	SL 200	BYI 02960 SL 200	USA	F
8	Mandarin	**	1.0	2	SL 200	BYI 02960 SL 200	USA	F

** sample value from later interval than the nominal PHI

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Table 6.7.2.2-29 (cont'd): Calculation of import-based MRL proposals for mandarin according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Results (Mandarin conc.)

Total number of data (n)	8	Standard deviation (SD)	0.307
Lowest residue	0.085	Percentage of censored data	0
Highest residue	1	Number of non-censored data	8
Median residue	0.510	Correction factor for censoring (CF)	1.000
Mean	0.472		

Proposed MRL estimate

Highest residue	1
Mean + 4 SD	1.702
CF × 3 mean	1.416
Unrounded MRL	1.702
Rounded MRL	2

Table 6.7.2.2-30: Calculation of import-based MRL proposals for orange according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Citrus fruit
Portion analysed :	fruit	Commodity :	**Orange** Brazil ST + foliar
Target value :	MRL	PHI :	0 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Orange	7	0.49**	I11-022-01 / I11-022	3	SL 200	Brazil	F
2	Orange	0	0.53	I11-022-02 / I11-022	3	SL 200	Brazil	F
3	Orange	14	0.36**	I11-022-03 / I11-022	3	SL 200	Brazil	F
4	Orange	0	0.21	I11-022-04 / I11-022	3	SL 200	Brazil	F
5	Orange	7	0.41**	I11-022-05 / I11-022	3	SL 200	Brazil	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

Results (Orange Brazil ST + foliar)

Total number of data (n)	5	Standard deviation (SD)	0.125
Lowest residue	0.21	Percentage of censored data	0
Highest residue	0.53	Number of non-censored data	5
Median residue	0.410	Correction factor for censoring (CF)	1.000
Mean	0.400		

Proposed MRL estimate

Highest residue	0.53
Mean + 4 SD	0.901
CF × 3 mean	1.200
Unrounded MRL	1.200
Rounded MRL	1.5

Table 6.7.2.2-31: Calculation of import-based MRL proposals for orange according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Citrus fruit
Portion analysed :	fruit	Commodity :	**Orange** Brazil foliar
Target value :	MRL	PHI :	0 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Orange	7	0.29**	I11-006-03 / I11-006	2	SL 200	Brazil	F
2	Orange	0	0.16	I11-006-04 / I11-006	2	SL 200	Brazil	F
3	Orange	7	0.28**	I11-006-05 / I11-006	2	SL 200	Brazil	F
4	Orange	0	0.23	I11-006-06 / I11-006	2	SL 200	Brazil	F
5	Orange	0	0.40	I11-006-07 / I11-006	2	SL 200	Brazil	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

Results (Orange Brazil foliar)

Total number of data (n)	5	Standard deviation (SD)	0.088
Lowest residue	0.16	Percentage of censored data	0
Highest residue	0.4	Number of non-censored data	5
Median residue	0.280	Correction factor for censoring (CF)	1.000
Mean	0.272		

Proposed MRL estimate

Highest residue	0.4
Mean + 4 SD	0.625
CF × 3 mean	0.816
Unrounded MRL	0.816
Rounded MRL	0.9

Table 6.7.2.2-32: Calculation of import-based MRL proposals for tree nuts according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	tree nuts
Portion analysed :	nutmeat without shell	Commodity :	**Almond/Pecan**
Target value :	MRL	PHI :	7 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No.[1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Almond	14	0.12**	RV204-10DA-A / RARVY016	2	SL 200	USA	F
2	Almond	7	<0.070	RV205-10DA-A / RARVY016	2	SL 200	USA	F
3	Almond	7	<0.070	RV206-10HA-A / RARVY016	2	SL 200	USA	F
4	Almond	7	<0.070	RV207-10HA-A / RARVY016	2	SL 200	USA	F
5	Almond	7	<0.070	RV208-10HA-A / RARVY016	2	SL 200	USA	F
6	Pecan	7	<0.070	RV209-10DA-A / RARVY016	2	SL 200	USA	F
7	Pecan	7	<0.070	RV210-10DA-A / RARVY016	2	SL 200	USA	F
8	Pecan	7	<0.070	RV211-10HA-A / RARVY016	2	SL 200	USA	F
9	Pecan	7	<0.070	RV212-10HA-A / RARVY016	2	SL 200	USA	F
10	Pecan	7	<0.070	RV213-10HA-A / RARVY016	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
value no. 1 is an outlier for t1
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-32 (cont'd): Calculation of import-based MRL proposals for tree nuts according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Results (Almond/Pecan)

Total number of data (n)	10	Standard deviation (SD)	0.016
Lowest residue	0.07	Percentage of censored data	90
Highest residue	0.12	Number of non-censored data	1
Median residue	0.070	Correction factor for censoring (CF)	0.400
Mean	0.075		

Proposed MRL estimate

Highest residue	0.12
Mean + 4 SD	0.138
CF × 3 mean	0.090
Unrounded MRL	0.138
Rounded MRL	0.15

Table 6.7.2.2-33: Calculation of import-based MRL proposals for tree nuts according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Tree nuts
Portion analysed :	nutmeat without shell	Commodity :	**Almond &pecan** diluted
Target value :	MRL	PHI :	7 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Almond	7	<0.070	RV204-10DA-B / RARVY016	2	SL 200	BYI 02960 SL 200	USA	F
2	Almond	7	<0.070	RV205-10DA-B / RARVY016	2	SL 200	BYI 02960 SL 200	USA	F
3	Almond	7	0.075	RV206-10HA-B / RARVY016	2	SL 200	BYI 02960 SL 200	USA	F
4	Almond	7	<0.070	RV207-10HA-B / RARVY016	2	SL 200	BYI 02960 SL 200	USA	F
5	Almond	7	<0.070	RV208-10HA-B / RARVY016	2	SL 200	BYI 02960 SL 200	USA	F
6	Pecan	7	0.071	RV209-10DA-B / RARVY016	2	SL 200	BYI 02960 SL 200	USA	F
7	Pecan	7	<0.070	RV210-10DA-B / RARVY016	2	SL 200	BYI 02960 SL 200	USA	F

[1] as given in the Tier 1 summaries
value no. 3 is an outlier for t1

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Table 6.7.2.2-33 (cont'd): Calculation of import-based MRL proposals for tree nuts according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
8	Pecan	7	<0.070	RV211-10HA-B / RARVY016	2	SL 200	BYI 02960 SL 200	USA	F
9	Pecan	7	<0.070	RV212-10HA-B / RARVY016	2	SL 200	BYI 02960 SL 200	USA	F
10	Pecan	7	<0.070	RV213-10HA-B / RARVY016	2	SL 200	BYI 02960 SL 200	USA	F

[1] as given in the Tier 1 summaries
value no. 3 is an outlier for t1

Results (tree nuts diluted)

Total number of data (n)	10	Standard deviation (SD)	0.002
Lowest residue	0.07	Percentage of censored data	80
Highest residue	0.075	Number of non-censored data	2
Median residue	0.070	Correction factor for censoring (CF)	0.467
Mean	0.071		

Proposed MRL estimate

Highest residue	0.075
Mean + 4 SD	0.077
CF x 3 mean	0.099
Unrounded MRL	0.099
Rounded MRL	0.1

Table 6.7.2.2-34: Calculation of import-based MRL proposals for apples according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Pomaceous fruit
Portion analysed :	fruit	Commodity :	**Apple** dilute spray
Target value :	MRL	PHI :	14 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Apple	14	0.17	RV050-11HA-B / RARVY013	2	SL 200	USA	F
2	Apple	13	0.17	RV051-11DA-B / RARVY013	2	SL 200	USA	F
3	Apple	14	0.14	RV052-11HA-B / RARVY013	2	SL 200	USA	F
4	Apple	14	0.12	RV053-11HA-B / RARVY013	2	SL 200	USA	F
5	Apple	28	0.63**	RV054-11DA-B / RARVY013	2	SL 200	USA	F
6	Apple	14	0.18	RV055-11HA-B / RARVY013	2	SL 200	USA	F
7	Apple	14	0.29	RV056-11HA-B / RARVY013	2	SL 200	USA	F
8	Apple	12	0.28	RV057-11HA-B / RARVY013	2	SL 200	USA	F
9	Apple	13	0.15	RV058-11HA-B / RARVY013	2	SL 200	USA	F
10	Apple	12	0.18	RV059-11DA-B / RARVY013	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
value no. 5 is an outlier for t1
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-34 (cont'd): Calculation of import-based MRL proposals for apples according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
11	Apple	14	0.16	RV060-11HA-B / RARVY013	2	SL 200	USA	F
12	Apple	14	0.22	RV061-11HA-B / RARVY013	2	SL 200	USA	F
13	Apple	21	0.19**	RV062-11DA-B / RARVY013	2	SL 200	USA	F
14	Apple	14	0.20	RV063-11HA-B / RARVY013	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
value no. 5 is an outlier for t1
** sample value from later interval than the nominal PHI

Results (Apple dilute)

Total number of data (n)	14	Standard deviation (SD)	0.127
Lowest residue	0.12	Percentage of censored data	0
Highest residue	0.63	Number of non-censored data	14
Median residue	0.180	Correction factor for censoring (CF)	1.000
Mean	0.220		

Proposed MRL estimate

Highest residue	0.63
Mean + 4 SD	0.730
CF × 3 mean	0.660
Unrounded MRL	0.730
Rounded MRL	0.8

Table 6.7.2.2-35: Calculation of import-based MRL proposals for apples according to the OECD calculator – based on GJR data (cf. 6.3.2)

Residue :	total residue of BYI 02960	Crop group :	Pomaceous fruit
Portion analysed :	fruit	Commodity :	**Apple** conc. spray
Target value :	MRL	PHI :	14 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Apple	14	0.31	RV050-11HA-A / RARVY013	2	SL 200	USA	F
2	Apple	21	0.19**	RV051-11DA-A / RARVY013	2	SL 200	USA	F
3	Apple	14	0.11	RV052-11HA-A / RARVY013	2	SL 200	USA	F
4	Apple	14	0.08	RV053-11HA-A / RARVY013	2	SL 200	USA	F
5	Apple	35	0.52**	RV054-11DA-A / RARVY013	2	SL 200	USA	F
6	Apple	14	0.14	RV055-11HA-A / RARVY013	2	SL 200	USA	F
7	Apple	14	0.13	RV056-11HA-A / RARVY013	2	SL 200	USA	F
8	Apple	12	0.25	RV057-11HA-A / RARVY013	2	SL 200	USA	F
9	Apple	13	0.12	RV058-11HA-A / RARVY013	2	SL 200	USA	F
10	Apple	12	0.23	RV059-11DA-A / RARVY013	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-35 (cont'd): Calculation of import-based MRL proposals for apples according to the OECD calculator – based on GJR data (cf. 6.3.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
11	Apple	14	0.12	RV060-11HA-A / RARVY013	2	SL 200	USA	F
12	Apple	14	0.29	RV061-11HA-A / RARVY013	2	SL 200	USA	F
13	Apple	28	0.26**	RV062-11DA-A / RARVY013	2	SL 200	USA	F
14	Apple	14	0.16	RV063-11HA-A / RARVY013	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

Results (Apple conc.)

Total number of data (n)	14	Standard deviation (SD)	0.116
Lowest residue	0.08	Percentage of censored data	0
Highest residue	0.52	Number of non-censored data	14
Median residue	0.175	Correction factor for censoring (CF)	1.000
Mean	0.208		

Proposed MRL estimate

Highest residue	0.52
Mean + 4 SD	0.671
CF x 3 mean	0.624
Unrounded MRL	0.671
Rounded MRL	0.7

Table 6.7.2.2-36: Calculation of import-based MRL proposals for pear according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Calculation of MRL proposals according to OECD Calculator

Residue :	total residue of BYI 02960	Crop group :	Pomaceous fruit
Portion analysed :	fruit	Commodity :	**Pear** conc. spray
Target value :	MRL	PHI :	14 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1] / Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Pear	14	0.38	RV064-11DA-A / RARVY013	2	SL 200	USA	F
2	Pear	14	0.45	RV065-11HA-A / RARVY013	2	SL 200	USA	F
3	Pear	13	0.12	RV066-11HA-A / RARVY013	2	SL 200	USA	F
4	Pear	14	0.23	RV067-11DA-A / RARVY013	2	SL 200	USA	F
5	Pear	14	0.43	RV068-11HA-A / RARVY013	2	SL 200	USA	F
6	Pear	35	0.33**	RV069-11DA-A / RARVY013	2	SL 200	USA	F
7	Pear	14	0.59	RV070-11HA-A / RARVY013	2	SL 200	USA	F
8	Pear	14	0.64	RV071-11DA-A / RARVY013	2	SL 200	USA	F
9	Pear	14	0.70	RV072-11HA-A / RARVY013	2	SL 200	Canada	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-36 (cont'd): Calculation of import-based MRL proposals for pome fruit according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Results (Pear conc.)

Total number of data (n)	9	Standard deviation (SD)	0.191
Lowest residue	0.12	Percentage of censored data	0
Highest residue	0.7	Number of non-censored data	9
Median residue	0.430	Correction factor for censoring (CF)	1.000
Mean	0.430		

Proposed MRL estimate

Highest residue	0.7
Mean + 4 SD	1.194
CF × 3 mean	1.290
Unrounded MRL	1.290
Rounded MRL	1.5

Table 6.7.2.2-37: Calculation of import-based MRL proposals for pear according to the OECD calculator – based on GJR data (cf. 6.3.2)

Residue :	total residue of BYI 02960	Crop group :	Pomaceous fruit
Portion analysed :	fruit	Commodity :	**Pear** diluted
Target value :	MRL	PHI :	14 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Pear	14	0.50	RV064-11DA-B / RARVY013	2	SL 200	USA	F
2	Pear	14	0.30	RV065-11HA-B / RARVY013	2	SL 200	USA	F
3	Pear	13	0.30	RV066-11HA-B / RARVY013	2	SL 200	USA	F
4	Pear	14	0.24	RV067-11DA-B / RARVY013	2	SL 200	USA	F
5	Pear	14	0.44	RV068-11HA-B / RARVY013	2	SL 200	USA	F
6	Pear	14	0.22	RV069-11DA-B / RARVY013	2	SL 200	USA	F
7	Pear	14	0.36	RV070-11HA-B / RARVY013	2	SL 200	USA	F
8	Pear	21	0.34**	RV071-11DA-B / RARVY013	2	SL 200	USA	F
9	Pear	14	0.32	RV072-11HA-B / RARVY013	2	SL 200	Canada	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-37 (cont'd): Calculation of import-based MRL proposals for pear according to the OECD calculator – based on GJR data (cf. 6.3.2)

Results (Pear diluted)

Total number of data (n)	9	Standard deviation (SD)	0.089
Lowest residue	0.22	Percentage of censored data	0
Highest residue	0.5	Number of non-censored data	9
Median residue	0.320	Correction factor for censoring (CF)	1.000
Mean	0.336		

Proposed MRL estimate

Highest residue	0.5
Mean + 4 SD	0.693
CF × 3 mean	1.007
Unrounded MRL	1.007
Rounded MRL	1

Table 6.7.2.2-38: Calculation of import-based MRL proposals for grapes according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Berries and small fruit
Portion analysed :	bunch of grapes	Commodity :	**Grape** foliar trtmt.
Target value :	MRL	PHI :	0 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Grape	0	0.51	RV092-10DA-A / RARVY007	2	SL 200	USA	F
2	Grape	0	0.44	RV093-10HA-A / RARVY007	2	SL 200	USA	F
3	Grape	0	0.48	RV094-10HA-A / RARVY007	2	SL 200	Canada	F
4	Grape	0	0.38	RV095-10DA-A / RARVY007	2	SL 200	Canada	F
5	Grape	0	0.58	RV096-10HA-A / RARVY007	2	SL 200	Canada	F
6	Grape	0	0.37	RV097-10HA-A / RARVY007	2	SL 200	Canada	F
7	Grape	0	2.0	RV098-10DA-A / RARVY007	2	SL 200	USA	F
8	Grape	21	0.63**	RV099-10DA-A / RARVY007	2	SL 200	USA	F
9	Grape	0	0.55	RV100-10HA-A / RARVY007	2	SL 200	USA	F
10	Grape	0	0.84	RV101-10HA-A / RARVY007	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-38 (cont'd): Calculation of import-based MRL proposals for grapes according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
11	Grape	0	0.37	RV102-10HA-A / RARVY007	2	SL 200	USA	F
12	Grape	3	0.49**	RV103-10HA-A / RARVY007	2	SL 200	USA	F
13	Grape	3	0.75**	RV104-10HA-A / RARVY007	2	SL 200	USA	F
14	Grape	7	1.2**	RV105-10HA-A / RARVY007	2	SL 200	USA	F
15	Grape	0	1.2	RV106-10HA-A / RARVY007	2	SL 200	USA	F
16	Grape	3	0.64**	RV107-10HA-A / RARVY007	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

Results (Grape)

Total number of data (n)	16	Standard deviation (SD)	0.430
Lowest residue	0.37	Percentage of censored data	0
Highest residue	2	Number of non-censored data	16
Median residue	0.565	Correction factor for censoring (CF)	1.000
Mean	0.714		

Proposed MRL estimate

Highest residue	2
Mean + 4 SD	2.433
CF × 3 mean	2.143
Unrounded MRL	2.433
Rounded MRL	3

Table 6.7.2.2-39: Calculation of import-based MRL proposals for blueberries according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Berries and small fruit
Portion analysed :	fruit	Commodity :	**Blueberry** IR-4
Target value :	MRL	PHI :	3 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Blueberry	3	2.39	10637.11-AU01 / IR-4 PR NO.10637	2	SL 200	Australia	F
2	Blueberry	3	1.007	10637.11-AU02 / IR-4 PR NO.10637	2	SL 200	Australia	F
3	Blueberry	3	0.327	10637.11-AU04 / IR-4 PR NO.10637	2	SL 200	Australia	F
4	Blueberry	3	0.960	10637.11-NZ02 / IR-4 PR NO.10637	2	SL 200	New Zealand	F
5	Blueberry	7	1.60**	10637.11-CL01 / IR-4 PR NO.10637	2	SL 200	Chile	F
6	Blueberry	3	1.31	10637.11-CL02 / IR-4 PR NO.10637	2	SL 200	Chile	F
7	Blueberry	3	1.79	10637.11-CL03 / IR-4 PR NO.10637	2	SL 200	Chile	F
8	Blueberry	3	0.407	10637.11-NS01 / IR-4 PR NO.10637	2	SL 200	Canada	F
9	Blueberry	3	0.891	10637.11-NS02 / IR-4 PR NO.10637	2	SL 200	Canada	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-39 (cont'd): Calculation of import-based MRL proposals for blueberries according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
10	Blueberry	3	1.64	10637.11-NS03 / IR-4 PR NO.10637	2	SL 200	Canada	F
11	Blueberry	3	0.506	10637.11-QC16 / IR-4 PR NO.10637	2	SL 200	Canada	F
12	Blueberry	3	1.04	10637.11-DK01 / IR-4 PR NO.10637	2	SL 200	Denmark	F
13	Blueberry	3	0.621	10637.11-UK01 / IR-4 PR NO.10637	2	SL 200	United Kingdom	F
14	Blueberry	3	0.731	10637.11-UK02 / IR-4 PR NO.10637	2	SL 200	United Kingdom	F
15	Blueberry	14	1.80**	10637.11-IT01 / IR-4 PR NO.10637	2	SL 200	Italy	F
16	Blueberry	3	0.193	10637.11-NZ01 / IR-4 PR NO.10637	2	SL 200	New Zealand	F
17	Blueberry	7	0.280**	10637.11-SP01 / IR-4 PR NO.10637	2	SL 200	Spain	F
18	Blueberry	2	2.60	10637.11-ME01 / IR-4 PR NO.10637	2	SL 200	USA	F
19	Blueberry	3	0.454	10637.11-MI01 / IR-4 PR NO.10637	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-39 (cont'd): Calculation of import-based MRL proposals for blueberries according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
20	Blueberry	3	0.479	10637.11-MI02 / IR-4 PR NO.10637	2	SL 200	USA	F
21	Blueberry	3	0.290	10637.11-MI03 / IR-4 PR NO.10637	2	SL 200	USA	F
22	Blueberry	3	0.843	10637.11-NC01 / IR-4 PR NO.10637	2	SL 200	USA	F
23	Blueberry	3	0.834	10637.11-NC02 / IR-4 PR NO.10637	2	SL 200	USA	F
24	Blueberry	3	1.079	10637.11-NJ01 / IR-4 PR NO.10637	2	SL 200	USA	F
25	Blueberry	3	1.21	10637.11-NJ02 / IR-4 PR NO.10637	2	SL 200	USA	F
26	Blueberry	3	0.626	10637.11-OR01 / IR-4 PR NO.10637	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-39 (cont'd): Calculation of import-based MRL proposals for blueberries according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Results (Blueberry IR-4)

Total number of data (n)	26	Standard deviation (SD)	0.645
Lowest residue	0.193	Percentage of censored data	0
Highest residue	2.6	Number of non-censored data	26
Median residue	0.867	Correction factor for censoring (CF)	1.000
Mean	0.996		

Proposed MRL estimate

Highest residue	2.6
Mean + 4 SD	3.575
CF × 3 mean	2.989
Unrounded MRL	3.575
Rounded MRL	4

Table 6.7.2.2-40: Calculation of import-based MRL proposals for tomato according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Fruit vegetables
Portion analysed :	fruit	Commodity :	**Tomato** soil trtmt.
Target value :	MRL	PHI :	45 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Tomato	45	<0.070	RV098-11HA-B / RARVY022	1	SL 200	USA	F
2	Tomato	45	0.33	RV099-11HA-B / RARVY022	1	SL 200	USA	F
3	Tomato	44	0.20	RV100-11HA-B / RARVY022	1	SL 200	USA	F
4	Tomato	43	0.16	RV101-11HA-B / RARVY022	1	SL 200	USA	F
5	Tomato	45	0.09	RV102-11HA-B / RARVY022	1	SL 200	USA	F
6	Tomato	43	0.08	RV103-11HA-B / RARVY022	1	SL 200	Canada	F
7	Tomato	45	0.83	RV104-11HA-B / RARVY022	1	SL 200	Canada	F
8	Tomato	70	0.82**	RV105-11DA-B / RARVY022	1	SL 200	USA	F
9	Tomato	44	<0.070	RV106-11HA-B / RARVY022	1	SL 200	USA	F
10	Tomato	45	0.08	RV107-11HA-B / RARVY022	1	SL 200	USA	F

[1] as given in the Tier 1 summaries
value no. 19 is an outlier for t1
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-40 (cont'd): Calculation of import-based MRL proposals for tomato according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
11	Tomato	50	1.1**	RV108-11DA-B / RARVY022	1	SL 200	USA	F
12	Tomato	45	0.23	RV109-11DA-B / RARVY022	1	SL 200	Canada	F
13	Tomato	70	0.81**	RV110-11DA-B / RARVY022	1	SL 200	USA	F
14	Tomato	70	0.14**	RV111-11DA-B / RARVY022	1	SL 200	USA	F
15	Tomato	44	0.20	RV112-11HA-B / RARVY022	1	SL 200	USA	F
16	Tomato	44	0.16	RV113-11HA-B / RARVY022	1	SL 200	USA	F
17	Tomato	69	0.63**	RV114-11DA-B / RARVY022	1	SL 200	USA	F
18	Tomato	60	0.11**	RV115-11DA-B / RARVY022	1	SL 200	USA	F
19	Tomato	60	1.9**	RV116-11DA-B / RARVY022	1	SL 200	USA	F

[1] as given in the Tier 1 summaries
value no. 19 is an outlier for t
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-40 (cont'd): Calculation of import-based MRL proposals for tomato according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Results (Tomato soil)

Total number of data (n)	19	Standard deviation (SD)	0.484
Lowest residue	0.07	Percentage of censored data	11
Highest residue	1.9	Number of non-censored data	17
Median residue	0.200	Correction factor for censoring (CF)	0.930
Mean	0.422		

Proposed MRL estimate

Highest residue	1.9
Mean + 4 SD	2.357
CF × 3 mean	1.176
Unrounded MRL	2.357
Rounded MRL	3

Table 6.7.2.2-41: Calculation of import-based MRL proposals for tomato according to the OECD calculator – based on GJR data (cf. 6.3.2)

Residue :	total residue of BYI 02960	Crop group :	Fruit vegetables
Portion analysed :	fruit	Commodity :	**Tomato** foliar
Target value :	MRL	PHI :	1 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Tomato	1	0.20	RV098-11HA-A / RARVY022	2	SL 200	USA	F
2	Tomato	1	0.15	RV099-11HA-A / RARVY022	2	SL 200	USA	F
3	Tomato	1	0.29	RV100-11HA-A / RARVY022	2	SL 200	USA	F
4	Tomato	1	0.12	RV101-11HA-A / RARVY022	2	SL 200	USA	F
5	Tomato	1	0.20	RV102-11HA-A / RARVY022	2	SL 200	USA	F
6	Tomato	1	0.33	RV103-11HA-A / RARVY022	2	SL 200	Canada	F
7	Tomato	1	0.12	RV104-11HA-A / RARVY022	2	SL 200	Canada	F
8	Tomato	21	0.16**	RV105-11DA-A / RARVY022	2	SL 200	USA	F
9	Tomato	1	0.20	RV106-11HA-A / RARVY022	2	SL 200	USA	F
10	Tomato	1	0.12	RV107-11HA-A / RARVY022	2	SL 200	USA	F
11	Tomato	7	0.16**	RV108-11DA-A / RARVY022	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-41 (cont'd): Calculation of import-based MRL proposals for tomato according to the OECD calculator – based on GJR data (cf. 6.3.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
12	Tomato	7	0.21**	RV109-11DA-A / RARVY022	2	SL 200	Canada	F
13	Tomato	1	0.52	RV110-11DA-A / RARVY022	2	SL 200	USA	F
14	Tomato	21	0.41**	RV111-11DA-A / RARVY022	2	SL 200	USA	F
15	Tomato	1	0.63	RV112-11HA-A / RARVY022	2	SL 200	USA	F
16	Tomato	1	0.35	RV113-11HA-A / RARVY022	2	SL 200	USA	F
17	Tomato	28	0.43**	RV114-11DA-A / RARVY022	2	SL 200	USA	F
18	Tomato	21	0.29**	RV115-11DA-A / RARVY022	2	SL 200	USA	F
19	Tomato	7	0.90**	RV116-11DA-A / RARVY022	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-41 (cont'd): Calculation of import-based MRL proposals for tomato according to the OECD calculator – based on GJR data (cf. 6.3.2)

Results (Tomato foliar)

Total number of data (n)	19	Standard deviation (SD)	0.204
Lowest residue	0.12	Percentage of censored data	0
Highest residue	0.9	Number of non-censored data	19
Median residue	0.210	Correction factor for censoring (CF)	1.000
Mean	0.305		

Proposed MRL estimate

Highest residue	0.9
Mean + 4 SD	1.119
CF × 3 mean	0.914
Unrounded MRL	1.119
Rounded MRL	1.5

Table 6.7.2.2-42: Calculation of import-based MRL proposals for chili peppers according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Fruiting veg.
Portion analysed :	fruit	Commodity :	**Chili (non-bell) pepper** soil trtmt.
Target value :	MRL	PHI :	45 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Chili / non-bell pepper	70	0.91**	RV127-11DA-B / RARVY022	1	SL 200	USA	F
2	Chili / non-bell pepper	43	0.37	RV128-11HA-B / RARVY022	1	SL 200	USA	F
3	Chili / non-bell pepper	44	0.18	RV129-11HA-B / RARVY022	1	SL 200	USA	F
4	Chili / non-bell pepper	60	0.73**	RV130-11DA-B / RARVY022	1	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI.

Results (Chili [non-bell] pepper, soil)

Total number of data (n)	4	Standard deviation (SD)	0.332
Lowest residue	0.18	Percentage of censored data	0
Highest residue	0.91	Number of non-censored data	4
Median residue	0.550	Correction factor for censoring (CF)	1.000
Mean	0.548		

Proposed MRL estimate

Highest residue	0.91
Mean + 4 SD	1.877
CF × 3 mean	1.643
Unrounded MRL	1.877
Rounded MRL	2

Table 6.7.2.2-43: Calculation of import-based MRL proposals for chili peppers according to the OECD calculator – based on GJR data (cf. 6.3.2)

Residue :	total residue of BYI 02960	Crop group :	Fruiting veg.
Portion analysed :	fruit	Commodity :	**Chili (non-bell) pepper** foliar
Target value :	MRL	PHI :	1 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Chili / non-bell pepper	28	0.40**	RV127-11DA-A / RARVY022	2	SL 200	USA	F
2	Chili / non-bell pepper	1	0.43	RV128-11HA-A / RARVY022	2	SL 200	USA	F
3	Chili / non-bell pepper	1	0.13	RV129-11HA-A / RARVY022	2	SL 200	USA	F
4	Chili / non-bell pepper	21	0.72**	RV130-11DA-A / RARVY022	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI.

Results (Chili [non-bell] pepper foliar)

Total number of data (n)	4	Standard deviation (SD)	0.241
Lowest residue	0.13	Percentage of censored data	0
Highest residue	0.72	Number of non-censored data	4
Median residue	0.415	Correction factor for censoring (CF)	1.000
Mean	0.420		

Proposed MRL estimate

Highest residue	0.72
Mean + 4 SD	1.385
CF × 3 mean	1.260
Unrounded MRL	1.385
Rounded MRL	1.5

Table 6.7.2.2-44: Calculation of import-based MRL proposals for sweet corn/maize according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Fruit vegetables / cereals
Portion analysed :	ear without husk	Commodity :	**Corn, sweet** - foliar
Target value :	MRL	PHI :	7 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Corn, sweet	6	0.26	RV041-10HA-A / RARVY002	2	SL 200	USA	F
2	Corn, sweet	14	0.21**	RV042-10DA-A / RARVY002	2	SL 200	USA	F
3	Corn, sweet	7	0.14	RV043-10HA-A / RARVY002	2	SL 200	USA	F
4	Corn, sweet	7	0.13	RV044-10HA-A / RARVY002	2	SL 200	USA	F
5	Corn, sweet	7	0.14	RV045-10HA-A / RARVY002	2	SL 200	USA	F
6	Corn, sweet	7	0.19	RV046-10HA-A / RARVY002	2	SL 200	USA	F
7	Corn, sweet	7	0.11	RV047-10HA-A / RARVY002	2	SL 200	Canada	F
8	Corn, sweet	7	0.16	RV048-10HA-A / RARVY002	2	SL 200	USA	F
9	Corn, sweet	14	0.26**	RV049-10DA-A / RARVY002	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-44 (cont'd): Calculation of import-based MRL proposals for sweet corn according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
10	Corn, sweet	7	<0.070	RV050-10HA-A / RARVY002	2	SL 200	Canada	F
11	Corn, sweet	5	<0.070	RV051-10HA-A / RARVY002	2	SL 200	USA	F
12	Corn, sweet	7	<0.070	RV052-10HA-A / RARVY002	2	SL 200	USA	F
13	Corn, sweet	7	0.078	RV053-10HA-A / RARVY002	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

Results (Corn, sweet - foliar)

Total number of data (n)	13	Standard deviation (SD)	0.068
Lowest residue	0.07	Percentage of censored data	23
Highest residue	0.26	Number of non-censored data	10
Median residue	0.140	Correction factor for censoring (CF)	0.846
Mean	0.145		

Proposed MRL estimate

Highest residue	0.26
Mean + 4 SD	0.418
CF x 3 mean	0.369
Unrounded MRL	0.418
Rounded MRL	0.5

Table 6.7.2.2-45: Calculation of import-based MRL proposals for sweet corn/maize according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Fruit vegetables / cereals
Portion analysed :	ear without husk	Commodity :	**Corn/maize, sweet** – seed trtmt
Target value :	MRL	PHI :	-

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Corn, sweet	76	0.08	RV045-10HA-C / RARVY002	1	FS 480	BYI 02960 FS 480	USA	F
2	Corn, sweet	73	0.13	RV048-10HA-C / RARVY002	1	FS 480	BYI 02960 FS 480	USA	F
3	Corn, sweet	72	0.13	RV041-10HA-C / RARVY002	1	FS 480	BYI 02960 FS 480	USA	F

[1] as given in the Tier 1 summaries
value no. 1 is an outlier for t

Results (Corn, sweet – seed trtmt)

Total number of data (n)	3	Standard deviation (SD)	0.029
Lowest residue	0.08	Percentage of censored data	0
Highest residue	0.13	Number of non-censored data	3
Median residue	0.130	Correction factor for censoring (CF)	1.000
Mean	0.113		

Proposed MRL estimate

Highest residue	0.13
Mean + 4 SD	0.229
CF × 3 mean	0.340
Unrounded MRL	0.340
Rounded MRL	0.4

Table 6.7.2.2-46: Calculation of import-based MRL proposals for celery according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Leaf and stem vegetables
Portion analysed :	stalk	Commodity :	**Celery**
Target value :	MRL	PHI :	1 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Celery	1	0.61	RV027-11DA / RARVY005	2	SL 200	BYI 02960 SL 200	USA	F
2	Celery	1	0.28	RV028-11DA / RARVY005	2	SL 200	BYI 02960 SL 200	USA	F
3	Celery	1	2.4	RV029-11DA / RARVY005	2	SL 200	BYI 02960 SL 200	USA	F
4	Celery	1	3.2	RV030-11DB / RARVY005	2	SL 200	BYI 02960 SL 200	USA	F
5	Celery	1	2.2	RV031-11HA / RARVY005	2	SL 200	BYI 02960 SL 200	USA	F
6	Celery	1	2.0	RV032-11HA / RARVY005	2	SL 200	BYI 02960 SL 200	Canada	F
7	Celery	1	1.1	RV033-11HA / RARVY005	2	SL 200	BYI 02960 SL 200	USA	F
8	Celery	1	3.6	RV034-11HA / RARVY005	2	SL 200	BYI 02960 SL 200	Canada	F

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Table 6.7.2.2-46 (cont'd): Calculation of import-based MRL proposals for celery according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
9	Celery	1	6.1	RV035-11HA / RARVY005	2	SL 200	BYI 02960 SL 200	USA	F
10	Celery	1	2.2	RV036-11HA / RARVY005	2	SL 200	BYI 02960 SL 200	USA	F

[1] as given in the Tier 1 summaries

Results (Celery)

Total number of data (n)	10	Standard deviation (SD)	1.680
Lowest residue	0.28	Percentage of censored data	0
Highest residue	6.1	Number of non-censored data	10
Median residue	2.200	Correction factor for censoring (CF)	1.000
Mean	2.369		

Proposed MRL estimate

Highest residue	6.1
Mean + 4 SD	9.087
CF × 3 mean	7.107
Unrounded MRL	9.087
Rounded MRL	9

Table 6.7.2.2-47: Calculation of import-based MRL proposals for dry beans according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Pulses
Portion analysed :	seed, dry	Commodity :	**Bean, dry**
Target value :	MRL	PHI :	7 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1] Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Bean	7	<0.070	RV190-11HA-B RARVY028	2	SL 200	USA	F
2	Bean	6	0.525	RV191-11HA-B RARVY028	2	SL 200	USA	F
3	Bean	6	0.081	RV192-11HA-B RARVY028	2	SL 200	USA	F
4	Bean	7	0.136	RV193-11HA-B RARVY028	2	SL 200	Canada	F
5	Bean	7	0.074	RV195-11HA-B RARVY028	2	SL 200	USA	F
6	Bean	28	0.304**	RV196-11DA-B RARVY028	2	SL 200	USA	F
7	Bean	7	0.165	RV197-11DA-B RARVY028	2	SL 200	USA	F
8	Bean	7	0.219	RV198-11DA-B RARVY028	2	SL 200	USA	F
9	Bean	35	0.417**	RV199-11DA-B RARVY028	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-47 (cont'd): Calculation of import-based MRL proposals for dry beans according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Results (Bean, dry)

Total number of data (n)	9	Standard deviation (SD)	0.163
Lowest residue	0.07	Percentage of censored data	11
Highest residue	0.525	Number of non-censored data	8
Median residue	0.165	Correction factor for censoring (CF)	0.926
Mean	0.221		

Proposed MRL estimate

Highest residue	0.525
Mean + 4 SD	0.873
CF × 3 mean	0.615
Unrounded MRL	0.873
Rounded MRL	0.9

Table 6.7.2.2-48: Calculation of import-based MRL proposals for dry peas according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Pulses
Portion analysed :	seed, dry	Commodity :	**Pea, dry**
Target value :	MRL	PHI :	7 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Pea	7	0.960	RV180-11HA-B / RARVY028	2	SL 200	Canada	F
2	Pea	7	0.629	RV181-11HA-B / RARVY028	2	SL 200	USA	F
3	Pea	7	0.077	RV182-11HA-B / RARVY028	2	SL 200	USA	F
4	Pea	7	1.74	RV183-11HA-B / RARVY028	2	SL 200	USA	F
5	Pea	7	0.257	RV184-11HA-B / RARVY028	2	SL 200	Canada	F
6	Pea	7	0.598	RV185-11HA-B / RARVY028	2	SL 200	Canada	F
7	Pea	14	5.31**	RV186-11DA-B / RARVY028	2	SL 200	USA	F
8	Pea	21	1.56**	RV187-11DA-B / RARVY028	2	SL 200	USA	F
9	Pea	12	0.512**	RV188-11DA-B / RARVY028	2	SL 200	Canada	F
10	Pea	33	1.27**	RV189-11DA-B / RARVY028	2	SL 200	Canada	F

[1] as given in the Tier 1 summaries
value no. 7 is an outlier for t1
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-48 (cont'd): Calculation of import-based MRL proposals for dry peas according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Results (Pea, dry)

Total number of data (n)	10	Standard deviation (SD)	1.513
Lowest residue	0.077	Percentage of censored data	0
Highest residue	5.31	Number of non-censored data	10
Median residue	0.795	Correction factor for censoring (CF)	1.000
Mean	1.291		

Proposed MRL estimate

Highest residue	5.31
Mean + 4 SD	7.344
CF × 3 mean	3.874
Unrounded MRL	7.344
Rounded MRL	8

Table 6.7.2.2-49: Calculation of import-based MRL proposals for peanuts according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Peanut
Portion analysed :	seed (nutmeat)	Commodity :	**Peanut**
Target value :	MRL	PHI :	7 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Peanut	6	0.087	RV120-10HA / RARVY010	2	SL 200	USA	F
2	Peanut	7	<0.070	RV121-10HA / RARVY010	2	SL 200	USA	F
3	Peanut	7	<0.070	RV122-10HA / RARVY010	2	SL 200	USA	F
4	Peanut	7	<0.070	RV123-10HA / RARVY010	2	SL 200	USA	F
5	Peanut	7	<0.070	RV124-10HA / RARVY010	2	SL 200	USA	F
6	Peanut	8	<0.070	RV125-10HA / RARVY010	2	SL 200	USA	F
7	Peanut	3	<0.070	RV126-10HA / RARVY010	2	SL 200	USA	F
8	Peanut	6	<0.070	RV127-10HA / RARVY010	2	SL 200	USA	F
9	Peanut	14	0.092**	RV128-10DA / RARVY010	2	SL 200	USA	F
10	Peanut	21	0.075**	RV129-10DA / RARVY010	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-49 (cont'd): Calculation of import-based MRL proposals for peanuts according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
11	Peanut	21	0.077**	RV130-10DA / RARVY010	2	SL 200	USA	F
12	Peanut	7	<0.070	RV131-10DA / RARVY010	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

Results (Peanut)

Total number of data (n)	12	Standard deviation (SD)	0.008
Lowest residue	0.07	Percentage of censored data	67
Highest residue	0.092	Number of non-censored data	4
Median residue	0.070	Correction factor for censoring (CF)	0.556
Mean	0.074		

Proposed MRL estimate

Highest residue	0.092
Mean + 4 SD	0.105
CF × 3 mean	0.124
Unrounded MRL	0.124
Rounded MRL	0.15

Table 6.7.2.2-50: Calculation of import-based MRL proposals for potatoes according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Potato (root & tuber)
Portion analysed :	tuber	Commodity :	**Potato**
Target value :	MRL	PHI :	7 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Potato	21	0.072**	RV178-10DA / RARVY015	2	SL 200	USA	F
2	Potato	6	<0.070	RV179-10HA / RARVY015	2	SL 200	USA	F
3	Potato	8	0.11	RV180-10HA / RARVY015	2	SL 200	USA	F
4	Potato	7	<0.070	RV181-10HA / RARVY015	2	SL 200	USA	F
5	Potato	7	<0.070	RV182-10HA / RARVY015	2	SL 200	USA	F
6	Potato	7	<0.070	RV183-10HA / RARVY015	2	SL 200	USA	F
7	Potato	7	0.10	RV184-10HA / RARVY015	2	SL 200	USA	F
8	Potato	7	0.081	RV185-10HA / RARVY015	2	SL 200	USA	F
9	Potato	7	<0.070	RV186-10HA / RARVY015	2	SL 200	USA	F
10	Potato	7	<0.070	RV187-10HA / RARVY015	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-50 (cont'd): Calculation of import-based MRL proposals for potatoes according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
11	Potato	7	<0.070	RV188-10HA / RARVY015	2	SL 200	USA	F
12	Potato	7	<0.070	RV189-10HA / RARVY015	2	SL 200	Canada	F
13	Potato	7	<0.070	RV190-10HA / RARVY015	2	SL 200	Canada	F
14	Potato	7	<0.070	RV191-10HA / RARVY015	2	SL 200	USA	F
15	Potato	7	0.094	RV192-10HA / RARVY015	2	SL 200	USA	F
16	Potato	7	<0.070	RV193-10HA / RARVY015	2	SL 200	USA	F
17	Potato	6	<0.070	RV194-10HA / RARVY015	2	SL 200	USA	F
18	Potato	7	<0.070	RV195-10HA / RARVY015	2	SL 200	USA	F
19	Potato	7	<0.070	RV196-10HA / RARVY015	2	SL 200	USA	F
20	Potato	7	0.12	RV197-10HA / RARVY015	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-50 (cont'd): Calculation of import-based MRL proposals for potatoes according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. 1/ / Study No.	No. of applic.	FL-Type	Country	Area of applic.
21	Potato	7	0.11	RV198-10HA / RARVY015	2	SL 200	Canada	F
22	Potato	7	<0.070	RV199-10HA / RARVY015	2	SL 200	Canada	F
23	Potato	7	0.074	RV200-10HA / RARVY015	2	SL 200	USA	F
24	Potato	7	0.079	RV201-10DA / RARVY015	2	SL 200	USA	F
25	Potato	21	0.098**	RV202-10DA / RARVY015	2	SL 200	USA	F
26	Potato	6	<0.070	RV203-10DA / RARVY015	2	SL 200	Canada	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

Results (Potato)

Total number of data (n)	26	Standard deviation (SD)	0.015
Lowest residue	0.07	Percentage of censored data	62
Highest residue	0.12	Number of non-censored data	10
Median residue	0.070	Correction factor for censoring (CF)	0.590
Mean	0.079		

Proposed MRL estimate

Highest residue	0.12
Mean + 4 SD	0.141
CF × 3 mean	0.140
Unrounded MRL	0.141
Rounded MRL	0.15

Table 6.7.2.2-51: Calculation of import-based MRL proposals for hops according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Stimulant plants
Portion analysed :	cone, kiln-dried	Commodity :	**Hops** conc.
Target value :	MRL	PHI :	21 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Hop	21	3.32	RV047-11HA-A / RARVY008	1	SL 200	BYI 02960 SL 200	USA	F
2	Hop	21	7.98	RV048-11HA-A / RARVY008	1	SL 200	BYI 02960 SL 200	USA	F
3	Hop	21	3.07	RV049-11HA-A / RARVY008	1	SL 200	BYI 02960 SL 200	USA	F

[1] as given in the Tier 1 summaries

Results (Hops conc.)

Total number of data (n)	3	Standard deviation (SD)	2.765
Lowest residue	3.07	Percentage of censored data	0
Highest residue	7.98	Number of non-censored data	3
Median residue	3.320	Correction factor for censoring (CF)	1.000
Mean	4.790		

Proposed MRL estimate

Highest residue	7.98
Mean + 4 SD	15.852
CF × 3 mean	14.370
Unrounded MRL	15.852
Rounded MRL	20

Table 6.7.2.2-52: Calculation of import-based MRL proposals for hops according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Stimulant plants
Portion analysed :	cone, kiln-dried	Commodity :	**Hops** diluted
Target value :	MRL	PHI :	21 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Hop	21	3.14	RV047-11HA-B / RARVY008	1	SL 200	BYI 02960 SL 200	USA	F
2	Hop	21	7.76	RV048-11HA-B / RARVY008	1	SL 200	BYI 02960 SL 200	USA	F
3	Hop	21	3.35	RV049-11HA-B / RARVY008	1	SL 200	BYI 02960 SL 200	USA	F

[1] as given in the Tier 1 summaries

Results (Hops diluted)

Total number of data (n)	3	Standard deviation (SD)	2.609
Lowest residue	3.14	Percentage of censored data	0
Highest residue	7.76	Number of non-censored data	3
Median residue	3.350	Correction factor for censoring (CF)	1.000
Mean	4.750		

Proposed MRL estimate

Highest residue	7.76
Mean + 4 SD	15.185
CF x 3 mean	14.250
Unrounded MRL	15.185
Rounded MRL	15

Table 6.7.2.2-53: Calculation of import-based MRL proposals for coffee according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Stimulant plants
Portion analysed :	bean, green	Commodity :	**Coffee** ("US" study)
Target value :	MRL	PHI :	0 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Coffee	0	0.273	RV232-11DA / RARVP074	4	SL 200	Guatemala	F
2	Coffee	21	0.206**	RV233-11DA / RARVP074	4	SL 200	Guatemala	F
3	Coffee	7	0.879**	RV234-11DA / RARVP074	4	SL 200	Mexico	F
4	Coffee	36	0.939**	RV246-11DA / RARVP074	4	SL 200	Mexico	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

Results (Coffee, "US" study)

Total number of data (n)	4	Standard deviation (SD)	0.388
Lowest residue	0.206	Percentage of censored data	0
Highest residue	0.939	Number of non-censored data	4
Median residue	0.576	Correction factor for censoring (CF)	1.000
Mean	0.574		

Proposed MRL estimate

Highest residue	0.939
Mean + 4 SD	2.127
CF × 3 mean	1.723
Unrounded MRL	2.127
Rounded MRL	3

Table 6.7.2.2-54: Calculation of import-based MRL proposals for coffee according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Stimulant plants
Portion analysed :	bean	Commodity :	**Coffee** (Brazilian study)
Target value :	MRL	PHI :	0 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Coffee	0	0.10	I11-008-01 / I11-008	4	SL 200	Brazil	F
2	Coffee	28	0.19**	I11-008-02 / I11-008	4	SL 200	Brazil	F
3	Coffee	21	0.11**	I11-008-04 / I11-008	4	SL 200	Brazil	F
4	Coffee	0	0.08	I11-008-05 / I11-008	4	SL 200	Brazil	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

Results (Coffee, Brazilian study)

Total number of data (n)	4	Standard deviation (SD)	0.048
Lowest residue	0.08	Percentage of censored data	0
Highest residue	0.19	Number of non-censored data	4
Median residue	0.105	Correction factor for censoring (CF)	1.000
Mean	0.120		

Proposed MRL estimate

Highest residue	0.19
Mean + 4 SD	0.313
CF × 3 mean	0.360
Unrounded MRL	0.360
Rounded MRL	0.4

Table 6.7.2.2-55: Calculation of import-based MRL proposals for barley according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Cereals
Portion analysed :	grain	Commodity :	**Barley**, foliar spray
Target value :	MRL	PHI :	21 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Barley	16	1.33	RV001-10HA-B / RARVY001	2	SL 200	USA	F
2	Barley	19	1.25	RV002-10HA-B / RARVY001	2	SL 200	USA	F
3	Barley	20	1.30	RV003-10DA-B / RARVY001	2	SL 200	USA	F
4	Barley	21	2.38	RV004-10HA-B / RARVY001	2	SL 200	Canada	F
5	Barley	22	0.725	RV005-10HA-B / RARVY001	2	SL 200	USA	F
6	Barley	29	0.926**	RV006-10DA-B / RARVY001	2	SL 200	USA	F
7	Barley	21	0.761	RV007-10HA-B / RARVY001	2	SL 200	USA	F
8	Barley	19	0.816	RV008-10HA-B / RARVY001	2	SL 200	USA	F
9	Barley	20	0.926	RV009-10HA-B / RARVY001	2	SL 200	USA	F
10	Barley	21	1.81	RV010-10HA-B / RARVY001	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
value no. 4 is an outlier for t1
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-55 (cont'd): Calculation of import-based MRL proposals for barley according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
11	Barley	21	0.814	RV011-10HA-B / RARVY001	2	SL 200	USA	F
12	Barley	21	0.575	RV012-10HA-B / RARVY001	2	SL 200	USA	F
13	Barley	34	1.19**	RV013-10DA-B / RARVY001	2	SL 200	Canada	F
14	Barley	20	0.778	RV014-10DA-B / RARVY001	2	SL 200	Canada	F
15	Barley	21	0.577	RV015-10HA-B / RARVY001	2	SL 200	Canada	F
16	Barley	21	0.943	RV016-10HA-B / RARVY001	2	SL 200	Canada	F
17	Barley	21	1.24	RV017-10HA-B / RARVY001	2	SL 200	Canada	F
18	Barley	21	0.703	RV018-10HA-B / RARVY001	2	SL 200	Canada	F
19	Barley	19	1.10	RV019-10HA-B / RARVY001	2	SL 200	Canada	F
20	Barley	20	0.516	RV020-10HA-B / RARVY001	2	SL 200	Canada	F

[1] as given in the Tier 1 summaries
value no. 4 is an outlier for t1
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-55 (cont'd): Calculation of import-based MRL proposals for barley according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Results (Barley, foliar spray)

Total number of data (n)	20	Standard deviation (SD)	0.450
Lowest residue	0.516	Percentage of censored data	0
Highest residue	2.38	Number of non-censored data	20
Median residue	0.926	Correction factor for censoring (CF)	1.000
Mean	1.033		

Proposed MRL estimate

Highest residue	2.38
Mean + 4 SD	2.834
CF × 3 mean	3.099
Unrounded MRL	3.099
Rounded MRL	3

Table 6.7.2.2-56: Calculation of import-based MRL proposals for barley according to the OECD calculator – based on GJR data (cf. 6.3.2)

Residue :	total residue of BYI 02960	Crop group :	Cereals
Portion analysed :	grain	Commodity :	**Barley** seed trtmt
Target value :	MRL	PHI :	-

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Barley	101	0.247	RV012-10HA-C / RARVY001	1	FS 480	BYI 02960 FS 480	USA	F
2	Barley	110	0.711	RV005-10HA-C / RARVY001	1	FS 480	BYI 02960 FS 480	USA	F
3	Barley	92	0.518	RV002-10HA-C / RARVY001	1	FS 480	BYI 02960 FS 480	USA	F

[1] as given in the Tier 1 summaries

Results (Barley seed trtmt)

Total number of data (n)	3	Standard deviation (SD)	0.233
Lowest residue	0.247	Percentage of censored data	0
Highest residue	0.711	Number of non-censored data	3
Median residue	0.518	Correction factor for censoring (CF)	1.000
Mean	0.492		

Proposed MRL estimate

Highest residue	0.711
Mean + 4 SD	1.424
CF × 3 mean	1.476
Unrounded MRL	1.476
Rounded MRL	1.5

Table 6.7.2.2-57: Calculation of import-based MRL proposals for sorghum according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Cereals
Portion analysed :	grain	Commodity :	**Sorghum**, foliar spray
Target value :	MRL	PHI :	21 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Sorghum	21	1.4	RV083-10HA-B / RARVY004	2	SL 200	USA	F
2	Sorghum	21	0.91	RV084-10HA-B / RARVY004	2	SL 200	USA	F
3	Sorghum	21	0.65	RV085-10HA-B / RARVY004	2	SL 200	USA	F
4	Sorghum	26	1.6**	RV086-10DA-B / RARVY004	2	SL 200	USA	F
5	Sorghum	21	0.69	RV087-10HA-B / RARVY004	2	SL 200	USA	F
6	Sorghum	20	0.89	RV088-10HA-B / RARVY004	2	SL 200	USA	F
7	Sorghum	21	0.43	RV089-10HA-B / RARVY004	2	SL 200	USA	F
8	Sorghum	21	0.56	RV090-10HA-B / RARVY004	2	SL 200	USA	F
9	Sorghum	21	0.52	RV091-10HA-B / RARVY004	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-57 (cont'd): Calculation of import-based MRL proposals for sorghum according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Results (Sorghum, foliar spray)

Total number of data (n)	9	Standard deviation (SD)	0.404
Lowest residue	0.43	Percentage of censored data	0
Highest residue	1.6	Number of non-censored data	9
Median residue	0.690	Correction factor for censoring (CF)	1.000
Mean	0.850		

Proposed MRL estimate

Highest residue	1.6
Mean + 4 SD	2.466
CF × 3 mean	2.550
Unrounded MRL	2.550
Rounded MRL	3

Table 6.7.2.2-58: Calculation of import-based MRL proposals for wheat according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Cereals
Portion analysed :	grain	Commodity :	**Wheat**, foliar spray
Target value :	MRL	PHI :	21 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Wheat	20	0.75	RV054-10HA-B / RARVY003	2	SL 200	USA	F
2	Wheat	21	0.27	RV055-10HA-B / RARVY003	2	SL 200	USA	F
3	Wheat	21	0.38	RV056-10HA-B / RARVY003	2	SL 200	USA	F
4	Wheat	21	0.78	RV057-10HA-B / RARVY003	2	SL 200	USA	F
5	Wheat	21	0.88	RV058-10HA-B / RARVY003	2	SL 200	Canada	F
6	Wheat	21	1.1	RV059-10HA-B / RARVY003	2	SL 200	USA	F
7	Wheat	35	1.8**	RV060-10DA-B / RARVY003	2	SL 200	USA	F
8	Wheat	21	0.31	RV061-10HA-B / RARVY003	2	SL 200	USA	F
9	Wheat	22	1.5	RV062-10HA-B / RARVY003	2	SL 200	USA	F
10	Wheat	21	0.91	RV063-10HA-B / RARVY003	2	SL 200	USA	F
11	Wheat	20	0.66	RV064-10HA-B / RARVY003	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-58 (cont'd): Calculation of import-based MRL proposals for wheat according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
12	Wheat	21	0.69	RV065-10HA-B / RARVY003	2	SL 200	USA	F
13	Wheat	28	0.66**	RV066-10DA-B / RARVY003	2	SL 200	USA	F
14	Wheat	21	0.11	RV068-10HA-B / RARVY003	2	SL 200	USA	F
15	Wheat	21	0.60	RV069-10HA-B / RARVY003	2	SL 200	USA	F
16	Wheat	21	0.093	RV070-10HA-B / RARVY003	2	SL 200	USA	F
17	Wheat	21	0.102	RV071-10HA-B / RARVY003	2	SL 200	USA	F
18	Wheat	20	0.25	RV072-10HA-B / RARVY003	2	SL 200	USA	F
19	Wheat	35	0.76**	RV073-10DA-B / RARVY003	2	SL 200	USA	F
20	Wheat	20	0.57	RV074-10HA-B / RARVY003	2	SL 200	USA	F
21	Wheat	21	2.7	RV075-10HA-B / RARVY003	2	SL 200	Canada	F
22	Wheat	21	0.72	RV076-10HA-B / RARVY003	2	SL 200	Canada	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-58 (cont'd): Calculation of import-based MRL proposals for wheat according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
23	Wheat	21	0.30	RV077-10HA-B / RARVY003	2	SL 200	Canada	F
24	Wheat	21	0.22	RV078-10HA-B / RARVY003	2	SL 200	Canada	F
25	Wheat	21	2.6	RV079-10HA-B / RARVY003	2	SL 200	Canada	F
26	Wheat	20	1.3	RV080-10HA-B / RARVY003	2	SL 200	Canada	F
27	Wheat	21	0.79	RV081-10HA-B / RARVY003	2	SL 200	Canada	F
28	Wheat	21	0.82	RV082-10DA-B / RARVY003	2	SL 200	Canada	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

Results (Wheat, foliar spray)

Total number of data (n)	28	Standard deviation (SD)	0.664
Lowest residue	0.093	Percentage of censored data	0
Highest residue	2.7	Number of non-censored data	28
Median residue	0.705	Correction factor for censoring (CF)	1.000
Mean	0.808		

Proposed MRL estimate

Highest residue	2.7
Mean + 4 SD	3.464
CF × 3 mean	2.424
Unrounded MRL	3.464
Rounded MRL	4

Table 6.7.2.2-59: Calculation of import-based MRL proposals for wheat according to the OECD calculator – based on GJR data (cf. 6.3.2)

Residue :	total residue of BYI 02960	Crop group :	Cereals
Portion analysed :	grain	Commodity :	**Wheat** seed trtmt
Target value :	MRL	PHI :	-

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Wheat	205	0.089	RV070-10HA-C / RARVY003	1	FS 480	BYI 02960 FS 480	USA	F
2	Wheat	103	0.29	RV062-10HA-C / RARVY003	1	FS 480	BYI 02960 FS 480	USA	F
3	Wheat	252	0.61	RV056-10HA-C / RARVY003	1	FS 480	BYI 02960 FS 480	USA	F

[1] as given in the Tier 1 summaries

Results (Wheat seed trtmt)

Total number of data (n)	3	Standard deviation (SD)	0.263
Lowest residue	0.089	Percentage of censored data	0
Highest residue	0.61	Number of non-censored data	3
Median residue	0.290	Correction factor for censoring (CF)	1.000
Mean	0.330		

Proposed MRL estimate

Highest residue	0.61
Mean + 4 SD	1.381
CF × 3 mean	0.989
Unrounded MRL	1.381
Rounded MRL	1.5

Table 6.7.2.2-60: Calculation of import-based MRL proposals for corn/maize according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Cereals
Portion analysed :	kernel	Commodity :	**Maize/Corn** foliar
Target value :	MRL	PHI :	21 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Maize/Corn	20	0.14	RV021-10HA-B / RARVY002	2	SL 200	BYI 02960 SL 200	USA	F
2	Maize/Corn	21	<0.070	RV022-10HA-B / RARVY002	2	SL 200	BYI 02960 SL 200	USA	F
3	Maize/Corn	21	<0.070	RV023-10HA-B / RARVY002	2	SL 200	BYI 02960 SL 200	USA	F
4	Maize/Corn	21	<0.070	RV024-10HA-B / RARVY002	2	SL 200	BYI 02960 SL 200	USA	F
5	Maize/Corn	20	<0.070	RV025-10HA-B / RARVY002	2	SL 200	BYI 02960 SL 200	USA	F
6	Maize/Corn	22	<0.070	RV026-10HA-B / RARVY002	2	SL 200	BYI 02960 SL 200	Canada	F
7	Maize/Corn	21	<0.070	RV027-10HA-B / RARVY002	2	SL 200	BYI 02960 SL 200	USA	F
8	Maize/Corn	21	<0.070	RV028-10HA-B / RARVY002	2	SL 200	BYI 02960 SL 200	USA	F
9	Maize/Corn	22	<0.070	RV029-10HA-B / RARVY002	2	SL 200	BYI 02960 SL 200	Canada	F

[1] as given in the Tier 1 summaries
value no. 1 is an outlier for tl

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Table 6.7.2.2-60 (cont'd): Calculation of import-based MRL proposals for corn/maize according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
10	Maize/Corn	21	<0.070	RV030-10HA-B / RARVY002	2	SL 200	BYI 02960 SL 200	USA	F
11	Maize/Corn	21	<0.070	RV031-10HA-B / RARVY002	2	SL 200	BYI 02960 SL 200	USA	F
12	Maize/Corn	21	0.071	RV032-10HA-B / RARVY002	2	SL 200	BYI 02960 SL 200	Canada	F
13	Maize/Corn	21	<0.070	RV033-10HA-B / RARVY002	2	SL 200	BYI 02960 SL 200	USA	F
14	Maize/Corn	21	<0.070	RV034-10HA-B / RARVY002	2	SL 200	BYI 02960 SL 200	Canada	F
15	Maize/Corn	21	<0.070	RV035-10HA-B / RARVY002	2	SL 200	BYI 02960 SL 200	USA	F
16	Maize/Corn	22	<0.070	RV036-10DA-B / RARVY002	2	SL 200	BYI 02960 SL 200	USA	F
17	Maize/Corn	19	<0.070	RV037-10DA-B / RARVY002	2	SL 200	BYI 02960 SL 200	Canada	F
18	Maize/Corn	19	<0.070	RV038-10DA-B / RARVY002	2	SL 200	BYI 02960 SL 200	USA	F
19	Maize/Corn	21	<0.070	RV039-10DA-B / RARVY002	2	SL 200	BYI 02960 SL 200	USA	F
20	Maize/Corn	20	<0.070	RV040-10HA-B / RARVY002	2	SL 200	BYI 02960 SL 200	USA	F

[1] as given in the Tier 1 summaries
value no. 1 is an outlier for t1

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Table 6.7.2.2-60 (cont'd): Calculation of import-based MRL proposals for corn/maize according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Results (Corn/maize foliar)

Total number of data (n)	20	Standard deviation (SD)	0.016
Lowest residue	0.07	Percentage of censored data	90
Highest residue	0.14	Number of non-censored data	2
Median residue	0.070	Correction factor for censoring (CF)	0.400
Mean	0.074		

Proposed MRL estimate

Highest residue	0.14
Mean + 4 SD	0.136
CF × 3 mean	0.088
Unrounded MRL	0.140
Rounded MRL	0.15

Table 6.7.2.2-61: Calculation of import-based MRL proposals for corn/maize according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Cereals
Portion analysed :	kernel	Commodity :	**Maize/Corn** seed trtmt.
Target value :	MRL	PHI :	--

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Maize/Corn	133	0.13	RV023-10HA-C / RARVY002	1	FS 480	BYI 02960 FS 480	USA	F
2	Maize/Corn	119	0.09	RV024-10HA-C / RARVY002	1	FS 480	BYI 02960 FS 480	USA	F
3	Maize/Corn	131	0.19	RV027-10HA-C / RARVY002	1	FS 480	BYI 02960 FS 480	USA	F

[1] as given in the Tier 1 summaries

Results (Corn/maize seed trtmt.)

Total number of data (n)	3	Standard deviation (SD)	0.050
Lowest residue	0.09	Percentage of censored data	0
Highest residue	0.19	Number of non-censored data	3
Median residue	0.130	Correction factor for censoring (CF)	1.000
Mean	0.137		

Proposed MRL estimate

Highest residue	0.19
Mean + 4 SD	0.338
CF × 3 mean	0.410
Unrounded MRL	0.410
Rounded MRL	0.5

Table 6.7.2.2-62: Calculation of import-based MRL proposals for cotton according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Cotton
Portion analysed :	seed, undelinted	Commodity :	**Cotton** foliar
Target value :	MRL	PHI :	14 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Cotton	14	<0.070	RV108-10HA / RARVY009	2	SL 200	USA	F
2	Cotton	14	0.19	RV109-10HA / RARVY009	2	SL 200	USA	F
3	Cotton	14	0.14	RV110-10HA / RARVY009	2	SL 200	USA	F
4	Cotton	19	0.093	RV111-10HA / RARVY009	2	SL 200	USA	F
5	Cotton	13	0.46	RV112-10HA / RARVY009	2	SL 200	USA	F
6	Cotton	14	0.078	RV113-10HA-A / RARVY009	2	SL 200	USA	F
7	Cotton	13	0.122	RV114-10HA-A / RARVY009	2	SL 200	USA	F
8	Cotton	14	0.14	RV115-10HA-A / RARVY009	2	SL 200	USA	F
9	Cotton	14	0.24	RV116-10DA / RARVY009	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-62 (cont'd): Calculation of import-based MRL proposals for cotton according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
10	Cotton	21	0.18**	RV117-10DA / RARVY009	2	SL 200	USA	F
11	Cotton	19	0.55**	RV118-10DA / RARVY009	2	SL 200	USA	F
12	Cotton	13	0.27	RV119-10DA / RARVY009	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

Results (Cotton foliar)

Total number of data (n)	12	Standard deviation (SD)	0.151
Lowest residue	0.07	Percentage of censored data	8
Highest residue	0.55	Number of non-censored data	11
Median residue	0.160	Correction factor for censoring (CF)	0.944
Mean	0.211		

Proposed MRL estimate

Highest residue	0.55
Mean + 4 SD	0.817
CF × 3 mean	0.598
Unrounded MRL	0.817
Rounded MRL	0.9

Table 6.7.2.2-63: Calculation of import-based MRL proposals for cotton according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Oilseeds
Portion analysed :	seed, undelinted	Commodity :	**Cotton**
Target value :	MRL	PHI :	0 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Cotton	179	<0.070	RV113-10HA-B / RARVY009	1	FS 480	BYI 02960 FS 480	USA	F
2	Cotton	136	0.087	RV114-10HA-B / RARVY009	1	FS 480	BYI 02960 FS 480	USA	F
3	Cotton	158	0.36	RV115-10HA-B / RARVY009	1	FS 480	BYI 02960 FS 480	USA	F

[1] as given in the Tier 1 summaries

Results (Cotton)

Total number of data (n)	3	Standard deviation (SD)	0.163
Lowest residue	0.07	Percentage of censored data	33
Highest residue	0.36	Number of non-censored data	2
Median residue	0.087	Correction factor for censoring (CF)	0.778
Mean	0.172		

Proposed MRL estimate

Highest residue	0.36
Mean + 4 SD	0.823
CF × 3 mean	0.402
Unrounded MRL	0.823
Rounded MRL	0.9

Table 6.7.2.2-64: Calculation of import-based MRL proposals for prickly pear according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Miscellaneous fruit
Portion analysed :	fruit	Commodity :	**Prickly pear cactus**
Target value :	MRL	PHI :	21 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Prickly Pear fruit	21	0.18	RV050-11HA-A / RARVP078	2	SL 200	BYI 02960 SL 200	USA	F
2	Prickly Pear fruit	20	0.18	RV051-11DA-A / RARVP078	2	SL 200	BYI 02960 SL 200	USA	F
3	Prickly Pear fruit	20	0.16	RV052-11HA-A / RARVP078	2	SL 200	BYI 02960 SL 200	USA	F
4	Prickly Pear fruit	21	0.13	RV053-11HA-A / RARVP078	2	SL 200	BYI 02960 SL 200	USA	F
5 (1A)	Prickly Pear pad	21	0.27	10722.11-CA*160/ RARVP078	2	SL 200	BYI 02960 SL 200	USA	F
6 (2A)	Prickly Pear pad	20	0.27	10722.11-CA*161/ RARVP078	2	SL 200	BYI 02960 SL 200	USA	F
7 (3A)	Prickly Pear pad	20	0.29	10722.11-CA*162/ RARVP078	2	SL 200	BYI 02960 SL 200	USA	F
8 (4A)	Prickly Pear pad	21	0.33	10722.11-CA*163/ RARVP078	2	SL 200	BYI 02960 SL 200	USA	F

[1] as given in the Tier 1 summaries

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Table 6.7.2.2-64 (cont'd): Calculation of import-based MRL proposals for prickly pear according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Results (Prickly pear cactus)

Total number of data (n)	8	Standard deviation (SD)	0.024
Lowest residue	0.13	Percentage of censored data	0
Highest residue	0.33	Number of non-censored data	8
Median residue	0.17	Correction factor for censoring (CF)	1.000
Mean	0.163		

Proposed MRL estimate

Highest residue	0.33
Mean + 4 SD	0.513
CF × 3 mean	0.676
Unrounded MRL	0.676
Rounded MRL	0.7

Table 6.7.2.2-65: Calculation of import-based MRL proposals for soybean according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Multiple use
Portion analysed :	seed, dry	Commodity :	**Soybean** foliar
Target value :	MRL	PHI :	21 d

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
1	Soybean	21	0.08	RV132-10DA-B / RARVY011	2	SL 200	USA	F
2	Soybean	21	0.41	RV133-10HA-B / RARVY011	2	SL 200	USA	F
3	Soybean	21	1.2	RV134-10DA-B / RARVY011	2	SL 200	USA	F
4	Soybean	20	0.08	RV135-10HA-B / RARVY011	2	SL 200	USA	F
5	Soybean	20	0.38	RV136-10HA-B / RARVY011	2	SL 200	USA	F
6	Soybean	28	1.2**	RV137-10DB-B / RARVY011	2	SL 200	Canada	F
7	Soybean	19	0.25	RV138-10HA-B / RARVY011	2	SL 200	USA	F
8	Soybean	20	0.20	RV139-10HA-B / RARVY011	2	SL 200	USA	F
9	Soybean	20	<0.070	RV140-10HA-B / RARVY011	2	SL 200	Canada	F
10	Soybean	22	0.73	RV141-10HA-B / RARVY011	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-65 (cont'd): Calculation of import-based MRL proposals for soybean according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Country	Area of applic.
11	Soybean	21	0.37	RV142-10HA-B / RARVY011	2	SL 200	USA	F
12	Soybean	20	0.08	RV143-10HA-B / RARVY011	2	SL 200	Canada	F
13	Soybean	21	0.08	RV144-10HA-B / RARVY011	2	SL 200	USA	F
14	Soybean	20	<0.070	RV145-10HA-B / RARVY011	2	SL 200	Canada	F
15	Soybean	21	<0.070	RV146-10DA-B / RARVY011	2	SL 200	USA	F
16	Soybean	20	3.6	RV147-10HA-B / RARVY011	2	SL 200	USA	F
17	Soybean	19	0.50	RV148-10HA-B / RARVY011	2	SL 200	USA	F
18	Soybean	19	0.65	RV149-10HA-B / RARVY011	2	SL 200	USA	F
19	Soybean	21	<0.070	RV150-10HA-B / RARVY011	2	SL 200	USA	F
20	Soybean	21	0.27	RV151-10HA-B / RARVY011	2	SL 200	USA	F

[1] as given in the Tier 1 summaries
value no. 16 is an outlier for t1
** sample value from later interval than the nominal PHI

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Table 6.7.2.2-65 (cont'd): Calculation of import-based MRL proposals for soybean according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Results (Soybean, foliar)

Total number of data (n)	20	Standard deviation (SD)	0.806
Lowest residue	0.07	Percentage of censored data	20
Highest residue	3.6	Number of non-censored data	16
Median residue	0.260	Correction factor for censoring (CF)	0.867
Mean	0.518		

Proposed MRL estimate

Highest residue	3.6
Mean + 4 SD	3.743
CF × 3 mean	1.347
Unrounded MRL	3.743
Rounded MRL	4

Table 6.7.2.2-66: Calculation of import-based MRL proposals for soybean according to the OECD calculator – based on GJR data (cf. 6.3.2 and 6.7.2.2)

Residue :	total residue of BYI 02960	Crop group :	Multiple use
Portion analysed :	seed, dry	Commodity :	**Soybean** seed trtmt.
Target value :	MRL	PHI :	--

No.	Crop	Days after application	Residue value (mg/kg)	Plot No. [1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Soybean	131	0.82	RV133-10HA-C / RARVY011	1	FS 480	BYI 02960 FS 480	USA	F
2	Soybean	138	0.50	RV135-10HA-C / RARVY011	1	FS 480	BYI 02960 FS 480	USA	F
3	Soybean	134	0.13	RV138-10HA-C / RARVY011	1	FS 480	BYI 02960 FS 480	USA	F

[1] as given in the Tier 1 summaries

Results (Soybean seed trtmt.)

Total number of data (n)	3	Standard deviation (SD)	0.345
Lowest residue	0.13	Percentage of censored data	0
Highest residue	0.82	Number of non-censored data	3
Median residue	0.500	Correction factor for censoring (CF)	1.000
Mean	0.483		

Proposed MRL estimate

Highest residue	0.82
Mean + 4 SD	1.865
CF × 3 mean	1.450
Unrounded MRL	1.865
Rounded MRL	2

• Summary of MRL proposals in plant matrices

MRLs for the total residue of BYI 02960 plus DFA have been proposed in this dossier based on primary crop and rotational crop uses, as described in section 6.3 and 6.6.3, respectively.

As BYI 02960 is to be registered worldwide, MRLs for commodities important in international trade would ideally be harmonized between in all regions. The following table summarizes all MRLs in plant matrices in this dossier and the appropriate proposal for a global, harmonized tolerance:

Table 6.7.2.2-67: BYI 02960 – Summary of EU MRL proposals (in mg/kg) based on the evaluation of EU and tolerance-relevant residue data presented above
(MRLs reflect the sum of BYI 02960 and DFA, expressed in parent equivalents)

Commodity	EU primary		EU rotational		GJR*	Harmonized proposal
	EU calc.	OECD calc.	orig.	new		
Citrus fruit	-	-	-		3.0	**3.0**
Tree nuts	-	-	-		0.15	**0.15**
Pome fruit	0.4	0.5	-		1.5	**1.5**
Grapes	0.9	1.0			3.0	**3.0**
Blueberries	-	-	-		4.0	**4.0**
Prickly pear	-	-	-		0.7	**0.7**
Root vegetables	-	-	0.3		*x*	**0.3**
Bulb vegetables	-	-	0.4	0.8**	0.3	**0.8****
Tomatoes/eggplants	0.7	0.9	1.0		3.0	**3.0**
Peppers	0.8	1.0	1.0		*x*	**1.0**
Chili peppers	-	-	1.0		3.0	**3.0**
Cucurbits, edible peel	0.9	1.5	1.0		*x*	**1.0**/1.5†
Watermelons	0.6	0.6	1.0		*x*	**1.0**
Sweet corn/maize	-	-	1.5	4.0**‡	0.4	**0.4** (4.0**)‡
Brassica vegetables	-	-	0.3		*x*	**0.3**
Lettuces/spinach	7.0	9.0	0.3		*x*	**7.0**/9.0†
Endive (scarole)	-	-	0.3		*x*	**0.3**
Legume vegetables	-	-	2.0		*x*	**2.0**
Stem vegetables	-	-	0.6		- 40 (celery)	**0.6 (general)** **40** (celery)
Pulses - dry beans - dry peas	-	-	6.0	10.0**	 0.9 8.0	**10.0** (general)**
Oilseeds - peanuts - soybean - cotton	-	-	0.4	0.8**	 0.15 4.0 0.9	**0.8** (general)** 4.0 (soybean) 0.9 (cotton)

x = these crops are not exported from GJR countries in significant quantities into the EU

* crops listed here are exported from GJR countries to the EU, calculated with the OECD model.
** these values are based on a re-evaluation of the data subsequent to the original GJR submission, incorporating all EU rotational crop data which became available later (using an extrapolation from the EU use pattern to the Australian use pattern as well as the envisaged Australian soil accumulation factor of 1.2).
† proposal depends on whether or not the OECD calculator is used for EU data
‡ proposal based on rotational cereals – depends on whether or not sweet corn/maize is regarded as a cereal crop

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Table 6.7.2.2-67 (cont'd): BYI 02960 – Summary of EU MRL proposals (in mg/kg) based on the evaluation of EU and tolerance-relevant residue data presented above

(MRLs reflect the sum of BYI 02960 and DFA, expressed in parent equivalents)

Commodity	EU primary EU calc.	EU primary OECD calc.	EU rotational *orig.*	EU rotational *new*	GJR*	Harmonized proposal
Potatoes (tuber veg.)	-	-	0.7	1.5**	0.15	**1.5****
Hops	4.0	4.0	-		20	**20**
Coffee	-	-	-		2.0	**2.0**
Cereals	-	-	1.5	4.0**		**4.0 (general)**
- barley					4.0	
- corn/maize					0.50	4.0** (corn)
- sorghum					4.0	
- wheat					4.0	

x= these crops are not exported from GJR countries in significant quantities into the EU

* crops listed here are exported from GJR countries to the EU, calculated with the OECD model.

** these values are based on a re-evaluation of the data subsequent to the original GJR submission, incorporating all EU rotational crop data which became available later (using an extrapolation from the EU use pattern to the Australian use pattern as well as the envisaged Australian soil accumulation factor of 1.2).

IIA 6.7.2.3 MRL Proposals in Animal Matrices Based on EUROPEAN Residue Data

Based on the proposed residue definition for risk assessment in animal matrices — the calculated total residues of BYI 02960, consisting of the sum of the residues of the parent compound and its metabolite DFA — and on the studies presented in this dossier, MRL proposals are presented below for animal tissues and products, resulting from exposure of livestock to feed crops treated with BYI 02960.

Note: The proposed residue definitions for both risk assessment and enforcement are different than the one used in the feeding studies for data collection, as while the former include only two components, the data gathering method determined 2 additional analytes, BYI 02960-acetyl-AMCP and BYI 02960-OH. However, as explained previously (section 6.7.1), these did not play a major role in any of the trials and thus they are not included in the MRL calculations summarized below.

The crop studies described in this dossier reflect only the "safe uses", i.e. lettuce and hops, as well as the rotational crop groups covered in the "major" study. Further uses will be submitted separately to cover numerous other crops; these uses are reflected in the crops affecting the dietary burden and thus the residue levels in animal matrices.

● Poultry

When chickens and other poultry are exposed to relevant residues of BYI 02960 via ingestion of plant materials, they are primarily exposed to two substances, the parent compound itself and its main metabolite, DFA. A feeding study was conducted by feeding parent compound to laying hens (KIIA 6.4.1/01), and, by way of "material balancing" including determination of residues in the excreta, transfer factors for DFA were calculated on the basis of the systemically available amount of DFA, and thus the residue values obtained in the study can be re-calculated to yield realistic worst-case MRLs based on exposure to both parent and DFA.

In the EU 1X animal group, representing the maximum proposed dietary burden of total residues of BYI 02960 in crops/matrices relevant to poultry feed, the following combined residue levels, comprising BYI 02960 and DFA, were observed in relevant poultry matrices taken at sacrifice:

Table 6.7.2.3-1: Combined residues of BYI 02960 and DFA in poultry matrices as determined in the feeding study (1X dose group)

Commodity	Residue levels (mg/kg)		
	combined residue	individual components	
		BYI 02960	DFA
eggs	0.061†	<0.01*†	0.051†
muscle	0.093	<0.01*	0.083
fat	0.039	<0.01*	0.029
liver	0.114	<0.01*	0.104

* LOQ for BYI 02960 = 0.01 mg/kg
† egg value based on the day-24 egg sample (cf. Table 6.4.1-3)

The dietary residues fed to the chickens were based on residue values in crops covered in this dossier (rotational turnips and cereals) as well as preliminary data from additional uses to be submitted later (kale and primary cereal uses). The contributions to the diet were as follows:

Table 6.7.2.3-2: Key data re. the make-up of the diet fed to chickens in the feeding study

Crop	Residue levels (mg/kg)			Levels in dry matter		Dietary burden (mg/kg feed)	Residue-to-burden factor
	total res.*	BYI 02960	DFA	% in crop	residue (mg/kg)		
wheat	0.78	0.01	0.77	86	0.91	0.635	1.428
kale	1.36	1.10	0.26	14	9.71	0.486	19.988
turnip	0.14	0.01	0.13	10	1.40	0.280	5.000
Totals:		1.12	1.16			1.401	

* "total residue" of BYI 02960 + DFA

Based on the feeding study results, transfer factors were calculated both for the *combined residue* of BYI 02960 and DFA derived from the feeding of BYI 02960 as well as for *DFA alone* derived from the exposure levels of the chickens to DFA in the feeding studies. (For details, cf. section 6.4.1 of this dossier.) Using these transfer factors, estimations of the residue levels reasonably expected to be determined after feeding of a *mixture* of BYI 02960 and DFA, as would be anticipated in the feed crops, can be calculated.

To do this, the residues fed must first be separated into the individual components. Using the residue-to-dietary-burden factors determined for the study, each component can be calculated as an individual contributor to the diet, as shown in table 6.7.2-13:

Table 6.7.2.3-3: Re-calculation of dietary burdens for the individual components of the relevant residue in poultry feed (BYI 02960 and DFA)

Crop	Residue levels (mg/kg)			Levels in dry matter		Dietary burden (mg/kg feed)	Residue-to-burden factor
	total res.*	BYI 02960	DFA	% in crop	residue (mg/kg)		
wheat	0.78	0.01		86	0.01	0.008	1.428
kale	1.36	1.10		14	7.86	0.393	19.988
turnip	0.14	0.01		10	0.10	0.020	5.000
Subtotal BYI 02960:		1.12				**0.421**	
wheat	0.78		0.77	86	0.90	0.627	1.428
kale	1.36		0.26	14	1.86	0.093	19.988
turnip	0.14		0.13	10	1.30	0.260	5.000
Subtotal DFA:			1.16			**0.980**	
Totals:		1.12	1.16			1.401	

* "total residue" of BYI 02960 + DFA

Using these dietary burden levels (0.421 mg/kg feed of BYI 02960 and 0.980 mg/kg feed of DFA) and the transfer factors derived in the feeding study study (for the low-dose group re. the total residue, and for the most relevant exposure scenario – again, the lowest, 0.5 mg/kg feed – for DFA), the following theoretical residue levels can be calculated for the feeding of BYI 02960 and DFA individually in ratios relevant to the worst-case residues expected in animal feed. They are summarized in the table below.

Table 6.7.2.3-4: Theoretical residues resulting from feeding BYI 02960 and DFA to poultry in a ratio relevant to the actual residues expected in feed commodities

Dietary burden (mg/ kg feed)	Matrix	Transfer factor*	Resulting residue (mg/kg)
BYI 02960			
0.421	egg	0.038	0.016
	muscle	0.062	0.026
	fat	0.026	0.011
	liver	0.076	0.032
DFA			
0.980	egg	0.097	0.095
	muscle	0.172	0.169
	fat	0.060	0.059
	liver	0.216	0.212

* for derivation of transfer factors, cf. section 6.4.1

Table 6.7.2.3-5 summarizes the results of the theoretical residues calculated above, matrix for matrix. The following levels of total residues of BYI 02960 and DFA (expressed in parent compound equivalents) can be expected after feeding of realistic worst-case residues in feed crops to poultry.

Table 6.7.2.3-5: Levels of the relevant residue of BYI 02960 (comprising BYI 02960 + DFA) in poultry tissues and eggs expected after feeding a worst-case diet containing residues due to treatment of crops with BYI 02960

Matrix	Residue levels* (mg/kg) based on feeding of			Proposed MRL
	BYI 02960	DFA	*Sum*	
egg	0.016	0.095	*0.111*	**0.15**
muscle	0.026	0.169	*0.195*	**0.20**
fat	0.011	0.059	*0.070*	**0.07**
liver	0.032	0.212	*0.244*	**0.30**

* all residue levels expressed in parent compound equivalents

Thus, on the basis of the feeding study in poultry, the following MRLs are proposed for the total residue of BYI 02960 and DFA in edible matrices: 0.15 mg/kg in eggs, 0.20 mg/kg in muscle, 0.07 mg/kg in fat, and 0.30 mg/kg in liver and edible offal.

● **Ruminants**

When cattle and similar animals are exposed to relevant residues of BYI 02960 via ingestion of plant materials, they are primarily exposed to two substances, the parent compound itself and its main metabolite, DFA. A feeding study was conducted by feeding parent compound to dairy cows (KIIA 6.4.2/01), and, by way of "material balancing" including determination of residues in the urine, transfer factors for DFA were calculated on the basis of the systemically available amount of DFA, and thus the residue values obtained in the study can be re-calculated to yield realistic worst-case MRLs based on exposure to both parent and DFA.

In the EU 1.3X animal group, representing slightly more than the maximum proposed dietary burden of total residues of BYI 02960 in crops/matrices relevant to ruminant feed, the following combined residue levels, comprising BYI 02960 and DFA, were observed in relevant cattle matrices taken at sacrifice:

Table 6.7.2.3-6: Combined residues of BYI 02960 and DFA in cattle matrices as determined in the feeding study (1.3X dose group)

Commodity	Residue levels (mg/kg)		
	combined residue	individual components	
		BYI 02960	DFA
milk	0.043†	0.023†	<0.02*†
muscle	0.063	0.043	<0.02*
fat	0.041	0.021	<0.02*
liver	0.165	0.145	<0.02*
kidney	0.180	0.159	0.021

* LOQ for DFA = 0.02 mg/kg, expressed in BYI 02960 equivalents
† milk value based on the day-28 milk sample (cf. Table 6.4.2-2)

The dietary residues fed to the cows were based on residue values in crops covered in this dossier (rotational turnips and cereals) as well as preliminary data from additional uses to be submitted later (kale and primary cereal uses). The contributions to the diet were as follows:

Table 6.7.2.3-7: Key data re. the make-up of the diet fed to dairy cows in the feeding study

Crop	Residue levels (mg/kg)			Levels in dry matter		Dietary burden (mg/kg feed)	Residue-to-burden factor
	total res.*	BYI 02960	DFA	% in crop	residue (mg/kg)		
wheat	0.78	0.01	0.77	86	0.91	0.050	18.140
kale	1.36	1.10	0.26	14	9.71	3.400	2.857
turnip	0.14	0.01	0.13	10	1.40	0.840	1.667
Totals:		1.12	1.16			4.290	

* "total residue" of BYI 02960 + DFA

Based on the feeding study results, transfer factors were calculated both for the *combined residue* of BYI 02960 and DFA derived from the feeding of BYI 02960 as well as for *DFA alone* derived from the exposure levels of the cows to DFA in the feeding studies. (For details, cf. section 6.4.2 of this dossier.) Using these transfer factors, estimations of the residue levels reasonably expected to be determined after feeding of a *mixture* of BYI 02960 and DFA, as would be anticipated in the feed crops, can be calculated.

To do this, the residues fed must first be separated into the individual components. Using the residue-to-dietary-burden factors determined for the feeding study, each component can be calculated as an individual contributor to the diet, as shown in Table 6.7.2.3-8:

Table 6.7.2.3-8: Re-calculation of dietary burdens for the individual components of the relevant residue in ruminant feed (BYI 02960 and DFA)

Crop	Residue levels (mg/kg) total res.*	BYI 02960	DFA	Levels in dry matter % in crop	residue (mg/kg)	Dietary burden (mg/kg feed)	Residue-to-burden factor
wheat	0.78	0.01		86	0.01	0.001	18.140
kale	1.36	1.10		14	7.86	2.750	2.857
turnip	0.14	0.01		10	0.10	0.060	1.667
Subtotal BYI 02960:		1.12				**2.811**	
wheat	0.78		0.77	86	0.90	0.049	18.140
kale	1.36		0.26	14	1.86	0.650	2.857
turnip	0.14		0.13	10	1.30	0.780	1.667
Subtotal DFA:			1.16			**1.479**	
Totals:		1.12	1.16			4.290	

* "total residue" of BYI 02960 + DFA

Using these dietary burden levels (2.811 mg/kg feed of BYI 02960 and 1.479 mg/kg feed of DFA) and the transfer factors derived in the feeding study (for the low-dose group re. the total residue, and for the most relevant exposure scenario – 1.45 mg/kg feed – for DFA), the following theoretical residue levels can be calculated for the feeding of BYI 02960 and DFA individually in ratios relevant to the worst-case residues expected in animal feed. They are summarized in the table below.

Table 6.7.2.3-9: Theoretical residues resulting from feeding BYI 02960 and DFA to cows in a ratio relevant to the actual residues expected in feed commodities

Dietary burden (mg/kg feed)	Matrix	Transfer factor* using apparent residues**	Transfer factor* using values "at LOQ"†	Resulting residue (mg/kg) using apparent residues**	Resulting residue (mg/kg) using values "at LOQ"†
BYI 02960					
2.811	milk	0.006	0.009	0.017	0.025
	muscle	0.012	0.013	0.034	0.037
	fat	0.007	0.009	0.020	0.025
	liver	0.035	0.036	0.098	0.101
	kidney	0.037	0.037	0.104	0.104
DFA					
1.479‡	milk		0.028		0.041
	muscle		0.094		0.139
	fat		0.068		0.101
	liver		0.091		0.135
	kidney		0.140		0.207

* for derivation of transfer factors, cf. section 6.4.2
** "apparent residues" used to derive factors include measured values below the tested LOQ
† when deriving factors, residue values of <LOQ were calculated as being at the LOQ, thus representing a worst case for exposure
‡ based on this dietary burden, the transfer factor chosen for DFA reflects the closest exposure rate, 1.45 mg/kg feed

Table 6.7.2.3-10 summarizes the results of the theoretical residues calculated above, matrix for matrix. The following levels of total residues of BYI 02960 and DFA (expressed in parent compound equivalents) can be expected after feeding of realistic worst-case residues in feed crops to cattle.

Table 6.7.2.3-10: Levels of the relevant residue of BYI 02960 (comprising BYI 02960 + DFA) in bovine tissues and milk expected after feeding a worst-case diet containing residues due to treatment of crops with BYI 02960

Matrix	Residue levels* (mg/kg) based on feeding of BYI 02960 "app."**	Residue levels* (mg/kg) based on feeding of BYI 02960 "at LOQ"†	DFA	*Sum* *"app."***	*Sum* *"at LOQ"*†	Proposed MRL*
milk	0.017	0.025	0.041	*0.058*	*0.067*	**0.07**
muscle	0.034	0.037	0.139	*0.173*	*0.176*	**0.20**
fat	0.020	0.025	0.101	*0.120*	*0.126*	**0.15**
liver	0.098	0.101	0.135	*0.233*	*0.236*	**0.30**
kidney	0.104	0.104	0.207	*0.311*	*0.311*	**0.40**

* all residue levels expressed in parent compound equivalents
** total reflects "apparent" residue levels (even if a component is below the LOQ), as shown in table 6.7.2-19
† total reflects residue levels of all components at or above the LOQ, as shown in table 6.7.2-19

Thus, on the basis of the feeding study in dairy cows, the following MRLs are proposed for the total residue of BYI 02960 and DFA in edible matrices: 0.07 mg/kg in milk, 0.20 mg/kg in muscle, 0.15 mg/kg in fat, 0.30 mg/kg in liver, and 0.40 mg/kg in kidney and other edible offal.

IIA 6.7.2.4 MRL Proposals in Animal Matrices Based on GLOBAL Residue Data

As BYI 02960 is to be registered worldwide, MRLs for animal commodities important in international trade would ideally be harmonized between in all regions.

► *Background:* GLOBAL JOINT REVIEW

As part of the Global Joint Review submission in the USA, Canada, Mexico, Brazil, and Australia, the maximum dietary burden of livestock was calculated on basis of the residues in the respective feed items. The dietary burden and the resulting residues in animal matrices, as well as MRL proposals were summarized in the "GJR dossier", submitted in October 2012. The highest MRL proposals in animal matrices resulted from the use of BYI 02960 in Australia, as presented below. The most critical diet was calculated on basis of the residues in feed items treated with BYI 02960, but as well from residues resulting from succeeding feed crops. The residues in succeeding feed crops were estimated on the basis of the residues determined in the European field rotational crop studies by extrapolation (adaption of maximum seasonal application rate).

• Poultry

According to APVMA guidelines, processed grains and plant protein meals (from rotational croppings) are considered to constitute no more than 20%, oilseeds (from rotational croppings) no more than 30% of the diet, while legume animal feeds (from primary or rotational croppings) or cereal grains (from rotational croppings) may constitute 100% of the diet for poultry. Therefore, given their relative contributions to dietary exposure and their relative MRLs, pulses (from rotational croppings) as legume feed commodities will be considered as the worst-case diet for the calculation of likely residues in poultry matrices.

Considering the moisture content of pulses of 10% (OECD guideline), the poultry dietary exposure based on a diet of 100% pulses can be calculated, as shown in Table 6.7.2.4-1.

Table 6.7.2.4-1: Dietary exposure to BYI 02960 residues by poultry

	Feed commodity	% in diet	Residue component	Residue (mg/kg) Fresh weight	Residue (mg/kg) Dry weight*	Livestock dietary exposure (mg/kg)
Poultry	Pulses	100%	BYI 02960 + DFEAF DFA Total	0 4.97 4.97	0 5.52 5.52	0 5.52

* Assuming moisture content of 10% in pulses (dry peas, DM=90%, OECD guideline)

Based on factors determined for the transfer of DFA residues to poultry matrices, as discussed in IIA 6.4.2, residues can be calculated as shown in Table 6.7.2.4-2.

Table 6.7.2.4-2: Calculated residues in poultry matrices from feeding DFA

Dietary burden (mg/ kg feed)	Matrix	Transfer factor*	Resulting residue (mg/ kg)
DFA			
5.52	eggs	0.078	0.431
	muscle	0.139	0.768
	fat	0.056	0.309
	liver	0.198	1.093

* Transfer factor derived from poultry feeding study:
DFA: 1X dose group = 1.85 mg DFA/kg dry feed (expressed in parent equivalents)

Based on these results, the following poultry commodity MRLs are proposed:

Edible offal (poultry)	1.0 mg/kg
Meat (poultry)	0.8 mg/kg
Eggs	0.5 mg/kg

● **Livestock**

Tomato pomace and green bean forage and fodder may constitute part of the diet for dairy and beef cattle.

According to APVMA guidelines, tomato pomace is considered to constitute no more that 10% of the diet, while based on previous APVMA considerations, legume animal feeds may constitute 70% of the diet for dairy cattle, and 100% of the diet for beef cattle. Therefore, given their relative contributions to dietary exposure and their relative MRLs, green bean feed commodities will be considered for calculation of likely residues in livestock. For dairy cattle, cereal grain-containing commodities from rotational cropping are proposed to make up 30% of the diet.

The highest total residue (BYI 02960, DFEAF, and DFA) for green bean feed commodities was 5.15 mg/kg found in fodder. This particular sample (cf. study BCS-0353, site C521) comprised 4.6 mg/kg BYI 02960 + DFEAF, and 0.54 mg/kg DFA, when all were expressed as BYI 02960 parent equivalents. The moisture content in fodder at this particular site was 85%. Cereal grain, from rotational crops, has been shown to contain residues of up to 1.75 mg/kg, all of which is DFA.

The livestock dietary exposure for cattle can be calculated, as shown in Table 6.7.2.4-3.

Table 6.7.2.4-3: Dietary exposure to BYI 02960 residues by cattle

	Feed commodity	% in diet	Residue component	Residue (mg/kg) Fresh weight	Dry weight*	Livestock dietary exposure (mg/kg)
Dairy Cattle	Bean fodder	70%	BYI 02960 + DFEAF DFA	4.6 0.54	30.67 3.60	21.47 2.52
	Cereal grain	30%	BYI 02960 + DFEAF DFA	0 1.75	0 1.99	0 0.60
	All feeds	100%	BYI 02960 + DFEAF DFA			21.47 3.12
Beef Cattle	Bean fodder	100%	BYI 02960 + DFEAF DFA	4.6 0.54	30.67 3.60	30.67 3.60

* Bean fodder: Calculated based on reported moisture content (85%) – refer to study report
Cereal grain: Assuming cereal grain moisture content of 88% (OECD guideline)

Based on transfer factors determined for transfer of BYI 02960 and DFA residues to livestock matrices, as discussed in IIA 6.4.2, residues are calculated as shown in Table 6.7.2.4-4.

Table 6.7.2.4-4: Calculated residues in livestock matrices from feeding BYI 02960 and DFA

Dietary burden (mg/ kg feed)	Matrix	Transfer factor*	Resulting residue (mg/kg)
BYI 02960			
Dairy: 21.47	milk	0.006	0.129
Beef: 30.67	muscle	0.013	0.399
	fat	0.006	0.184
	liver	0.035	1.073
	kidney	0.038	1.165
DFA			
Dairy: 3.12	milk	0.030	0.094
Beef: 3.60	muscle	0.097	0.349
	fat	0.086	0.310
	liver	0.097	0.349
	kidney	0.131	0.472

* Transfer factor derived from cattle feeding study:
BYI 02960: 6.3X EU dose group = 23 mg BYI 02960/kg dry feed
DFA: 34X EU dose group = 3.9 mg DFA/kg dry feed (expressed in parent equivalents)

By summing residues calculated from feeding BYI 02960 and DFA, the total residue in animal matrices can be determined (Table 6.7.2.4-5).

Table 6.7.2.4-5: Total BYI 02960 residues in livestock matrices

Matrix	Total residue (mg/kg)
milk	0.223
muscle	0.748
fat	0.494
liver	1.422
kidney	1.637

Based on these results, the following mammalian commodity MRLs are proposed:

Edible offal (mammalian)	2.0 mg/kg
Meat (mammalian)	1.0 mg/kg
Milks	0.3 mg/kg

● Summary of MRL proposals in animal matrices

MRLs for the total residue of BYI 02960 plus DFA have been proposed in this dossier based on primary crop and rotational-crop uses described in sections 6.3 and 6.6.3, respectively.

As BYI 02960 is to be registered worldwide, MRLs for commodities important in international trade would ideally be harmonized between in all regions. The following table summarizes all MRLs in animal tissues in this dossier and the appropriate proposal for a global, harmonized tolerance:

Table 6.7.2.4-6: BYI 02960 – Summary of EU MRL proposals (in mg/kg) based on the evaluation of EU and tolerance-relevant residue data presented above
(MRLs reflect the sum of BYI 02960 and DFA, expressed in parent equivalents)

Commodity	"EU" proposal	Harmonized GJR proposal*	New, additional proposal in EU dossier**
Eggs	0.15	0.3	**0.5**†
Poultry meat (muscle)	0.20	0.5	**0.8**†
Poultry fat	0.07	0.2	**0.3**†
Poultry liver/offal	0.30	0.5	**1.0**†
Milk	0.07	0.3	**0.3**
Bovine meat (muscle)	0.20	1.0	**1.0**
Bovine fat	0.15	0.5	**0.5**
Bovine liver	0.30	2.0	**2.0**‡
Bovine kidney	0.40	2.0	**2.0**‡
Other bovine offal	0.40	2.0	**2.0**

Values in bold print are now considered to be the internationally harmonized proposals
* values according to dossier submitted in November (based on primary crop uses only)
** values based on Australian feeding calculations, also considering rotational crop data
† values re-calculated using revised dietary burden in Australian diet (incorporating full EU rotational crop data set, extrapolated to Australian use pattern and using Australian soil accumulation factor).
‡ not applicable in Australia (no MRLs are set there on this commodity, however values calculated on basis of Australian worst-case diet)

IIA 6.8 Proposed pre-harvest intervals, re-entry or withholding periods

IIA 6.8.1 Pre-harvest interval (in days) for each relevant crop

The envisaged pre-harvest intervals for EU uses are as described above in the field residue trials section of this chapter (point KIIA 6.3.1). For:

- lettuce grown in greenhouses, the critical PHI is 3 days.
- lettuce grown outdoors, the critical PHI is also 3 days, based on the "home & garden" use.
- fruiting vegetables of all natures, the PHI is 3 days for both field and greenhouse uses.
- grapes, the PHI is 14 days.
- pome fruit, the PHI is 14 days.
- hops, the PHI is 21 days.

IIA 6.8.2 Re-entry period (in days) for livestock, to areas to be grazed

BYI 02960-containing products are not intended for use in areas to be grazed by livestock. Therefore, a re-entry period does not need to be established.

IIA 6.8.3 Re-entry period for man to crops, buildings or spaces treated

Under practical conditions there is no reason to enter a crop shortly after treatment. Even if done, one would wait until the spray solution has dried on the plant surface, at least. Under these circumstances, re-entry exposure was evaluated based on measured dislodgeable foliar residues as well as on conservative model assumptions. Exposure was estimated to be within acceptable levels and no unacceptable risk is anticipated for workers entering the treated crop and performing re-entry activities when standard work clothing is worn (shoes, socks, long pants, and long sleeves).
Therefore, setting a specific re-entry period is not indicated.

b) Buildings
Not relevant.

c) Spaces
Not relevant

IIA 6.8.4 Withholding period (in days) for animals feedingstuffs

Lettuce, apples:
Due to the time between last treatment and harvest, as defined by the GAPs, it is not necessary to set a withholding period for use of treated plants as animal feedingstuffs. The withholding period is covered by the vegetation period of the crop. However, a poultry feeding study with parent BYI 02960 was conducted at dose rates which reflect maximum possible exposure to livestock based

on uses in numerous crops (many of which will be submitted in a separate, future submission). That study covers all aspects of residues in livestock and thus no specific withholding period is required.

Hops, grapes, fruiting vegetables:
Not relevant for these crops since they are not used as animal feedingstuffs.

IIA 6.8.5 Waiting period between last application and sowing or planting

Not applicable, because BYI 02960-containing products are not intended for use on crops covered in this dosier prior to sowing or planting.

IIA 6.8.6 Waiting period between application and handling treated products

The use of BYI 02960-containing products is intended in lettuce, fruiting vegetables, pome fruit, grapes, and hops prior to harvest. The proposed pre-harvest interval is 3 days for the vegetable crops, 14 days for the fruit crops, and 21 days for hops, as stated previously. There is no need to handle treated crops before harvest.

IIA 6.8.7 Waiting period before sowing/planting succeeding crops

A full program of residue trials in rotational crops is presented either in this dossier (the "main", multi-crop, multi-rotation study, and various single-crop single-rotation trials with additional crops). The data collected in these studies yield information on the level of residues to be expected in following crops, and are reflected in the dietary risk assessment. Therefore, no waiting period needs to be specified.

IIA 6.9 Estimation of exposure through diet and other means

IIA 6.9.1 TMDI calculations

The assessment of the chronic uptake of BYI 02960 residues with food is made based on the proposed MRLs as shown in this dossier (cf. section 6.7.2) and the Acceptable Daily Intake (ADI) of 0.078 mg/kg bw/day, which was established based on the lowest NOAELs obtained in a chronic toxicity study in the most sensitive species. The lowest NOAELs has been observed in the rat 2-generation reproduction study based on body weight effects in females and in the 1-year dog study based on histopathological findings in the skeletal muscle (cf. section 3, point 5.11).

In order to evaluate the potential chronic exposure to BYI 02960 residues through the diet, the Theoretical Maximum Daily Intakes (TMDI) of residues was estimated using the EFSA PRIMo consumer exposure model. The MRLs as summarized in table 6.7.2.2-67 were used as the basis for calculation.

For agricultural and "home & garden" uses, the calculated TMDI values are summarized in table 6.9.1-1 below. (Details of the individual TMDI calculations are shown in table 6.9.1-2.)

Table 6.9.1-1: BYI 02960 – Summary of the TMDI calculation (EFSA PRIMo model rev. 2.0) Top ten ADI usage results including top contributors

TMDI (% ADI)	Diet	Highest contributor to the diet (% ADI)	Commodity	2nd–highest contributor to the diet (% ADI)	Commodity
126.5	WHO cluster diet B	43.8	Wheat	12.7	Maize/corn
102.8	NL child	24.3	Wheat	15.6	Citrus fruit
100.7	DE child	24.4	Pome fruit	21.1	Wheat
85.0	FR toddler	15.4	Root and tuber vegetables (incl. potatoes)	15.2	Milk, cream, cheese, butter, etc.
81.2	DK child	28.2	Wheat	22.7	Rye
81.1	IE adult	11.8	Maize	11.8	Maize
77.5	UK Toddler	20.1	Wheat	10.4	Pulses, dry
74.5	WHO cluster diet D	33.4	Wheat	8.6	Root and tuber vegetables (incl. potatoes)
72.5	WHO cluster diet E	20.2	Wheat	10.1	Root and tuber vegetables (incl. potatoes)
71.3	UK Infant	14.9	Milk, cream, cheese, butter, etc.	13.4	Wheat

The TMDI, calculated according to the EFSA PRIMo model, amounts to between 19.4% (PL general population) and 126.5% (WHO Cluster Diet B) of the ADI. The "top ten" most critical values ranged from 71.3% to 126.5% of the ADI. Three ADI usage values in these evaluations are above 100%; thus, due to this, a further, more refined risk assessment is required.

(It should be noted that these calculations represent an overestimate of the true residue intake. All models fail to consider the fact that the percentage of the total area of a crop treated with BYI 02960 is far below 100%; most treated crops contain residues well below the MRL at harvest; residues are usually reduced during storage, preparation, commercial processing, and cooking; and, it is not realistic to assume that every commodity for which an MRL is proposed or exists has been treated with BYI 02960 over the lifetime of the consumer — in fact, most commodities will not have been treated with the compound and will not contain any BYI 02960 residues at all.)

Table 6.9.1-2: BYI 02960 – Details of the TMDI calculation (EFSA PRIMo model rev. 2.0)

BYI 02960			
Status of the active substance:	new	Code no.	
LOQ (mg/kg bw):	0.04	proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	0.078	ARfD (mg/kg bw):	0.35
Source of ADI:	KIIA 5	Source of ARfD:	KIIA 5
Year of evaluation:	2012	Year of evaluation:	2012

Calculation based on MRLs described in table 6.7.2.2-67

Chronic risk assessment

TMDI (range) in % of ADI minimum - maximum: 19 – 126

No of diets exceeding ADI: 3

Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)
126.5	WHO Cluster diet B	43.8	Wheat	12.7	Maize	11.9	Tomatoes	0.3
102.8	NL child	24.3	Wheat	15.6	Citrus fruit	13.0	Pome fruit	0.2
100.7	DE child	24.4	Pome fruit	21.1	Wheat	17.7	Citrus fruit	0.2
85.0	FR toddler	15.4	Root and tuber vegetables	15.2	Milk and cream,	13.4	Wheat	0.1
81.2	DK child	28.2	Wheat	22.7	Rye	7.4	Root and tuber vegetables	0.1
81.1	IE adult	11.8	Maize	11.8	Maize	10.3	Citrus fruit	0.3
77.5	UK Toddler	20.1	Wheat	10.4	PULSES, DRY	8.9	Citrus fruit	0.1
74.5	WHO cluster diet D	33.4	Wheat	8.6	Root and tuber vegetables	3.9	Tomatoes	0.1
72.5	WHO cluster diet E	20.2	Wheat	10.1	Root and tuber vegetables	6.9	Table and wine grapes	0.1
71.3	UK Infant	14.9	Milk and cream,	13.4	Wheat	9.1	Root and tuber vegetables	0.1
70.8	ES child	22.7	Wheat	9.0	Citrus fruit	6.1	PULSES, DRY	0.1
65.3	IT kids/toddler	34.1	Wheat	7.7	Other cereal	5.5	Tomatoes	0.1
64.5	WHO Cluster diet F	18.5	Wheat	8.4	Root and tuber vegetables	4.4	Citrus fruit	0.1
56.7	WHO regional European diet	15.2	Wheat	8.8	Root and tuber vegetables	4.2	Tomatoes	0.1
56.5	PT General population	20.1	Wheat	10.6	Table and wine grapes	4.0	Rice	0.1
52.7	FR infant	13.7	Root and tuber vegetables	9.9	Milk and cream,	5.4	Pome fruit	0.1
52.6	SE general population 90th percentile	16.4	Wheat	10.6	Root and tuber vegetables	5.3	Citrus fruit	0.2
49.7	FR all population	16.9	Wheat	15.8	Table and wine grapes	3.0	Root and tuber vegetables	0.1
47.2	NL general	10.6	Wheat	7.1	Citrus fruit	5.9	Root and tuber vegetables	0.1
47.2	ES adult	12.0	Wheat	5.6	Citrus fruit	4.8	Lettuce	0.1
46.9	IT adult	21.2	Wheat	4.5	Tomatoes	3.6	Other cereal	0.1
39.3	UK vegetarian	10.5	Wheat	5.5	PULSES, DRY	4.0	Citrus fruit	0.0
33.4	DK adult	10.3	Wheat	5.7	Table and wine grapes	3.7	Root and tuber vegetables	0.0
32.7	LT adult	6.7	Root and tuber vegetables	5.5	Rye	5.4	Wheat	0.0
32.1	UK Adult	8.6	Wheat	4.4	Table and wine grapes	3.1	Root and tuber vegetables	0.0
26.0	FI adult	5.0	Wheat	4.3	Citrus fruit	3.5	Rye	0.0
19.4	PL general population	7.8	Root and tuber vegetables	4.5	Pome fruit	3.4	Tomatoes	0.0

Conclusion:

The estimated Theoretical Maximum Daily Intakes based on MS and WHO diets and pTMRLs were in the range of 19.4 % to 126 % of the ADI.
For 3 diets the ADI is exceeded. Further refinements of the dietary intake estimates have not been performed. A public health risk can not be excluded at the moment.

IIA 6.9.2 NEDI/IEDI calculations

As the TMDI calculation for BYI 02960 showed that residues at the level of the proposed MRLs exceed the ADI in one case, a refined risk assessment was conducted using STMR values instead of MRLs. The STMRs are summarized in the table below (cf. sections 6.3.1, 6.3.2, and 6.6.3 for the residue data, and 6.7.2 for the evaluation). MRL values were used for animal commodities.

Table 6.9.2-1: BYI 02960 – Summary of STMRs used in higher-tiered chronic dietary risk assessment, based on the evaluation of EU and tolerance-relevant residue data presented above
(all values expressed in mg/kg)

Commodity	STMR	Source	Dossier chap.
Citrus fruit - lemons - mandarins - oranges - grapefruits	 0.29 0.51 0.26 0.21	} GJR data package*	6.3.2
Tree nuts	<0.07	GJR data package*	6.3.2
Pome fruit - apples - pears	 0.18 0.43	} GJR data package*	6.3.2
Grapes	0.57	GJR data package*	6.3.2
Blueberries	0.87	GJR data package* (IR-4)	6.3.2
Prickly pear	0.22	GJR data package* (IR-4)	6.3.2
Root vegetables	0.08	EU rotational data package (root)	6.6.3.1
Bulb vegetables	0.18	EU rotational data package (bulb)**	6.6.3.1
Tomatoes/eggplants	0.32	EU rotational data package (fruiting)†	6.6.3.1
Peppers	0.32	EU rotational data package (fruiting)	6.6.3.1
Chili peppers	0.55	GJR data package*	6.3.2
Cucumbers/zucchini	0.32	EU rotational data package (fruiting)	6.6.3.1
Watermelons	0.32	EU rotational data package (fruiting)	6.6.3.1
Sweet corn/maize	0.14	GJR data package*	6.3.2
Brassica vegetables	0.08	EU rotational data package (leafy)	6.6.3.1
Lettuces/spinach	2.2	EU primary use	6.3.1
Endive (scarole)	0.08	EU rotational data package (leafy)	6.6.3.1
Legume vegetables	0.50	EU rotational data package (legume)	6.6.3.1
Stem vegetables - celery - others	 2.2 0.08	 GJR data package* EU rotational data package (stem)	 6.3.2 6.6.3.1
Pulses	3.35	EU rotational data package (pulses)**	6.6.3.1

* crops listed here are exported from GJR countries to the EU
** STMR value based on recalculation to reflect Australian use pattern and soil accumulation factor (cf. section 6.7.2)
† STMR value from EU rotational crop trials higher for this crop than the corresponding US primary-use value

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Table 6.9.2-1 (cont'd): BYI 02960 – Summary of STMRs used in higher-tiered chronic dietary risk assessment, based on the evaluation of EU and tolerance-relevant residue data presented above
(all values expressed in mg/kg)

Commodity	STMR	Source	Dossier chap.
Oilseeds			
- peanuts	0.22	EU rotational data pkg. (oilseeds)**	6.6.3.1
- soybean	0.26	GJR data package*	6.3.2
- cotton	0.16	GJR data package*	6.3.2
- others	0.22	EU rotational data pkg. (oilseeds)**	6.6.3.1
Potatoes (tuber veg.)	0.29	EU rotational data package (tuber)**	6.6.3.1
Hops	3.3	GJR data package*	6.3.2
Coffee	0.58	GJR data package*	6.3.2
Cereals			
- barley	0.93	GJR data package*	6.3.2
- corn/maize	0.945	EU rotational data package (cereals)**	6.6.3.1
- sorghum	0.69	GJR data package*	6.3.2
- wheat	0.71	GJR data package*	6.3.2
- others	0.945	EU rotational data package (cereals)**	6.6.3.1

* crops listed here are exported from GJR countries to the EU
** STMR value based on recalculation to reflect Australian use pattern and soil accumulation factor (cf. section 6.7.2)

The NEDI/IEDI (national/international estimation of dietary intake) calculations of residues were again conducted using the EFSA PRIMo consumer exposure model. For agricultural and "home & garden" uses, the calculated IEDI values are summarized in table 6.9.2-2 below. (Details of the individual IEDI calculations are shown in table 6.9.2-3.)

Table 6.9.2-2: BYI 02960 – Summary of the IEDI/NEDI calculation (EFSA PRIMo model rev. 2.0) Top ten ADI usage results including top contributors

NEDI/ IEDI (% ADI)	Diet		Highest contributor to the diet (% ADI)	Commodity	2nd–highest contributor to the diet (% ADI)	Commodity
23.4	WHO cluster diet B	→	7.8	Wheat	3.0	Maize/corn
18.4	NL child	→	4.3	Wheat	2.6	Milk and cream, etc.
17.6	IE adult	→	2.8	Maize	2.1	Apples
16.3	DE child	→	3.7	Wheat	2.8	Wheat
16.2	DK child	→	5.4	Rye	5.0	Sugar beet
16.0	UK Toddler	→	3.6	Wheat	3.3	Barley
14.9	FR toddler	→	3.6	Milk and cream, etc.	2.4	Lettuce
14.7	UK Infant	→	3.5	Milk and cream, etc.	2.4	Rye
14.3	WHO cluster diet D	→	5.9	Wheat	1.5	Potatoes
14.1	ES child	→	4.0	Wheat	1.2	Wheat

(It should be noted that these calculations still represent an overestimate of the true residue intake. All models fail to consider the fact that the percentage of the total area of a crop treated with BYI 02960 is far below 100%; residues are often reduced during storage, preparation [e.g. peeling], commercial processing, and cooking; and, it is not realistic to assume that every commodity for which a registration is proposed or exists has been treated with BYI 02960 over the lifetime of the consumer — in fact, most commodities will not have been treated with the compound and will not contain any BYI 02960 residues at all.

The calculations also include STMRs based on rotational use, which, under realistic conditions, will play even less of a role than would values based on primary use of BYI 02960; it is unrealistic to evaluate chronic consumption of entire classes of commodities grown on fields treated just previously with BYI 02960 and on which the primary crops failed.)

The NEDI/IEDI, calculated according to the EFSA PRIMo model, amounts to between 3.2% (PL general population) and 23.4% (WHO Cluster Diet B) of the ADI. No ADI usage values in any of these evaluations are above 100%; in fact, they are all below 25%. Thus, the use of BYI 02960 does not pose a risk to consumers if used according to the GAPs as described in this dossier.

Table 6.9.2-3: BYI 02960 – Details of the NEDI/IEDI calculation (EFSA PRIMo model rev. 2.0)

BYI 02960			
Status of the active substance:	new	Code no.	flupyradifurone
LOQ (mg/kg bw):	0.04	proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	0.078	ARfD (mg/kg bw):	0.35
Source of ADI:	KIIA 5	Source of ARfD:	KIIA 5
Year of evaluation:	2012	Year of evaluation:	2012

The NEDI/IEDI risk assessment is conducted on the basis of STMRs as described above in Table 6.9.2-1.

Chronic risk assessment

	TMDI (range) in % of ADI minimum - maximum
	3 - 23
No of diets exceeding ADI:	---

Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)
23.4	WHO Cluster diet B	7.6	Wheat	3.0	Maize	1.6	Table and wine grapes	0.0
18.4	NL child	4.3	Wheat	2.6	Milk and cream,	2.2	Potatoes	0.0
17.6	IE adult	2.8	Maize	2.7	Wheat	1.5	Barley	
16.3	DE child	3.7	Wheat	2.8	Apples	1.3	Milk and cream,	0.0
16.2	DK child	5.4	Rye	5.0	Wheat	1.1	Milk and cream,	
16.0	UK Toddler	3.6	Wheat	3.3	Beans	2.3	Sugar beet (root)	
14.9	FR toddler	3.6	Milk and cream,	2.4	Wheat	2.0	Spinach & similar (leaves)	0.0
14.7	UK Infant	3.5	Milk and cream,	2.4	Wheat	2.1	Beans	
14.3	WHO cluster diet D	5.8	Wheat	1.5	Potatoes	0.7	Rice	0.0
14.1	ES child	4.0	Wheat	1.2	Lettuce	1.1	Milk and cream,	
13.6	WHO cluster diet E	3.6	Wheat	1.4	Potatoes	1.3	Table and wine grapes	0.0
12.6	IT kids/toddler	6.1	Wheat	1.8	Other cereal	0.8	Lettuce	0.0
12.5	PT General population	3.6	Wheat	2.0	Table and wine grapes	2.0	Potatoes	
12.1	WHO Cluster diet F	3.3	Wheat	1.3	Potatoes	0.9	Rye	
11.1	WHO regional European diet	2.7	Wheat	1.5	Potatoes	1.1	Lettuce	0.0
9.6	ES adult	2.1	Wheat	1.5	Lettuce	0.6	Barley	
9.4	SE general population 90th percentile	2.9	Wheat	1.5	Potatoes	1.1	Milk and cream,	
9.3	FR all population	3.0	Table and wine grapes	3.0	Wheat	0.5	Other lettuce and other salad	0.0
9.3	IT adult	3.8	Wheat	1.1	Lettuce	0.9	Other cereal	0.0
9.1	FR infant	2.3	Milk and cream,	1.5	Potatoes	1.3	Spinach & similar (leaves)	
8.8	NL general	1.8	Wheat	1.0	Potatoes	0.6	Table and wine grapes	0.0
7.9	UK vegetarian	1.9	Wheat	1.5	Beans	0.7	Table and wine grapes	
6.4	UK Adult	1.5	Wheat	0.9	Beans	0.8	Table and wine grapes	
6.3	LT adult	1.3	Rye	1.2	Potatoes	1.0	Wheat	
6.3	DK adult	1.8	Wheat	1.1	Table and wine grapes	0.8	Rye	
4.8	FI adult	0.9	Wheat	0.8	Rye	0.5	Milk and cream,	
3.2	PL general population	1.3	Potatoes	0.5	Apples	0.4	Tomatoes	

Conclusion:
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.
A long-term intake of residues of BYI 02960 is unlikely to present a public health concern.

IIA 6.9.3 NESTI/IESTI calculations

The short-term dietary risk assessment for BYI 02960 was calculated based on the uses presented above (sections 6.3, 6.4, and 6.6.3) and on the Acute Reference Dose (ARfD) of 0.35 mg/kg body weight, which was derived from the acute neurotoxicity study in rats (cf. section 3, point 5.11).

The intake estimation was calculated using the EFSA PRIMo model (Version 2a) including diets from various countries in Europe. In a first, very conservative approach, the MRL values derived from supervised residues trials (total residues; as summarized in table 6.7.2.2-07) were used in the calculations for the edible part of plant commodities (as opposed to the standard approach using HR values). For animal matrices, MRL values were also used. The results of the calculations are summarized in the table below.

Table 6.9.3-1: BYI 02960 – IESTI calculation (EFSA/PRIMo rev. 2)
Calculation based on MRL values*

IESTI 1		IESTI 2	
% of the ARfD	**Commodity**	**% of the ARfD**	**Commodity**
Children			
83.9	Sweet corn	59.9	Sweet corn
65.9	Potatoes	56.1	Table grapes
56.1	Table grapes	52.2	Beans
53.8	Lettuce	47.1	Potatoes
52.3	Oranges*	45.2	Spinach
Adults	***(gen. population)***		
27.2	Table grapes	27.2	Table grapes
24.9	Sweet corn	21.3	Aubergines (eggplants)
22.0	Lettuce	20.3	Wine grapes
21.3	Aubergines (eggplants)	18.8	Purslane
20.7	Purslane	18.0	Beans

* Citrus values based on MRL-P of 1.38 mg/kg; MRL for the RAC 3.0mg/kg × avg. peeling factor 0.46 (cf. chapter 6)

The results summarised in table 6.9.3-1 indicate that the maximum contribution to the ARfD is approx. 84% for sweet corn (children, IESTI 1 calculation), and thus far below 100%. The second-highest value is for potatoes, at approx. 66%. (It should be noted that the intended primary use in lettuces does not include broad-leafed endive; use in "scarole" will not be registered in the EU and thus will not appear on any label. It is, however, included in the underlying risk-assessment calculation, due to the proposed MRL for rotational leafy vegetables.) The uses in citrus fruit were assessed incorporating the peeling factor, in order to include only the edible components of the fruit.

Despite using the most conservative approach for the assessment of the acute risk (based on MRLs instead of HRs), it is evident that no acute risk for consumers will arise from the uses of BYI 02960 as presented in this dossier.

IIA 6.10 Other/special studies

Report:	**KIIA 6.10/01, [redacted], [redacted]; 2012**
Title:	Systemicity of flupyradifurone and specific metabolites in tomato (foliar/soil application), melon (soil application) and cucumber (foliar application) under greenhouse conditions - Flupyradifurone SL 200 (200 g/L)
Report No & Document No:	MR-12/052 Date: 2012-07-11 M-434311-01-1
Guidelines:	Following Directive 91/414/EEC, residues in or on treated products, food and feed
GLP:	No

Executive Summary

The systemicity of BYI 02960, formulated as an SL 200, has been investigated in plants cultivated under greenhouse conditions using semi-quantitative autoradiographic methods and quantitative analysis. Besides the parent compound BYI 02960, also its key metabolites difluoroacetic acid (DFA), BYI 02960-difluoroethyl-amino-furanone (DFEAF) and 6-chloronicotinic acid (6-CNA) were included in the analysis.

In a first step, tomato, melon, and cucumber plants were treated with parent compound labelled either at the [pyridinylmethyl-^{14}C] or the [ethyl-1-^{14}C] moiety. The laballing positions allowed to trace either parent compound and the metabolite 6-CNA or parent compound and the metabolites DFA and DFEAF, respectively. The uptake and the the distribution of BYI 02960 and its metabolites was visualized by semi-quantitative autoradiography after defined droplet application of BYI 02960 200 SL at different points of the leaves or leaf axils. In a second step, a specially designed residue study was conducted in cucumber. Defined droplet application was conducted on cucumber leaves with non-radiolabelled BYI 02960 (formulated as an SL 200). Different plant parts were were sampled at different time points and analyzed for parent and the metabolites 6-CNA, DFA and DFEAF to elucidate the translocation behavior of the different compounds.

The autoradiographs showed a rapid acropetal uptake of radiolabelled compounds into the plant and translocation mainly via the <u>xylem</u> in direction of the transpiration stream followed by a translaminar distribution into adjacent plant cells. Radioactivity accumulated at the leaf margins over time. The autoradiograms indicated also a low translocation of radioactivity via the <u>phloem</u> into plant parts below the application points.

Analysis of cucumber leaves and fruits in the specially designed residue study confirmed that the parent compound and metabolite DFEAF were translocation mainly via the <u>xylem</u>. Transport of DFEAF from leaves into fruits was not observed, the concentration of the metabolite was always below the limit of quantification in cucumber fruits. Metabolite DFA was formed in treated leaves and translocated via the <u>phloem</u> into cucumber fruits growing in adjacent leaf axils of treated leaves and even in cucumber fruits growing in leaf axils of untreated leaves. This behavior was also observed for metabolite 6-CNA, however it was less distinct and only some cucumber fruits showed 6-CNA residues.

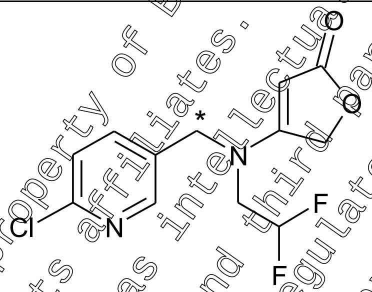
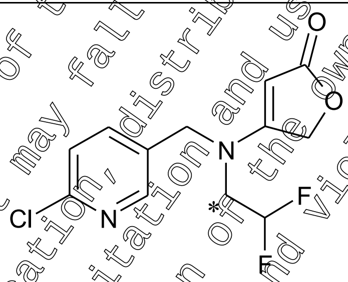
These analytical results are in line with the predictions made by the transport model according to Bromilow et al. which links the physico-chemical properties of compounds to their transport patterns in plants.

I. Materials and Methods

Autoradiography

A. Materials

1. Test Material

Test material for foliar and soil application of tomato plants and for soil application of melons	
Chemical structure	 * position of the radiolabel
Radiolabelled test material	[pyridinylmethyl-^{14}C]BYI 02960
Specific radioactivity	4.37 MBq/mg (118.08 µCi/mg)
Chemical Purity	> 99% (HPLC)
Radiochemical purity	> 99% (HPLC and TLC)
Test material for foliar application of cucumber plants	
Chemical structure	
Radiolabelled test material	[ethyl-1-^{14}C]BYI 02960
Specific radioactivity	3.93 MBq/mg (106.28 µCi/mg)
Chemical Purity	> 99% (HPLC)
Radiochemical purity	> 99% (HPLC and TLC)

Water solubility: 3240 mg/L
Log Pow at 25°C: 1.2
Koc: 98 mL/g

The radiolabelled test compounds were formulated as an SL 200.

2. Plants and Soil:

Crop	Soil
Tomato, variety "Rentita"	Sandy loam; pH $CaCl_2$ 6.7; total carbon 1.1%; sand 70.1%, silt 20.3%, clay 9.6%; pot. cation exchange capacity 57.7 mmol/kg
Cantaloupe (melon), variety "Magenta F1"	Sandy loam; pH $CaCl_2$ 6.7; total carbon 1.1%; sand 70.1%, silt 20.3%, clay 9.6%; pot. cation exchange capacity 57.7 mmol/kg
Cucumber, variety "Roxanna"	"Einheitserde ED 73"

B. Study Design

Experimental conditions:

Tomato, foliar application:

The tomato plants were cultivated in 5 L planting buckets filled with a sanly loam soil in a greenhouse of the test facility (controlled temperature, humidity and light conditions). Application of the formulated test compound was conducted with a micropipette according to three different scenarios:

Scenario 1:

10 µL droplet on center midrib of tomato leaf 7 containing 25 kBq [pyridinylmethyl-^{14}C] BYI 02960 added to a spray solution of 0.5 L BYI 02960 SL 200 in 300 L water/ha.

Scenario 2:

2x5 µL droplets on either side of the midrib of 2 center pinnate leaves of tomato leaf 8. 1 kBq [pyridinylmethyl-^{14}C]BYI 02960 added to a spray solution of 0.5 L BYI 02960 SL 200 in 300 L water/ha.

Scenario 3:

10 µL droplet on main stem above leaf 8. 25 kBq [pyridinylmethyl-^{14}C]BYI 02960 added to a spray solution of 0.5 L BYI 02960 SL 200 in 300 L water/ha.

Plants/shoots were sampled one and four days after the treatment, pressed and dried for 72 h at room temperature. The dried shoots were placed on phosphor images (Fuji-Fujix BAS Cassette 2040) for 72 h. The images were analysed with a Fujifilm BAS 2500 scanner and semi-quantitative evaluation was performed with the AIDA Image Analyzer v.4.14.

Tomato and melon, soil drench application:

The tomato/melon plants were cultivated in 5 L planting buckets filled with a sanly loam soil in a greenhouse of the test facility (controlled temperature, humidity and light conditions). The formulated test compound [pyridinylmethyl-^{14}C]BYI 02960 was applied with a measuring cylinder in a circular ring cavity of 11 cm in diameter around each plant, to achieve a homogeneous distribution of radioactivity in each pot. The drench solution was prepared by adding a defined amount of the radiolabelled active substance to the non-radiolabelled formulation BYI 02960 SL 200. Each tomato plant received 24 mg and each melon plant 36 mg parent BYI 02960.

Tomato plants/shoots were sampled 1, 3, 7, 14 and 21 days after the treatment and the melon plant at 31 days after treatment, pressed and dried between two sheets of absorbent filter paper at 50 °C for 24 h. The dried shoots were placed on phosphor images (Fuji-Fujix BAS Cassette 2040) for 6 days.

The images were analysed with a Fujifilm BAS 2500 scanner and semi-quantitative evaluation was performed with the AIDA Image Analyzer v.4.14.

Cucumber, foliar application:

The cucumber plants were cultivated in 5 L planting buckets filled with Einheitserde ED 73 in a greenhouse of the test facility (controlled temperature, humidity and light conditions). Application of the formulated test compound was conducted with a micropipette according to two different scenarios:

Scenario 1:

2 single droplets (2 x 10 µL) on either side of the center midrib of leaf 4. Each droplet contained 25 kBq [ethyl-1-^{14}C]BYI 02960.

Scenario 2:

A single 10 µL droplet onto leaf axil of leaf 4. Each droplet contained 25 kBq [ethyl-1-^{14}C]BYI 02960.

Plants/shoots were sampled 1, 4, 7 and 14 days after the treatment, pressed and dried for 48 h at room temperature. The dried shoots were placed on phosphor images (Fuji-Fujix BAS Cassette 2040) for 96 h. The images were analysed with a Fujifilm BAS 2500 scanner and semi-quantitative evaluation was performed with the AIDA Image Analyzer v.4.14.

Specially designed residue study

One trial in cucumber was conducted in the greenhouse, as follows:

22 cucumber plants (variety Roxana), cultivated in 30 L-planting pots, were treated with BYI 02960 SL 200. Two applications were made, each at a nominal rate of 0.125 kg a.s./ha x m canopy height (CH); the water rate was 750 L/ha x m CH, reflecting local practice. The canopy height of the plants was approx. 2 m since the main shoot of the cucumber plants was trimmed at that height. The first application was conducted at a BBCH stage of approx. 17-19, 13 days before the first harvest of fruits; the second application was conducted 10 days later. The spray liquid was applied onto 5 marked leaves using a lab sprayer which allowed to treat only the upper surface of the leaves. The five treated leaves (leaf level 1 to 5) were located above five untreated leaves (leaf level 0). Above the treated leaves were another six untreated leves (leaf level 6 to 11). During application, the soil of the planting pots was covered with aluminium foil and the leaves, fruitlets and shoot parts of the leaf levels 0 and 6 to 11 were protected by PE bags and foil to prevent contamination.

Mature cucumbers were sampled 3, 7, 14, 21 and 28 days after the last sampling. At each sampling date, 4 fruits were collected from the treated zone (leaf level 1 to 5), 4 fruits from the untreated zone located above (leaf level 5 to 11) and 4 fruits from the untreated zone located below (leaf level 0).

The samples were analyzed for the parent compound and its metabolites 6-CNA, DFA and DFEAF by LC-MS/MS using methods 01304. The respective LOQs for the 4 analytes were 0.01, 0.01, 0.02, and 0.01 mg/kg (all in parent equivalents).

II. Findings

Autoradiography

The translocation experiments with [pyridinylmethyl-^{14}C]- and [ethyl-1-^{14}C]BYI 02960 after foliar application of tomato and cucumber plants showed a rapid acropetal uptake of the radioactivity into the plant and translocation mainly via the xylem in direction of the transpiration stream followed by a translaminar distribution into adjacent plant cells. Radioactivity accumulated at the leaf margins over time. Autoradiographs indicated also a translocation of radioactive compounds via the phloem into plant parts below and above the application points *viz.* leaves, stems, petioles, tendrils, flowers and fruitlets. The phloem transport was more distinct after application of [ethyl-1-^{14}C]BYI 02960.

The translocation behavior of [pyridinylmethyl-^{14}C]BYI 02960 and its metabolites in tomato and melon after soil drench application was comparable to the behavior after foliar aooplication. The radioactivity (parent BYI 02960 and metabolites) was rapidly taken up via the root system and translocated within 1-24 (31) days after treatment via the xylem in direction of the transpiration stream into the shoot followed by a translaminar distribution into the leaves. Over time, radiolabelled compounds accumulated at the leaf margins while leaf laminae were gradually depleted.

Several models have been proposed to explain and predict the transport patterns of agricultural chemicals in plants. In general, they suggest that the extent to which a chemical is moved systemically in plants is principally regulated by its physico-chemical properties. According to the Bromilow model (1991), the two typical characteristics that have been highly correlated with xylem and phloem systemicity of chemicals in plants are the octanol/water partition coefficient log K_{OW} and the dissociation constant pKa of the compound. For non-dissociating chemicals the log K_{OW} is the predominant parameter, and models established with diverse pesticides demonstrate that those with a log K_{OW} in the range of -3 to 0 are ambimobile, 0 to 4 are xylem mobile, and over 4 they are generally non-systemic.

Of course, the discrete ranges of log K_{OW} in this classification are subject to exceptions and there are compounds that fall out of these general classes. In addition, if the molecules possess an ionisable functionality (e.g. carboxylic, amino, sulfonyl urea functions etc.) this can dramatically alter the transport patterns in plants due to differences in the pH present in the different plant compartments. It is known that the xylem is slightly acid (pH < 7) and the phloem slightly basic (pH > 7). The apparent transport patterns of chemicals can also be significantly modified by a number of factors including metabolism, adsorption to cellular constituents, phytotoxicity, and sequestration of the compounds in vacuoles.

On the basis of the translocation model, the observed translocation behaviour of BYI 02960 can be assigned to the parent compound and the metabolites detected in the plant metabolism studies:
BYI 02960 does not possess chemical groups that can be ionized/dissociated at a physiological pH and a log K_{OW} being in the range of 0 to 4; therefore the transport models predict mobility in the xylem, only. Metabolite BYI 02960-difluoroethyl- amino-furanone (DFEAF) does also not possess chemical groups that can be ionized/dissociated at a physiological pH, however a log K_{OW} being in the range of -3 to 0. Thus the metabolite is ambimobile and can be transported in the xylem and the phloem. Metabolite difluoroacetic acid (DFA), which is a strong acid with a pKa of 1.1 and a log K_{OW} of < -3 is

expected to be transported via the phloem according to the models. The minor metabolite 6-CNA, which is a weak acid (pK_a = 3.2) should show very good phloem mobility, as well.

To confirm the model predictions, the specially designed residue study was evaluated.

Specially designed residue study

In the specially designed residue study, BYI 02960 was applied on cucumber leaf sheaths (leaf 1 to 5) and the residue levels of BYI 02960, DFA, DFEAF and 6-CNA were determined in mature fruits of lower and higher plant parts at different time points (3, 7, 14, 21 and 28 days after application). Only DFA was detected in significant concentrations in fruits, i.e. in cucumbers growing in adjacent leaf axils of the treated leaves and even in cucumbers growing in leaf axils of untreated leaves, indicating the phloem mobility of this metabolite. Highest DFA levels (approx. 0.5 mg/kg) in fruits of the untreated zone were found in cucumbers sampled 14 and 21 days after application. DFEAF was not detected in cucumber fruits of the untreated zone, and parent compound BYI 02960 and 6-CNA were detected in trace levels and in some fruit samples, only. However, this is not very surprising since DFEAF and 6-CNA were only very minor or minor metabolites in all metabolism studies and therefore the expected concentration levels have to be very low; parent compound BYI 02960 was not expected to be phloem mobile due to its pysicochemical properties. Certainly the study showed that DFA is phloem mobile and can be transported within the plant along with the flow of photosynthesis products. This finding is agreement with the observation of the autoradiography experiments which showed that the phloem transport was more distinct after application of [ethyl-1-^{14}C]BYI 02960.

III. Conclusions

The translocation behaviour and the systemicity, predicted by the translocation model of Bromilow et al. on the basis of the physicochemical properties (log Kow and pKa) of the parent compound and its major metabolites, was confirmed in translocation experiments with radiolabelled parent compound (by semi-quantitative autoradiographic methods) and in an additional residue experiment in cucumber (analysis of leaves and fruits after application of selected leaves or plant parts). Following foliar spray or soil drench application, a rapid acropetal uptake of BYI 02960 into the plant is observed. Translocation of the parent compound is mainly via the xylem in direction of the transpiration stream. A translaminar distribution into adjacent plant cells is also observed. The major plant metabolite DFA shows phloem mobility and can therefore be redistributed, along with the flow of photosynthesis products, out of the leaves into e.g. developing seeds and fruits. Theoretically, a higher proportion of 6-CNA was expected to be translocated via the phloem due to its more favourable physicochemical properties, however this was not confirmed by the experiments. Metabolite DFA was the predominant compound translocated via the phloem.

Report:	**KIIA 6.10/02, [redacted]; 2012**
Title:	Uptake of aged BYI 02960 residues in succeeding crops
Report No. & Document No.:	Not applicable (position paper) M-434690-01-1
Guidelines:	Not applicable
GLP:	Not applicable

Background

The new insecticide BYI 02960 (common name: flupyradifurone) can be used in a wide range of food and feed crops after foliar or soil application.

The aerobic degradation of BYI 02960 in soil was investigated in laboratory and field studies. The primary metabolic pathway of BYI 02960 in soil is molecular cleavage resulting in the metabolites difluoroacetic acid (DFA) and 6-chloronicotinic acid (6-CNA). DFA has been identified in all soils tested, with a maximum percentage of 34%. 6-CNA was identified in several soils tested with a maximum percentage of 17%. Further microbial breakdown led to the formation of significant amounts of carbon dioxide (up to 54%) and soil-bound residues.

The biotransformation of BYI 02960 was studied in several EU and US soils under standardized aerobic laboratory conditions, as well as in a terrestrial field dissipation study performed at different sites in Europe and North America. BYI 02960 was found to be moderately degradable in aerobic soil under laboratory as well as under field conditions. The clear biphasic degradation kinetics indicates that the compound is less available for biotransformation with time, probably due to a time-dependent sorption behavior in soil. The data for the metabolite 6-CNA indicate that it is very rapidly degraded in soil, with a mean DT_{50} of < 1 week. The metabolite DFA yielded a slightly longer DT_{50}, i.e. it was calculated to be in the range of approx. 2 months. The calculated DT_{50} of BYI 02960 ranged between 8.3 and 251 days in the field dissipation studies.. In general, the field dissipation observed for BYI 02960 residues, i.e. for BYI 02960 and its main soil metabolite DFA, was comparable to that found within the standardized laboratory studies. Applying the mean SFO model, a DT_{50} of 204.2 days can be estimated for BYI 02960 residues.

Therefore, the exposure of following crops to BYI 02960 soil residues cannot be excluded and thus the metabolism of BYI 02960 was investigated in representative rotational crops (wheat, Swiss chard and turnips) following soil application of either [pyridinylmethyl-UL-^{14}C] or [furanone-4-^{14}C] radio-labelled active substance. The application rates were slightly above the anticipated US maximum field rate of 400 g a.s./ha. [Ethyl-1-^{14}C]BYI 02960 was not available for a confined rotational crop (CRC) study when the studies were started. Therefore, no detection of ^{14}C-difluoroacetic acid was possible. To estimate the residue levels of difluoroacetic acid in the crop samples, non-radiolabelled difluoroacetic acid was analyzed in the samples originating from the CRC studies with the furanone label by HPLC-MSMS according to the conditions of residue analytical method 01304 (see KIIA 6.2.1/12).

The nature and level of residues in succeeding crops is influenced by the amount of active ingredient applied to the soil, by the degradation behavior in soil, and by the uptake of parent compound and soil metabolites by the roots.

Aim of the position paper

The aim of the position paper submitted here (KIIA 6.10/02) is to evaluate if the plant uptake of BYI 02960 residues changes with time, i.e. if the ageing of the soil residues (e.g. due to formation of bound residues and increased sorption over time) results in lower plant uptake and therefore in lower plant residues.

Confined rotational crop studies

The metabolism of the insecticide BYI 02960 was investigated in the representative rotational crops wheat, Swiss chard, and turnips from three consecutive rotations. Two studies were conducted, one with [furanone-4-^{14}C]BYI 02960 and the other with [pyridinylmethyl-^{14}C]BYI 02960. [^{14}C]BYI 02960 was formulated as an SL 200 and sprayed onto the soil of a planting container (approx. 1 m^2). The actual application rate corresponded to 436 g a.s./ha or 433 g a.s./ha, and was slightly above the anticipated maximum seasonal US field rate of 400 g a.s./ha. The crops were each sown at 29, 135, and 296 days after the soil application, representing the first, second, and third rotations, respectively.

Intermediate raw agricultural commodities (RACs) investigated were immature Swiss chard as well as wheat forage and wheat hay. All other RACs (wheat straw, wheat grain, Swiss chard, turnip leaves, and turnip roots) were harvested at maturity.

The TRR values for all RACs are given in the following table.

Table 6.10-1: TRR values in the different RACs of the three rotations after soil application of [furanone-4-^{14}C]BYI 02960 (436 g a.s./ha)

Rotation	TRR [mg/kg]							
	Wheat				Swiss chard		Turnips	
	forage	hay	straw	grain	imm.	mature	leaves	roots
1st rotation	0.783	2.003	6.290	0.478	0.848	0.871	0.679	0.074
2nd rotation	0.193	1.081	1.519	0.103	0.311	0.263	0.158	0.014
3rd rotation	0.111	0.254	0.462	0.047	0.180	0.152	0.090	0.008

Table 6.10-2: TRR values in the different RACs of the three rotations after soil application of [pyridinylmethyl-^{14}C]BYI 02960 (433 g a.s./ha)

Rotation	TRR [mg/kg]							
	Wheat				Swiss chard		Turnips	
	forage	hay	straw	grain	imm.	mature	leaves	roots
1st rotation	1.407	2.409	9.015	0.177	1.358	1.483	0.815	0.072
2nd rotation	0.308	1.009	2.148	0.057	0.332	0.438	0.239	0.022
3rd rotation	0.117	0.321	0.491	0.017	0.135	0.130	0.083	0.008

Since no confined rotational crop study was conducted with [ethyl-1-^{14}C]BYI 02960, hypothetical TRR values were estimated on the basis of the (non-radioactive) DFA concentrations measured by HPLC-MS/MS in the crop matrices collected in the study with [furanone-4-^{14}C]BYI 02960.

Table 6.10-3: Summary of difluoroacetic acid residues measured by LC-MS/MS in rotational crop matrices after soil application of BYI 02960

Metabolism study	Rotation	Crop	Sample material	Residues [mg/kg]	Residues [mg a.s. equiv./kg]
Metabolism of [furanone-4-^{14}C]BYI 02960 in Confined Rotational Crops	1st rotation	wheat	forage	0.09	0.27
			hay	0.32	0.96
			straw	0.20	0.60
			grain	1.15	3.45
		Swiss chard	intermediate	0.08	0.24
			mature	0.16	0.48
		turnip	leaves	0.08	0.24
			roots	0.02	0.06
	2nd rotation	wheat	forage	0.02	0.06
			hay	0.14	0.42
			straw	0.06	0.18
			grain	0.26	0.78
		Swiss chard	intermediate	0.04	0.12
			mature	0.05	0.15
		turnip	leaves	0.03	0.09
			roots	< 0.01	< 0.03
	3rd rotation	wheat	forage	< 0.01	< 0.03
			hay	0.01	0.03
			straw	0.02	0.06
			grain	0.05	0.15
		Swiss chard	intermediate	< 0.01	< 0.03
			mature	0.01	0.03
		turnip	leaves	< 0.01	< 0.03
			roots	< 0.01	< 0.03

The TRR values for all matrices were estimated by subtracting the concentrations of all metabolites label-specific to the [furanone-4-^{14}C]label, and then adding the measured DFA concentration.

Example:
[Furanone-4-^{14}C]BYI 02960: TRR (forage, 1st rotation) = 0.783 mg/kg
Label-specific metabolites:

- BYI 02960-aminofuranone: 0.015 mg/kg
- BYI 02960-mercapto-lactic acid: 0.013 mg/kg
- BYI 02960-bromo-aminofuranone: 0.016 mg/kg
- BYI 02960-difluoroethyl-amino-furanone-OH-glyc: 0.025 mg/kg
- BYI 02960-difluoroethyl-amino-furanone: 0.077 mg/kg

⇨ Sum of label specific metabolites: 0.146 mg/kg
⇨ DFA concentration measured in wheat forage: 0.27 mg/kg

Estimated TRR: 0.783 mg/kg – 0.146 mg/kg + 0.27 mg/kg = 0.907

Table 6.10-4: Estimated TRR values in the different RACs of the three rotations after soil application of [ethyl-1-^{14}C]BYI 02960 (436 g a.s./ha)

Rotation	Estimated TRR [mg/kg]							
	Wheat				Swiss chard		Turnips	
	forage	hay	straw	grain	imm.	mature	leaves	roots
1st rotation	0.907	2.525	5.522	3.588	0.932	1.169	0.906	0.128
2nd rotation	0.221	1.137	1.273	0.812	0.372	0.344	0.245	0.042
3rd rotation	0.079	0.152	0.334	0.197*	0.179	0.122	0.117	0.038

* TRR was not corrected for label-specific metabolites since no identification of residues was possible due to the low absolute residue level. Thus:
hypothetical residue = TRR (furanone label) + DFA concentration

The measured and the estimated TRR values show that the residues in all plant matrices decline from the first to the third rotation.

Estimation of plant uptake

To estimate the plant uptake at different time points, the ratio of "BYI 02960 residues in soil at sowing of crop" to "measured residue in crop matrix at harvest" was calculated for all three rotations.

The BYI 02960 soil residues were estimated on the basis of a single first-order kinetic model (SFO) with a mean DT_{50} of 204.2 days, which reflects a conservative scenario.

Table 6.10-5: Estimated BYI 02960 residues in soil according to the SFO model (DT_{50} = 204.2 days, mixing depth = 0.1 m)

Time [d]	Initial application rate: 436 g a.s./ha	Initial application rate: 433 g a.s./ha
	BYI 02960 residues in soil [mg/kg]	
0	0.291	0.289
29 (1st rotation)	0.263	0.262
135 (2nd rotation)	0.184	0.183
296 (3rd rotation)	0.106	0.106

The rotational crops were sown at day 29 (1st rotation), day 135 (2nd rotation), and day 296 (3rd rotation). After harvest of the immature/mature crop, the TRR in each crop matrix was determined.

Table 6.10-6: [Furanone-4-^{14}C]BYI 02960: TRR values after initial application of 436 g a.s./ha and calculated ratio (soil residue/ crop residue)

Rotation	TRR [mg/kg]							
	Wheat				Swiss chard		Turnips	
	forage	hay	straw	grain	imm.	mature	leaves	roots
1st rotation	0.783	2.003	6.290	0.478	0.848	0.871	0.679	0.074
2nd rotation	0.193	1.081	1.519	0.103	0.311	0.263	0.158	0.014
3rd rotation	0.111	0.254	0.462	0.047	0.180	0.152	0.090	0.008
Ratio (residues in soil / residues in plant)								
1st rotation	0.336	0.131	0.042	0.550	0.310	0.302	0.387	3.554
2nd rotation	0.953	0.170	0.121	1.786	0.592	0.700	1.165	13.143
3rd rotation	0.955	0.417	0.229	2.255	0.589	0.697	1.178	13.250

Table 6.10-7: [Pyridinylmethyl-^{14}C]BYI 02960: TRR values after initial application of 433 g a.s./ha and calculated ratio (soil residue/ crop residue)

Rotation	TRR [mg/kg]							
	Wheat				Swiss chard		Turnips	
	forage	hay	straw	grain	imm.	mature	leaves	roots
1st rotation	1.407	2.409	9.015	0.177	1.358	1.483	0.815	0.072
2nd rotation	0.308	1.009	2.148	0.057	0.332	0.438	0.230	0.022
3rd rotation	0.117	0.321	0.491	0.017	0.135	0.130	0.083	0.008
Ratio (residues in soil / residues in plant)								
1st rotation	0.186	0.109	0.029	1.480	0.193	0.177	0.321	3.639
2nd rotation	0.594	0.181	0.085	3.211	0.551	0.418	0.796	8.318
3rd rotation	0.906	0.330	0.216	6.235	0.785	0.815	1.277	13.250

Table 6.10-8: [Ethyl-1-^{14}C]BYI 02960: Hypothetical TRR values after initial application of 436 g a.s./ha and calculated ratio (soil residue/ crop residue)

Rotation	Hypothetical TRR [mg/kg]							
	Wheat				Swiss chard		Turnips	
	forage	hay	straw	grain	imm.	mature	leaves	roots
1st rotation	0.907	2.525	5.522	3.588	0.932	1.169	0.906	0.128
2nd rotation	0.221	1.137	1.273	0.812	0.372	0.344	0.245	0.042
3rd rotation	0.079	0.152	0.334	0.197*	0.179	0.122	0.117	0.038
Ratio (residues in soil / residues in plant)								
1st rotation	0.290	0.104	0.048	0.073	0.282	0.225	0.290	2.055
2nd rotation	0.833	0.162	0.145	0.227	0.495	0.535	0.751	4.381
3rd rotation	1.342	0.697	0.317	0.538	0.592	0.869	0.906	2.789

* TRR was not corrected for label-specific metabolites since no identification of residues was possible due to the low absolute residue level, thus:
hypothetical residue = TRR (furanone label) + DFA concentration

Regarding the ratios, it becomes obvious that aged soil residues are less accessible for plant uptake. Considering the ratio "*soil residues at 29 days / crop residue at harvest of 1st rotation*" as the initial ratio, all ratios calculated for the second or third rotation are higher, independent of the crop. From the first to the second rotation, the ratio increases by a factor ranging between 1.3 and 3.7; and from the first to the third rotation, by a factor of 1.4 to 7.4. Thus, an increasing ratio was observed for all crops over the time. For Swiss chard and turnip root,s the ratio calculated for the third rotation was slightly lower compared to the second rotation with regard to one radiolabel; however the ratios for the later rotations were always higher than those calculated for the first rotation. Therefore it can be concluded that aged soil residues will result in lower crop residues due to a limited uptake. The proportion which can be taken up can be estimated on the basis of the calculated ratios.

Example for wheat forage (furanone-label):

Soil concentration at 29 days (sowing of crops of 1st rotation): 0.263 mg/kg
Concentration in wheat forage at harvest (1st rotation): 0.783 mg/kg
⇨ Ratio (residues in soil / residues in plant): 0.336

Soil concentration after 296 days (sowing of crops of 3rd rotation): 0.106 mg/kg

Assuming that the same proportion of residues is always taken up by the plant within a defined period, the residue concentration in the plant can be calculated on basis of the soil concentration and the ratio estimated for the 1st rotation:
Concentration in the plant = soil concentration / ratio = 0.106 mg/kg / 0.336 = 0.315 mg/kg

However, the actual measured concentration in the plant was significantly lower (0.111 mg/kg), indicating that the soil residues were less accessible (only 35% was accessible for plant uptake).

The accessible amount was calculated for each crop matrix, as summarized in table 6.10-9.

Table 6.10-9: Accessible amount of aged residues for different crops after approx. 1 year (350 days)

Label	Accessible amount of aged residues (%)							
	Wheat				Swiss chard		Turnips	
	forage	hay	straw	grain	imm.	mature	leaves	Roots
furanone-label	35	31	18	24	53	43	33	27
pyridinylmethyl-label	21	33	13	24	25	22	25	27
ethyl-label	22	15	15	14	48	26	32	74*
average:	**26**	**26**	**15**	**21**	**42**	**30**	**30**	**43**

* overestimated value, residue of main metabolite was below the LOQ, but calculated at LOQ

These calculations indicate that a maximum 42% to 43% of the aged soil residue is accessible for plant uptake. Thus, when estimating plant residues of crops grown on soil which was treated annually at the maximum rate of 450 g BYI 02960/ha, two processes have to be considered – on the one hand, the concentration of the residues in the soil until a plateau concentration is reached at steady state, and on the other, the accessibility of the residues due to ageing processes.

Based on the half-life of BYI 02960 in soil of 204.4 days, and with an annual application of 450 g a.s./ha, soil concentrations can be calculated at various times until a steady-state peak concentration is reached. These values are shown in table 6.10-10.

Table 6.10-10: Estimated soil concentrations according to the SFO model and resulting key parameters

Half-life (d)	204.4
Annual application (g a.s./ha)	450
Soil concentration (mg a.s./kg soil) in the surface 10 cm immediately after 1st application (Year 0)	0.30
Soil concentration (mg a.s./kg soil) in the surface 10 cm immediately before 2nd application (Year 1)	0.09
Soil concentration (mg a.s./kg soil) in the surface 10 cm prior to next annual application at steady state	0.12
Annual carryover (% of residues present immediately after the previous year's application)	29.1
Steady state peak concentration (mg a.s./kg soil)	0.42 (1.41 × initial value)
Year when steady state has reached	~ year 3

The steady-state peak concentration of 0.42 mg/kg is comprised of 0.30 mg/kg from the immediately preceding annual application, and 0.12 mg/kg carried over from previous applications. The 0.12 mg/kg portion is aged soil residue, of which, as was shown in table 6.10-9, at most 42% is accessible to plants. Therefore the concentration of residue accessible for plant uptake at the steady-state peak concentration is 0.30 mg/kg + (42% of 0.12 mg/kg ⇒ 0.05 mg/kg) = 0.35 mg/kg; this value is 1.17 times (0.35 mg/kg/0.30 mg/kg = 1.17) the concentration in soil immediately following a single application at the annual rate.

Therefore, following annual applications of BYI 02960 at 450 g a.s./ha to the point at which the steady-state peak soil concentration is reached, the soil residues accessible for plant uptake can be considered to be a maximum of 1.2 times the residue levels accessible following a single application at the annual rate.

IIA 6.11 Summary and evaluation of residue behaviour and reasonable grounds

IIA 6.11.1 Summary and evaluation of residue behaviour

Summary of plant metabolism:

The metabolism of BYI 02960 was investigated in five target crops (tomato, potato, apple, cotton and rice) following application of [furanone-4-^{14}C]BYI 02960 and [pyridinylmethyl-^{14}C]BYI 02960. Additionally, [ethyl-1-^{14}C]BYI 02960 was applied in one tomato metabolism study. In all other plant metabolism studies, the fate of the difluoroethane moiety of the active substance was tracked by analysing extracts of all RACs for non-radiolabelled difluoroacetic acid, the most plausible metabolite which can be formed from the moiety after cleavage of the parent compound. The analysis of difluoroacetic acid was initiated after detecting difluoroacetic acid as a major soil metabolite in the aerobic soil degradation studies.

The active substance was applied either as an SL formulation for drench and foliar application, an FS formulation for seed/tuber treatment or as a granule to cover the special application technique in rice in Japan.

One to two spray applications were conducted in apples, cotton and rice with a maximum seasonal application rate of 400 g a.s./ha. In rice, additionally a granule application was conducted at the same maximum seasonal application rate. Soil treatments were performed in tomato (drench application) and in potato (in-furrow application) at a maximum seasonal application rate of 600 g a.s./ha. Tuber treatment of potatoes was also conducted with a dressing rate of 10 g a.s./dt (corresponding to approx. 250 g a.s./ha).

An overview of the use pattern from the metabolism studies in target plants is summarized in Table 6.11.1-1

Table 6.11.1-1 Use patterns in the target plant metabolism studies

Crop	Radiolabel	Appl. technique	No. of appl.	Actul single application rate	Appl. interval [days]	BBCH growth stage	PHI [days]
Tomato	[furanone-4-^{14}C], [pyridylmethyl-^{14}C], [ethyl-1-^{14}C]	drench appl.	2	300 g a.s./ha 300 g a.s./ha 300 g a.s./ha	14	14-15 51-59	56-86[1]
Potato	[furanone-4-^{14}C], [pyridylmethyl-^{14}C]	tuber treatment	1	10 g a.s./dt = 245 g a.s./ha or = 270 g a.s./ha	-	03	97
Potato	[furanone-4-^{14}C], [pyridylmethyl-^{14}C]	in-furrow appl.	1	626 g a.s./ha 626 g a.s./ha	-	03	97
Apple	[furanone-4-^{14}C], [pyridylmethyl-^{14}C]	spray appl.	1	86 g/(ha x m CH) 87 g/(ha x m CH)	-	69	98
Apple	[furanone-4-^{14}C], [pyridylmethyl-^{14}C]	spray appl.	2	86 & 86 g/(ha x m CH) 85 & 87 g/(ha x m CH)	14	69 85	14
Cotton	[furanone-4-^{14}C], [pyridylmethyl-^{14}C]	spray appl.	1	209 g a.s./ha	-	16	169
Cotton	[furanone-4-^{14}C], [pyridylmethyl-^{14}C]	spray appl.	2	209 & 176 g a.s./ha 206 & 177 g a.s./ha	155	15-16 95-97	14
Rice	[furanone-4-^{14}C], [pyridylmethyl-^{14}C]	granular appl.	1	409 g a.s./ha 434 g a.s./ha	-	13-15	127
Rice	[furanone-4-^{14}C], [pyridylmethyl-^{14}C]	spray appl.	2	175 & 240 g a.s./ha 178 & 236 g a.s./ha	97	13-15 87-89	29

[1] harvest period of approx. 4 weeks since tomato fruits ripen continuously

The total radioactive residues (TRR) of the raw agricultural commodities (RACs) of all target crops are summarized in Table 6.11.1-2. The TRR values were low in all edible matrices (max. 1.286 mg/kg in apple fruits in the double spray experiment).

Table 6.11.1-2 Total radioactive residues (TRR) in plant matrices under investigation

RAC		**TRR (mg/kg)** [furanone-4-UL-^{14}C]	**TRR (mg/kg)** [pyridinylmethyl-^{14}C]	**TRR (mg/kg)** [ethyl-1-^{14}C]
Tomato fruits	drench appl.	0.096	0.130	0.201
Tomato flowers	drench appl.	0.721	1.254	2.230
Potato tubers	tuber treatment	0.078	0.076	(0.441)[3]
Potato tubers	in-furrow	0.171	0.115	(0.618)[3]
Apple fruits	single spray	0.280	0.079	(0.760)[3]
Apple leaves	single spray	38.957	56.715	n.c.
Apple fruits[1]	double spray	1.133	1.868	n.c.
Apple fruits[2]	double spray	1.286	0.545	(1.221)[3]
Apple leaves	double spray	102.919	134.841	(99.846)[3]
Cotton intermediate	single spray	12.391	14.153	n.c.
Cotton gin trash	single spray	0.191	0.310	(0.367)[3]
Cotton lint	single spray	0.009	0.007	n.c.
Cotton seeds	single spray	0.013	0.045	(0.135)[4]
Cotton gin trash	double spray	2.767	2.344	(2.351)[3]
Cotton lint	double spray	4.993	8.846	n.c.
Cotton seeds	double spray	0.016	0.068	(0.125)[3]
Rice kernels	granule appl.	0.140	0.050	(0.288)[3]
Rice husks	granule appl.	1.404	1.602	(2.973)[3]
Rice straw	granule appl.	2.879	3.280	(4.325)[3]
Rice kernels	spray appl.	0.659	0.620	(0.661)[3]
Rice husks	spray appl.	24.098	23.957	(24.450)[3]
Rice straw	spray appl.	19.891	24.731	(24.790)[3]

1 with surface wash
2 without surface wash
3 estimated TRR in hypothetical metabolism study with [ethyl-1-^{14}C]BYI 02960 (for explanation see below)
4 worst case TRR in hypothetical metabolism study with [ethyl-1-^{14}C]BYI 02960 since no analysis of the seed extract was performed and therefore no information on label-specific metabolites is available; DFA residue was added to TRR determined in metabolism study
n.c. not calculated since intermediate extract was not analysed for DFA residues

Example for estimation of a hypothetical TRR (TRR of apple fruit in the single application experiment):

1. DFA was analysed in the apple extract obtained in the metabolism study with [furanone-4-^{14}C]BYI 0260
   ⇨ 0.23 mg DFA/kg, corresponding to 0.69 mg a.s. equiv./kg (see KIIA 6.2.1/12)
2. TRR determined in apple fruit extract: 0.280 mg a.s. equiv./kg (see KIIA 6.2.1/06)
   ⇨ all label-specific metabolites detected are subtracted from the TRR to get a TRR that is based on parent compound and metabolites common to all three radiolabels only (= corrected TRR):
   0.280 mg/kg – 0.201 mg/kg (glucose) – 0.009 mg/kg (BYI 02960-difluoroethyl-amino-furanone) = 0.070 mg/kg
3. A hypothetical TRR is calculated by adding the DFA residue to the corrected TRR:
   0.070 mg/kg + 0.69 mg/kg = 0.76 mg/kg

Corresponding TRR values of sample matrices were very well comparable when considering the studies performed with [furanone-4-^{14}C]BYI 02960 and [pyridinylmethyl-^{14}C]BYI 0296. Only for the apple and some of the cotton matrices significant differing TTR values were determined. These differences can be traced back to some label-specific metabolites. These metabolites show a different uptake and/or translocation behaviour compared to the parent compound and concentrate in varying compartments of the crop. For example, radiolabelled glucose, a natural product formed after complete cleavage of the furanone moiety of the parent compound, can be found in high concentrations in the repository organ of apples – the fruits. Thus, the TRR in fruits is significant higher in the study performed with [furanone-4-^{14}C]BYI 02960, which allows the detection of the natural compound by incorporated radioactivity. Another example is metabolite 6-CNA, a weak acid that shows a pronounced phloem mobility and is therefore transported selectively into the cotton seeds as phloem sink. This behaviour seems even more distinct for the metabolite difluoroacetic acid. Based on the "cold analysis" of the metabolite in representative extracts of all plant metabolism studies, high concentrations of difluoroacetic acid are present in potato tubers, all fruits and in seeds/kernels. Thus, the hypothetical TRR values estimated for these matrices are generally higher compared to the measured TRR values in the studies performed with [furanone-4-^{14}C]BYI 02960 and [pyridinylmethyl-^{14}C]BYI 0296. The tomato metabolism study with [ethyl-1-^{14}C]BYI 02960 confirmed these results. It showed also very high concentrations of difluoroacetic acid in fruits (> 80% of the TRR) and a TRR that was significant higher (by a factor of approx. 2) compared to the studies performed with the other radiolabels.

Thus metabolite difluoroacetic acid was the main compound detected in tomato fruits and flowers, in potato tubers, in apple fruits after early spray application of the a.s., in rice kernels after granule application and in cotton seeds in both application scenarios and in cotton gin trash after early spray application. The difluoroacetic acid proportion was generally higher if the crop was treated at an early growth stage, only. Certainly, a second late application with the active substance shifted the proportion in favour of the parent compound. Thus, parent compound was the main constituent in apple fruits, in rice kernels and as well in cotton gin trash after a second late spray treatment. However, parent compound was always an prominant constituent of the residue. In rice husks and straw, as well as in the cotton intermediate, parent compound was the main compound even after one early application. In tomato fruits and potato tubers, parent compound was the second most common constituent considering all application scenarios. Overall, major compounds detected in the studies were the metabolites 6-CNA, BYI 02960-CHMP-glyc and -CHMP-di-glyc, glucose, BYI 02960-difluoroethyl-amino-furanone and BYI 02960-OH-glyc besides difluoroacetic acid and parent compound. The amounts of parent compound and these metabolites in edible matrices of target crops are shown in Table 6.11.1-3 (single application) and Table 6.11.1-4 (double application).

Table 6.11.1-3 Residues [mg a.s. equiv./kg] of BYI 02960 and major metabolites in edible matrices after one application

Compound (BYI 02960-)	**potato tubers**				**apple fruits**		**rice kernels**		**cotton seeds**	
	tuber treatment		in-furrow appl.		foliar appl.		granule appl.		foliar appl.	
Label:	F	P	F	P	F	P	F	P	F	P
TRR:	**0.078**	**0.076**	**0.171**	**0.115**	**0.280**	**0.079**	**0.140**	**0.050**	**0.013[2]**	**0.045[2]**
BYI 02960	0.031	0.031	0.097	0.051	0.021	0.034	0.032	0.035		
DFA		0.39[1]		0.54[1]	0.69[1]			0.06[1]		0.09[1]
glucose/carbohydr.	---		---		0.201		0.038			
6-CNA		0.016		0.021		0.004		0.002		
CHPM-di-glyc		0.003		0.006		---		---		
CHMP-glyc		0.003		0.003		0.004		---		
difluoroethyl-amino-furanone	0.003		0.005		0.009		---			
OH-glyc	0.005	0.005	0.007	0.005	0.001	0.004	---	---		

1 LC-MS/MS analysis of non-radiolabelled DFA in the extract obtained in the metabolism study
2 analysis of the extracts was not feasible due low extraction efficiency and high matrix load in the extracts

Table 6.11.1-4 Residues [mg a.s. equiv./kg] of BYI 02960 and major metabolites in edible matrices after two applications

Compound (BYI 02960-)	**tomato fruits**			**apple fruits -** with surface wash		**apple fruits -** w/o surface wash		**rice kernels**		**cotton seeds**	
	drench application			spray application				spray appl.		spray appl.	
Label:	F	P	E	F	P	F	P	F	P	F	P
TRR:	**0.096**	**0.130**	**0.201**	**1.133**	**1.868**	**1.286**	**0.545**	**0.659**	**0.620**	**0.016[2]**	**0.068[2]**
BYI 02960	0.034	0.031	0.020	0.809	1.652	0.946	0.467	0.373	0.467		
DFA			0.174				0.12[1]		0.24[1]		0.06[1]
glucose/carbohydr.	0.026			0.193		0.182		0.023			
6-CNA		0.017			0.009		0.008		0.019		
CHPM-di-glyc		0.048			---		---		---		
CHMP-glyc		0.007			0.010		0.005		---		
difluoroethyl-amino-furanone	0.010		0.004	0.007		0.003		---			
OH-glyc	0.005	0.004	0.001	0.014	0.024	0.014	0.009	---	---		

1 LC-MS/MS analysis of non-radiolabelled DFA in the extract obtained in the metabolism study
2 analysis of the extracts was not feasible due low extraction efficiency and high matrix load in the extracts

Except for the metabolite difluoroacetic acid, the amounts of the single metabolites in edible matrices were very low. Only the natural compound glucose was found at levels > 0.1 mg/kg in one crop matrix, namely apple fruits. Thus parent compound, difluoroacetic acid and glucose are the only compounds which accounted for residue concentrations > 0.05 mg/kg in edible crops. Since glucose is a natural compound with no toxicological concern, parent compound BYI 02960 and metabolite difluoroacetic acid were the two compounds analysed for in the plant residue trials in the EU. Additionally, metabolite BYI 02960-difluoroethyl-amino-furanone was included in the residue definition for data collection since it was expected as a major metabolite in leafy crops after soil application as indicated by the confined rotational crop studies.

Metabolism studies conducted in five crops representing four diverse crop groups (fruiting crops, root crops, oilseeds and cereals) showed similar profiles, with the unchanged parent compound and metabolite difluoroacetic acid representing the major part of the residue. Analysis of a variety of crops from European field trials shows that the residues are, in fact, dominated by parent compound and difluoroacetic acid. Of course, short pre-harvest intervals in the field trials increased the proportion of parent in the total residue.

The proposed metabolic pathway in plants (primary and rotational crops) is shown in Figure 6.11.1-1. The metabolism in all plants was very similar. The main reactions involved were:

- Oxidative cleavage of the difluoroethylamine bond and formation of difluoroacetic acid,
- complete degradation of the furanone moiety and incorporation of carbon atoms into the natural compound pool, e.g. into glucose/carbohydrates,
- cleavage of the pyridinylmethylamine bond and formation of BYI 02960-difluoroethylamino-furanone and BYI 02960-CHMP / BYI 02960-6-CNA,
- formation of BYI 02960-CHMP was followed by conjugation with carbohydrates and sulphate or by oxidation of the methylene group to a carboxylic group and subsequent conjugation with glycerol and glucuronic acid,
- hydroxylation of the furanone or the difluoroethyl moiety followed by conjugation with carbohydrates and sulphate, and
- oxidative degradation of the furanone moiety to an acetic acid group followed either by conjugation with a carbohydrate or by further oxidation or degradation of the moiety.
- Halogenation (bromination/chlorination) of the furanone moiety of the parent compound was most probably a process which took place in the soil.

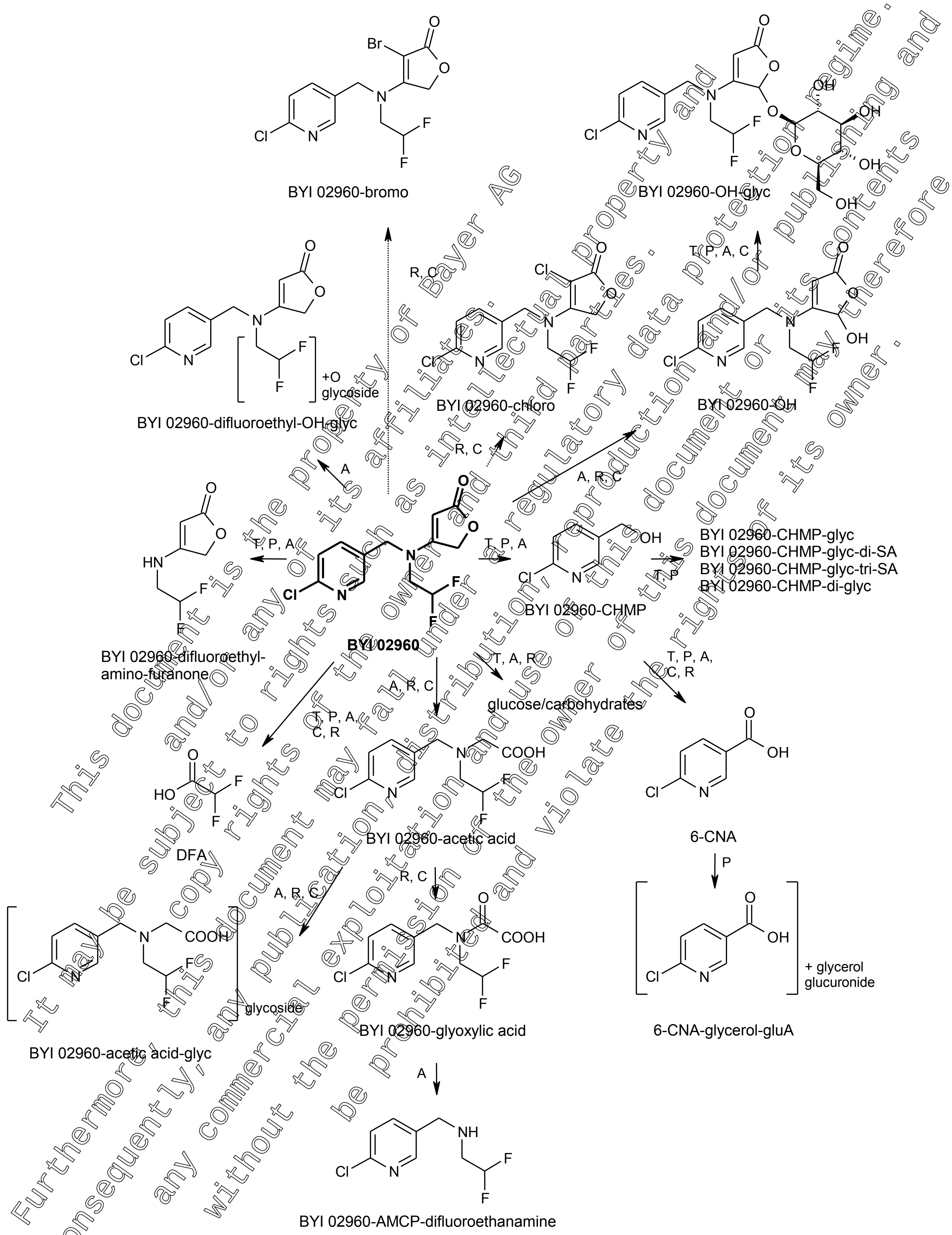
Thus, oxidative cleavage of the molecule, oxidation and hydroxylation were the primary transformation steps followed by conjugation reactions with glycosides, sulphate and glucuronic acid.

Generally, these main metabolic reactions were also observed in the rat studies on absorption, distribution, metabolism and elimination (ADME) of BYI 02960 (refer to KIIA 5.1). Parent compound and all major plant metabolites, or at least subsequent metabolites which imply the presence of the plant metabolites as transient metabolites were detected, although BYI 02960 shows a more moderate degradation behaviour in rats compared to plants.

In the ADME studies, parent compound was highly bioavailable and rather moderately metabolized. Generally, the metabolic profiles in urines and faeces were very similar for both sexes and the dose rates tested, but male rats exhibited a higher rate of metabolite formation compared to female animals. In all low dosed tests with male and female rats the unchanged active substance was found at 40.9% to 77.7% of the dose. Plant metabolite 6-CNA and its conjugates are covered by the rat metabolites 6-CNA and BYI 02960-hippuric acid, which were detected in sum at a maximum of 16.8% of the dose rate. Both metabolites were considered together since hippuric acid is the subsequent metabolite of 6-CNA and can only be formed via 6-CNA. The hydroxylated parent compound BYI 02960-OH accounted for 10.8% to 28.9% of the dose and even additional conjugates of this metabolite were detected in the rat. Thus toxicological coverage is given. Metabolite BYI 02960-difluoroethyl-amino-furanone (DFEAF) was detected at lower levels. It represented up to 3.5% of the dose, only. Therefore additional toxicity testings were initiated and it was shown that the metabolite was neither acutely toxic nor exhibits a genotoxic potential. Subacute administration of BYI 02960-difluoroethyl-amino-furanone to rats revealed that it is less toxic than parent and thus covered by the endpoints derived for the parent compound BYI 02960.

A detailed view on the toxicological coverage of all plant metabolites is summarized in Section 3 KIIA 5.10.

Figure 6.11.1-1 Proposed metabolic pathway of BYI 02960 in target plants



T	Tomato	R	Rice	glyc	glycoside	di-glyc	diglycoside
P	Potato	C	Cotton	glyc-di-SA	glycoside-disulphate	gluA	glucuronic acid
A	Apple			glyc-tri-SA	glycoside-trisulphate		

Summary of livestock metabolism:

The metabolism of Flupyradifurone (BYI 02960) was investigated in laying hens as a model for poultry and lactating goats as a model for ruminants following oral administration of [pyridinylmethyl-^{14}C]BYI 02960 and [furanone-4-^{14}C]BYI 02960 for both species.

Six hens were orally dosed once daily in the morning for 14 consecutive days with an aqueous 0.5% Tragacanth® suspension of 1.0 mg/kg body weight which corresponded to approximately 16.7 mg a.s./kg dry feed/day. The animals were sacrificed six hours after the last administration. Total radioactive residues were determined daily in the eggs and excreta, and at sacrifice in the dissected organs and tissues (muscle, fat, liver, kidney, skin and eggs from ovary/oviduct). Eggs, muscle, fat, liver and excreta were extracted and analysed for parent compound and metabolites.

One goat was orally dosed once daily for five consecutive days in the morning after milking with 1.0 mg of the active substance per kg body weight which corresponded to approximately 26.6 mg a.s./kg dry feed/day. The animal was sacrificed about six hours after the last administration. Total radioactive residues (TRR) were determined in milk and excreta at various sampling intervals, and in muscle, fat, kidney and liver at sacrifice. Milk, edible organs and tissues and urine were analysed for parent compound and metabolites.

In case of laying hens the overall recovery of radioactivity was high (96.1% of the total dose) after administration of [pyridinylmethyl-^{14}C]BYI 02960. However, following the dosage of [furanone-4-^{14}C]BYI 02960 the recovery was lower (82.2% of the total dose). This is probably due to the partial instability of the labelling position and the formation of $^{14}CO_2$, an observation which was also made in rat studies with the [furanone-4-^{14}C]-labelled test compound (KIIA 5.1). The total radioactive residues in the eggs and edible tissues as well as the concentrations of the identified metabolites are summarised in Table 6.11.1-5.

For lactating goats the recovery of radioactivity was also higher for the pyridinylmethyl-label (88.8% of the total dose) as compared to the furanone-4-label (78.9% of the total dose). The same explanation as for the hen studies would be applicable here. The total radioactive residues in the milk and edible tissues as well as the concentrations of the identified metabolites are summarised in Table 6.11.1-6.

Table 6.11.1-5 Radioactive residues of parent compound and metabolites in eggs and edible organs and tissues of laying hens following oral administration of 14 daily doses of [pyridinylmethyl-^{14}C]- or [furanone-4-^{14}C] BYI02960 at a dose rate of 1.0 mg/kg

	Pyridinylmethyl-^{14}C								Furanone-4-^{14}C							
	Eggs (day 3-13)		Muscle		Fat		Liver		Eggs (day 2-7)		Muscle		Fat		Liver	
Total radioactivity (TRR): (mg/kg)	0.084		0.070		0.021		0.435		0.540		0.183		0.427		2.178	
BYI 02960-	%TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Endogenous fatty acids									52.0	0.281	8.1	0.015	95.9	0.410	51.5	1.121
lactato-mercaptyl-nicotinic acid	4.0	0.003	3.6	0.002			15.5	0.068								
acetyl-cysteinyl-nicotinic acid							0.3	0.001								
6-CNA	7.2	0.006	8.8	0.006	1.8	<0.001	6.4	0.028								
des-difluoroethyl-OH-SA			2.1	0.001	5.6	0.001	3.1	0.014	0.1	0.001	0.5	0.001			0.2	0.004
acetyl-AMCP	23.1	0.019	40.2	0.028	28.5	0.006	6.3	0.027								
des-difluoroethyl	8.9	0.007	9.9	0.007	5.0	0.001	1.8	0.008	1.2	0.006	2.6	0.005			0.8	0.017
AMCP-difluoroethanamine-SA							0.3	0.001								
OH-SA	5.1	0.004	1.8	0.001	16.2	0.003	22.5	0.098	0.6	0.003					5.1	0.112
OH	18.0	0.015	8.1	0.006	5.5	0.001	1.5	0.007	2.3	0.013	2.4	0.004			0.8	0.018
Parent compound	19.8	0.017	9.8	0.007	15.3	0.003	0.9	0.004	2.3	0.013	2.9	0.005			0.5	0.010
Total identified	86.2	0.072	84.2	0.059	77.9	0.016	58.6	0.255	58.5	0.316	16.5	0.030	95.9	0.410	58.9	1.282

Table 6.11.1-6: Radioactive residues of parent compound and metabolites in milk and edible organs and tissues of lactating goats following oral administration of 5 daily doses of [pyridinylmethyl-^{14}C]- or [furanone-4-^{14}C] BYI02960 at a dose rate of 1.0 mg/kg

	Pyridinylmethyl-^{14}C									
	Milk		Muscle		Fat		Kidney		Liver	
TRR (mg/kg):	0.186		0.356		0.106		1.869		1.215	
BYI 02960-	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Cysteinyl-nicotinic acid							6.1	0.114	4.8	0.058
Hippuric acid	9.1	0.017					9.5	0.178	0.8	0.010
Methylthio-glyoxylic acid	1.5	0.003	1.3	0.005						
OH-gluA (isomer 1)							6.0	0.112		
OH-gluA (isomer 2)							9.3	0.175	1.4	0.016
OH-gluA (isomer 3)							8.4	0.158		
OH-gluA (isomer 4)							7.5	0.141		
AMCP-difluoroethanamine							1.1	0.020	1.2	0.015
Des-difluoroethyl										
OH							16.0	0.299		
Parent compound	88.8	0.165	98.0	0.349	99.2	0.105	34.8	0.650	84.6	1.028
Total identified	99.3	0.184	99.4	0.353	99.2	0.105	98.8	1.847	92.8	1.128
	Furanone-4-^{14}C									
	Milk		Muscle		Fat		Kidney		Liver	
TRR (mg/kg):	1.046		0.539		0.265		1.472		1.746	
BYI 02960-	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Lactose	66.8	0.698								
OH-gluA (isomer 1)							2.2	0.032		
OH-gluA (isomer 2)							2.2	0.032		
OH-gluA (isomer 3)							4.7	0.069		
OH-gluA (isomer 4)							3.5	0.052		
Des-difluoroethyl							1.3	0.019		
OH			1.8	0.010	2.9	0.008	14.6	0.215		
Parent compound	23.9	0.250	88.1	0.475	80.5	0.213	50.5	0.744	59.8	1.045
Total identified	90.7	0.948	89.9	0.484	83.4	0.221	79.0	1.163	59.8	1.045

The concentrations of the identified metabolites in the different matrices are basically in the same order of magnitude independent of the label employed. However, after administration of the furanone-labelled test compound, the concentrations of the total radioactivity in eggs and edible tissues of laying hens as well as in milk and fat of lactating goats are higher. This is attributable to the fact that the radioactivity originating from this label is incorporated into natural compounds like fatty acids in all poultry tissues and lactose in the milk of goats.

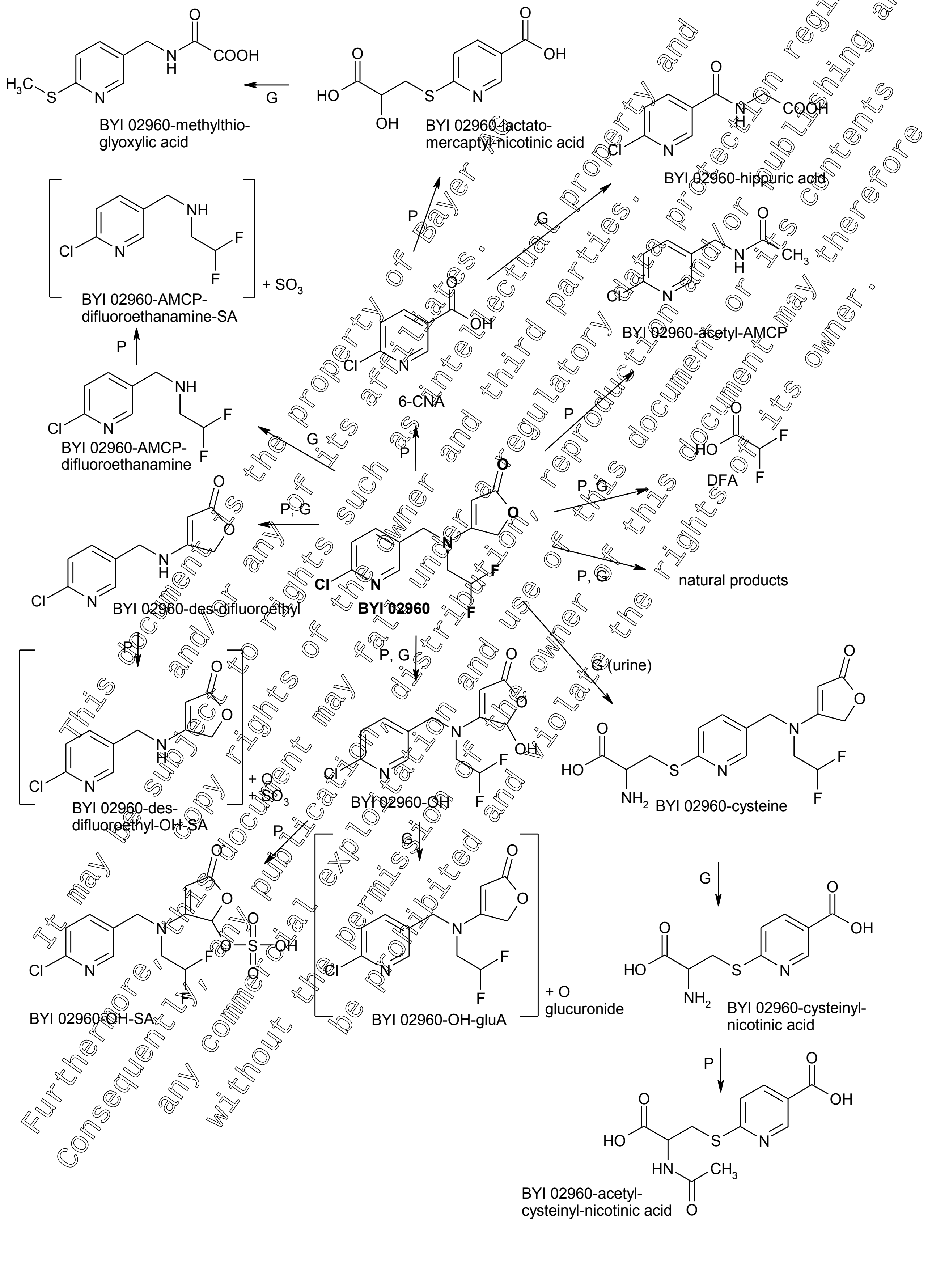
Notwithstanding these observations, the unchanged parent compound is a significant, if not the dominating constituent of the residue in milk, eggs and edible tissues of both species. Other metabolites determined in comparable concentrations are the natural compound lactose in the milk of goats after administration of [furanone-4-^{14}C]BYI 02960, and BYI 02960-acetyl-AMPC in eggs and tissues of poultry after administration of [pyridinylmethyl-^{14}C] BYI 02960.

The proposed metabolic pathway of BYI 02960 in edible tissues of livestock, milk and eggs is shown in Figure 6.11.1-2. The main metabolic reactions involved were:

- Hydroxylation in position 5 of the furanone ring forming BYI 02960-hydroxy followed by conjugation with sulfuric acid to BYI 02960-OH-SA
- Hydroxylation followed by conjugation with glucuronic acid forming two diastereomeric conjugates of BYI 02960-OH (BYI 02960-OH-gluA, isomer 2 and 3), the hydroxylation and conjugation being in the 5-position of the furanone ring. One isomer (BYI 02960-OH-gluA, isomer 4) with hydroxylation and conjugation in the difluoroethyl side chain and one isomer (BYI 02960-OH-gluA, isomer 1) with hydroxylation and conjugation in an unknown position
- Oxidative cleavage of the pyridinylmethyl moiety forming BYI 02960-6-CNA as well as subsequent total degradation of the furanone ring forming smaller carbon units (C-1- or C-2-fragments), entering the carbon pool of endogenous compounds and then being used either for the biosynthesis of fatty acids of lactose
- Substitution of the chloro group of BYI 02960-6-CNA with glutathione followed by degradation resulting in the conjugates BYI 02960-acetyl-cysteinyl-nicotinic acid and BYI 02960-lactato-mercaptyl-nicotinic acid
- Cleavage of the difluoroethyl group forming BYI 02960-des-difluoroethyl followed by hydroxylation and conjugation with sulfuric acid to BYI 02960-des-difluoroethyl-OH-SA
- Cleavage of the furanone ring and conjugation with sulfonic acid forming BYI 02960-AMCP-difluoroethanamine-SA
- Cleavage of the furanone ring and the difluoroethyl group forming an amine followed by acetylation to BYI 02960-acetyl-AMCP and BYI 02960-AMCP-difluoroethanamine
- Cleavage of the difluoroethyl group forming BYI 02960-des-difluoroethyl and difluoroacetic acid

Difluoroacetic acid was determined in selected livestock samples by high resolution LC-MS subsequently to the metabolism studies since rat studies conducted with [ethyl-1-^{14}C]BYI 02960 showed major amounts of this metabolite in organs and tissues. Extrapolation of rat data suggested high difluoroacetic acid levels in livestock tissues as well which was confirmed by the non-radioactive LC-MS analyses. Based on these findings, it was concluded that difluoroacetic acid is a major livestock metabolite and should be - besides parent compound - part of the residue definition for data collection, risk assessment and enforcement.

Figure 6.11.1-2 Metabolic pathway of BYI 02960 in milk, eggs and edible organs and tissues of lactating goats and laying hens following oral administration of [pyridinylmethyl-^{14}C]- or [furanone-4-^{14}C] BYI02960 (G: Goat, P: Poultry)



These main metabolic reactions were also observed in the rat studies on absorption, distribution, metabolism and elimination (ADME) of BYI 02960 (refer to KIIA 5.1) and therefore the toxicological coverage of the livestock metabolites is given. Parent compound and all major plant metabolites, or at least subsequent metabolites which imply the presence of the livestock metabolites as transient metabolites were detected.
In the ADME studies, parent compound was highly bioavailable and rather moderately metabolised. Generally, the metabolic profiles in urines and faeces were very similar for both sexes and the dose rates tested, but male rats exhibited a higher rate of metabolite formation compared to female animals. In all low dosed tests with male and female rats the unchanged active substance was found between 40.9% and 77.7% of the given dose. The hydroxylated parent compound including its conjugates are major rat and livestock metabolites. The same is true for 6-CNA and its glycine conjugate hippuric acid. Also BYI 02960-des-difluoroethyl was found in rats. In livestock, some further conjugates of 6-CNA occur, i.e. BYI 02960-lactato-mercaptyl-nicotinic acid, BYI 02960-cysteinyl-nicotinic acid and BYI 02960-acetyl-cysteinyl-nicotinic acid. The formation of these conjugates is considered a typical detoxification reaction so that these metabolites would also be covered by 6-CNA. It should also be noted that these metabolites occur only at very low concentrations in the livestock metabolism studies which have been conducted at exaggerated dose levels. Finally, there is a group of livestock metabolites which do no longer contain the furanone ring (BYI 02960-AMCP-difluoroethanamine, BYI 02960-AMCP-difluoroethanamine-SA and BYI 02960-acetyl-AMCP). There is no equivalent metabolite in the rat. These metabolites occur at maximum concentrations of 0.028 mg/kg (muscle of poultry) so that one would expect residues below 0.01 mg/kg in the poultry feeding study at the 1X-dose level (see also KIIA 5.10). BYI 02960-acetyl-AMCP as the main metabolite of this group was included in the analytical method for data collection used in the poultry feeding study (KIIA 6.4.1). With the exception of one muscle sample in which a concentration of 0.003 mg/kg was determined, the residue levels of BYI 02960-acetyl-AMCP were in all cases below the LOD of 0.003 mg/kg thus confirming the assumption made on the basis of the results of the metabolism study.

Summary of confined rotational crop metabolism:

The metabolism of BYI 02960 residues in the rotational crops wheat (small grain), Swiss chard (leafy crop) and turnip (root crop) was investigated at a nominal application rate of 400 g a.s./ha. The plant back intervals were 29, 135 and 296 days for all crops. The studies were conducted with [furanone-4-^{14}C]BYI 02960 and [pyridinylmethyl-^{14}C]BYI 02960. A study with [ethyl-1-^{14}C]BYI 02960 was not conducted and therefore non-radiolabelled difluoroacetic acid was determined in all extracts obtained in the CRC study conducted with [furanone-4-^{14}C]BYI 02960 to gain information on the fate of the difluoroethane moiety of the active substance.

The total radioactive residues (TRR) of the raw agricultural commodities (RACs) of the rotational crops in the three subsequent rotations are summarized in Table 6.11.1-7. The TRR values of all matrices declined significantly form the 1st to the 3rd rotation.

Table 6.11.1-7 TRR values in the different RACs of the three rotations after soil application of BYI 02960

TRR [mg/kg]	wheat				Swiss chard		turnips	
	[furanone-4-^{14}C]BYI 02960							
	forage	hay	straw	grain	imm.	mature	leaves	roots
1st rotation	0.783	2.003	6.290	0.478	0.848	0.871	0.679	0.074
2nd rotation	0.193	1.081	1.549	0.103	0.311	0.263	0.158	0.014
3rd rotation	0.111	0.254	0.462	0.047	0.180	0.152	0.090	0.008
	[pyridinylmethyl-^{14}C]BYI 02960							
1st rotation	1.407	2.409	9.015	0.177	1.358	1.483	0.815	0.072
2nd rotation	0.308	1.009	2.148	0.057	0.332	0.438	0.230	0.022
3rd rotation	0.117	0.321	0.491	0.017	0.135	0.130	0.083	0.008

Corresponding TRR values showed similar residue levels when comparing the studies performed with [furanone-4-^{14}C]BYI 02960 and [pyridinylmethyl-^{14}C]BYI 02960. Generally, the TRR values were slightly higher in the crops of 1st and 2nd rotation of the study performed with [pyridinylmethyl-^{14}C]BYI 02960, except for wheat grains, where it was the opposite way round due to the selective transport of glucose as a label specific metabolite into the RAC.

The levels of parent compound decreased with increasing plant back intervals but nevertheless parent formed a main portion of the residues in all of the RACs in all rotations, except for wheat grains. Other major metabolites (accounting for >10% of the TRR in at least one RAC in one rotation) were

- DFA, which was the main metabolite in wheat grains (all rotations) and in turnip roots (1st rotation) and a major metabolite in all other RACs
- 6-CNA-glucerol-gluA (3 isomers), which were major in and specific for all wheat commodities and accounted in sum for 11% to 33% of the TRR considering all rotations
- BYI 02960-difluoroethyl-amino-furanone, which was a major metabolite in all Swiss chard samples in all rotations and accounted for up to 17% of the TRR
- BYI 02960-OH-glyc, which was major in Swiss chard and turnip leaves in all rotations
- BYI 02960-glyoxylic acid, which was only a major metabolite in wheat forage, hay and straw and in turnip roots of the first rotation, in subsequent rotations it was detected in minor amounts, only

- BYI 02960-bromo-amino-furanone, which was only major in wheat hay of the 3rd rotation
- BYI 02960-OH, which was major in wheat grains of the 1st rotation, only
- Glucose/carbohydrates, which were identified as the main portion in wheat grains after exhaustive extraction and as a major metabolite in turnip roots after conventional extraction.

The amounts of parent compound and these major metabolites in the matrices of confined rotational crops are shown in Table 6.11.1-8 to Table 6.11.1-10 for all rotations.

Table 6.11.1-8 Residues [mg a.s. equiv./kg] of BYI 02960 and major metabolites in the matrices of rotational crops (1st rotation)

Compound (BYI 02960-)	wheat forage		wheat hay		wheat straw		wheat grain	
Label:	F	P	F	P	F	P	F	P
TRR:	**0.783**	**1.407**	**2.003**	**2.409**	**6.290**	**9.015**	**0.478**	**0.177**
BYI 02960	0.365	0.640	0.672	0.676	2.459	3.261	0.002	0.015
DFA	0.27[1]		0.96[1]		0.60[1]		3.45[1]	
glucose/carbohydr.	---		---		---		0.338	
bromo-amino-furanone	0.016		0.033		0.172			---
difluoroethyl-amino-furanone	0.077		0.205		0.374		---	
glyoxylic acid	0.124	0.172	0.227	0.176	0.965	0.615	0.024	0.011
OH-glyc	0.028	0.048	0.067	0.135	0.242	0.296	0.007	0.009
6-CNA-glycerol-gluA (2 + 3)		0.199		0.569		1.900		0.036
OH	0.010	0.019	0.038	0.052	0.161	0.239	0.011	0.019

(2 + 3) isomer 2 and/or isomer 3
F = [furanone-4-^{14}C]-label P = [pyridinylmethyl-^{14}C]-label

Compound (BYI 02960-)	Swiss chard intermediate		Swiss chard mature		turnip leaves		turnip roots	
Label:	F	P	F	P	F	P	F	P
TRR:	**0.848**	**1.358**	**0.871**	**1.483**	**0.679**	**0.815**	**0.074**	**0.072**
BYI 02960	0.460	0.779	0.371	0.687	0.437	0.508	0.041	0.042
DFA	0.24[1]		0.48[1]		0.24[1]		0.06[1]	
glucose/carbohydr.	---		---		---		0.003	
bromo-amino-furanone	---		---		---		---	
difluoroethyl-amino-furanone	---		0.010		---		---	
glyoxylic acid	0.031	0.021	0.041	0.039	0.045	0.021	0.009	0.006
OH-glyc	0.072	0.101	0.119	0.162	0.076	0.076	<0.001	0.002
6-CNA-glycerol-gluA (2 + 3)		---		---		---		---
OH	0.017	0.024	0.017	0.023	0.012	0.011	<0.001	<0.001

[1] LC-MS/MS analysis of non-radiolabelled DFA in the extract obtained in the confined rotation crop study performed with [furanone-4-^{14}C]BYI 02960
(2 + 3) isomer 2 and/or isomer 3
F = [furanone-4-^{14}C]-label P = [pyridinylmethyl-^{14}C]-label

Table 6.11.1-9 Residues [mg/kg] of BYI 02960 and major metabolites in the matrices of rotational crops (2nd rotation)

Compound (BYI 02960-)	wheat forage		wheat hay		wheat straw		wheat grain	
Label:	F	P	F	P	F	P	F	P
TRR:	**0.193**	**0.308**	**1.081**	**1.009**	**1.519**	**2.148**	**0.103**	**0.057**
BYI 02960	0.124	0.183	0.314	0.283	0.538	0.804	0.001	0.001
DFA	0.06[1]		0.42[1]		0.18[1]		0.78[1]	
glucose/carbohydr.	---		---		---		---	
bromo-amino-furanone	0.006		0.107		0.093		---	
difluoroethyl-amino-furanone	0.016		0.075		0.090		---	
glyoxylic acid	<0.001	---	0.020	0.010	0.018	0.036	0.001	0.001
OH-glyc	0.007	0.008	0.037	0.045	0.08	0.112	0.002	0.003
6-CNA-glycerol-gluA (2 + 3)	---	0.044	---	0.242	---	0.472	---	0.007
OH	0.003	0.005	0.021	0.019	0.047	0.079	0.003	0.004

(2 + 3) isomer 2 and/or isomer 3
F = [furanone-4-^{14}C]-label P = [pyridinylmethyl-^{14}C]-label

Compound (BYI 02960-)	Swiss chard intermediate		Swiss chard mature		turnip leaves		turnip roots	
Label:	F	P	F	P	F	P	F	P
TRR:	**0.311**	**0.332**	**0.263**	**0.438**	**0.158**	**0.230**	**0.014**	**0.022**
BYI 02960	0.171	0.170	0.072	0.108	0.108	0.153	0.004	0.011
DFA/carbohydr.	0.12[1]		0.15[1]		0.09[1]		<0.03[1]	
glucose	---		---		---		0.002	
bromo-amino-furanone	---		---		---		---	
difluoroethyl-amino-furanone	0.032		0.046		0.002		---	
glyoxylic acid	---	---	---	---	0.002	---	<0.001	---
OH-glyc	0.036	0.058	0.047	0.111	0.020	0.025	<0.001	0.001
6-CNA-glycerol-gluA (2 + 3)		---		---		---		---
OH	0.006	0.013	0.006	0.016	0.002	0.004	---	---

[1] LC-MS/MS analysis of non-radiolabelled DFA in the extract obtained in the confined rotation crop study performed with [furanone-4-^{14}C]BYI 02960
(2 + 3) isomer 2 and/or isomer 3
F = [furanone-4-^{14}C]-label P = [pyridinylmethyl-^{14}C]-label

Table 6.11.1-10 Residues [mg/kg] of BYI 02960 and major metabolites in the matrices of rotational crops (3rd rotation)

Compound (BYI 02960-)	**wheat forage**		**wheat hay**		**wheat straw**		**wheat grain**	
Label:	F	P	F	P	F	P	F	P
TRR:	**0.111**	**0.117**	**0.254**	**0.321**	**0.462**	**0.491**	**0.047**	**0.017**
BYI 02960	0.048	0.053	0.047	0.063	0.096	0.129	0.001	0.002
DFA	<0.03[1]		0.03[1]		0.06[1]		0.15[1]	
glucose/carbohydr.	---		---		---		---	
bromo-amino-furanone	0.006		0.027		0.034		---	
difluoroethyl-amino-furanone	0.013		0.021		0.024		---	
glyoxylic acid	---	0.001	0.001	---	---	0.013	---	---
OH-glyc	0.003	0.004	0.006	0.010	0.016	0.014	0.001	0.001
6-CNA-glycerol-gluA (2 + 3)		0.022		0.095		0.140		0.002
OH	0.001	0.001	0.004	0.005	0.010	0.010	0.001	0.001

(2 + 3) isomer 2 and/or isomer 3
F = [furanone-4-^{14}C]-label P = [pyridinylmethyl-^{14}C]-label

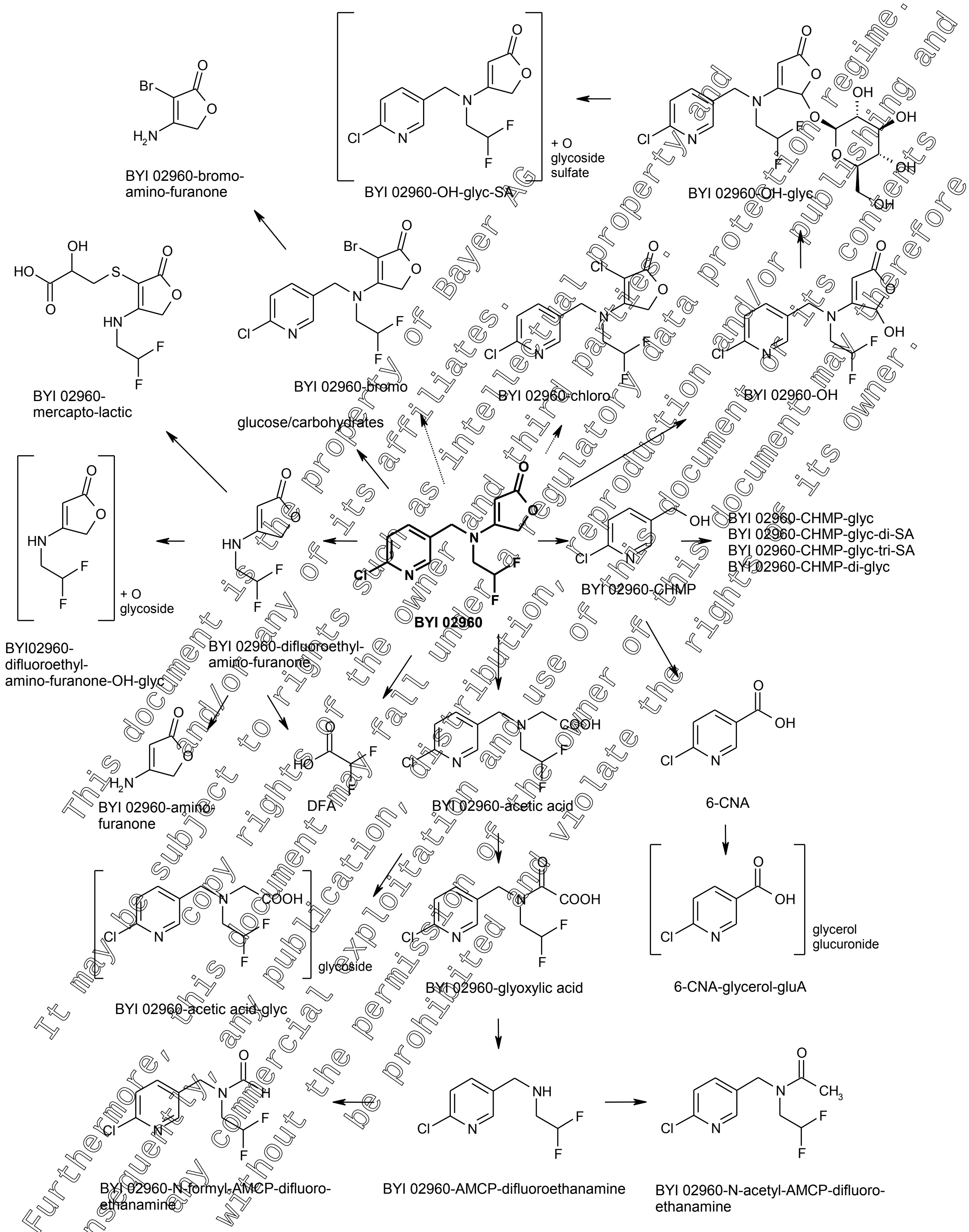
Compound (BYI 02960-)	**Swiss chard intermediate**		**Swiss chard mature**		**turnip leaves**		**turnip roots**	
Label:	F	P	F	P	F	P	F	P
TRR:	**0.180**	**0.135**	**0.152**	**0.130**	**0.090**	**0.083**	**0.008**	**0.008**
BYI 02960	0.066	0.042	0.051	0.036	0.065	0.058	0.006	0.005
DFA	<0.03[1]		0.03[1]		<0.03[1]		<0.03[1]	
glucose/carbohydr.	---		---		---		<0.001	
bromo-amino-furanone	---		---		---		---	
difluoroethyl-amino-furanone	0.025		0.024		0.001		---	
glyoxylic acid	<0.001	0.003	---	0.001	0.002	---	---	---
OH-glyc	0.040	0.033	0.033	0.036	0.009	0.008	<0.001	<0.001
6-CNA-glycerol-gluA (2 + 3)		---		---		---		---
OH	0.007	0.005	0.005	0.004	0.001	---	---	---

[1] LC-MS/MS analysis of non-radiolabelled DFA in the extract obtained in the confined rotation crop study performed with [furanone-4-^{14}C]BYI 02960
(2 + 3) isomer 2 and/or isomer 3
F = [furanone-4-^{14}C]-label P = [pyridinylmethyl-^{14}C]-label

The proposed metabolic pathway is very similar to the one of the target plants. As observed in target plants the metabolic reactions involved were hydroxylation and oxidative cleavage of the active substance followed by additional oxidation and conjugation processes. No additional metabolic routes were detected, only additional metabolites were identified, e.g. additional conjugates or existing metabolites were subjected to further oxidation reactions.

A pathway for succeeding crops is proposed in Figure 6.11.1-3.

Figure 6.11.1-3 Proposed metabolic pathway of BYI 02960 in confined rotational crops



As field rotational crop studies became necessary, residue data have been collected on parent BYI 02960, difluoroacetic acid and BYI 02960-difluoroethyl-amino-furanone. These three compounds are adequate to assess the dietary risk of BYI 02960. Parent compound and difluoroacetic acid are major components detected in all RACs of all rotations. Since BYI 02960-difluoroethyl-amino-furanone occurred in high levels in Swiss chard matrices (representative for leafy crops) and first analysis on difluoroacetic acid indicated only marginal levels of this metabolite in these matrices, BYI 02960-difluoroethyl-amino-furanone was chosen as additional component to represent the relevant **residue definition for data gathering** and **risk assessment** in plants. All three compounds are specific to the use of BYI 02960 and suitable marker compounds for estimating residue levels of other metabolites, if necessary. All other metabolites, not included in the residue definition, show no toxicity concerns nor are they generally observed across most crop matrices.

Toxicological coverage of metabolites was either shown in the rat ADME studies, in additional toxicological tests or by estimating the toxicological concern of the metabolite for the consumer by applying the TTC (Threshold of Toxicological Concern) concept (see Section 3 KIIA 5.10).

Studies were conducted to assess the **storage stability** of frozen samples. During a storage period of 18 months under deep-freezer conditions, the components of the relevant residues of BYI 02960 (including parent compound, BYI 02960-difluoroethyl-amino-furanone, and DFA) were stable in orange fruit, spinach leaves and tomato fruit, wheat grain, bean seed, coffee bean and soybean seed, and sugar cane, representing a wide array of plant-based sample materials. (The study summarized here will be continued until a final storage period of 2 years.) In addition, over a storage period of 43 days under deep-freezer conditions, DFA was shown to be stable in bovine fat, kidney, liver, and muscle. (Animal matrices were not stored for longer periods in the studies presented in this dossier.) These results validate the residue values reported in supervised field trials, processing studies, and feeding studies with respect to storage stability of samples frozen prior to analysis.

Full sets of **field residue trials** were presented, allowing the evaluation of the residue behaviour of BYI 02960 in the "safe use" crops lettuce and hops, as well as in numerous other "primary" crops (pome fruit, grapes, and various fruiting vegetables) in the field and, where relevant, in greenhouses. Residue determinations in these crops formed the basis for MRL calculations and dietary risk assessment. In addition to the EU uses, crop residue data from the Global Joint Review dossier were presented for a wide array of commodities traded from GJR countries to the EU, including citrus and pome fruit; fruiting, stem, and tuber vegetables; tree nuts; pulses; oilseeds; cereals; and coffee.

Based on these trials, in which residues of BYI 02960 itself and its metabolite make up by far the major proportion of the residue in crops, the proposed **enforcement residue definition** for BYI 02960 in *plant* commodities is parent compound + DFA, expressed in parent equivalents.

Processing trials were also conducted to support the intended uses. In a radioactive hydrolysis study simulating processing conditions, no breakdown products of BYI 02960 >0.5% were determined, thus confirming the residue definition's validity for use in processing "field trials". In an extensive package of processing data, Processing Factors were elucidated, as shown in the following table:

Summary of Processing Factors for important end commodities, as documented in EU and global studies in this dossier
(study data: cf. section IIA 6.5.4)

RAC	Processed commodity	Avg. Proc. Factor (PF)	
		EU study	GJR study
Orange	juice	<0.25	
	marmalade	0.25	
	oil	<0.25	<1
Apple	juice	0.65	
	sauce	0.81	
	dried fruit	1.8	
Peach	preserve (canned fruit)	0.50	
Grape	juice	0.68	
	wine	0.42, 0.56	
	jelly	0.31	
	raisin (dried fruit)	2.5	
Lettuce	washed inner leaves	0.67	
Tomato	juice	0.70	
	preserve (canned fruit)	0.72	
	puree	1.4	
	paste	1.7	
	dried fruit	1.9	
Cucumber	pickles (preserve)	0.78	
	sour pickles (fermented)	0.57	
Potato	flakes		1.3
	crisps		<1
	boiled tuber		<1
Coffee	roasted bean		<1
	instant coffee		3
Hops	beer	0.01	
Barley	beer	0.085	
	pearl barley	0.14	
Wheat	germ	1.1	1.3
	white flour	0.35	<1
	white bread	0.30	<1
	whole-meal flour	1.5	<1
	whole-meal bread	0.95	<1
	semolina	0.95	
	pasta		<1
Corn	bran		1.5
	flour		<1
	starch		<1
	oil		<1
Cotton	oil		<1
Peanut	oil		<1
Soybean	oil		<1
	milk		<1
	flour		<1
Sugar beet	refined sugar	<0.5	

Field rotational crop trials were also conducted to evaluate the effect of previous application of BYI 02960 on following crops. In large-scale trials, using multiple rotations (simulating crop failure, re-use of the field in the same season, and re-use in the following season) and multiple crop groups (a root crop, a leafy crop, and a cereal), it was evident that total residues in all relevant food and feed matrices were generally highest in the first rotation. Subsequently, based on early draft guidance available in 2010 and as discussed with the MSs Austria and the Netherlands (RMS), 7 further sets of single-rotation, single-crop rotational crop trials were conducted (in rotational tuber, stem, fruiting, bulb, and legume vegetables; pulses; and oilseeds). Residue determinations in these crops formed the basis for MRL calculations and dietary risk assessment.

Animal feeding studies were conducted in both dairy cattle and laying hens. The studies were conducted in a manner that allows their use in multiple registration regions (EU, NAFTA, Australia). Feeding studies should allow the evaluation of the effects of feeding a representative residue to livestock. As the primary residues of BYI 02960 in both plants and in livestock chiefly comprise parent BYI 02960 and its metabolite DFA, the feeding studies were also designed to allow "material balancing" in order to evaluate levels and calculate transfer factors for both the total residues and DFA, despite feeding parent compound only. This study design is specific to BYI 02960. Both studies showed that the primary components of the residue are, in fact, parent and DFA. Plateau residue levels were achieved for milk and eggs; residues were evaluated for all dose groups (4 per study). Transfer factors were calculated for all relevant matrices for both the total residue of BYI 02960 + DFA as well as for DFA alone. The basic study data as well as the evaluation of DFA transfer factors allowed MRL calculations for realistic worst-case animal diet conditions.

Based on these studies, in which residues of BYI 02960 itself and its metabolite make up by far the major proportion of the residue in all relevant tissues, the proposed **enforcement residue definition** for BYI 02960 in *animal* matrices is parent compound + DFA, expressed in parent equivalents.

MRLs for the uses of BYI 02960 described in this dossier (including primary uses and rotational crops as well as residues in edible animal commodities) were proposed, as follows:

Summary of MRL proposals – based on primary and rotational EU uses as well as on residue data from "global" uses for import-relevant crops
(study data: cf. sections IIA 6.3.1, 6.3.2, 6.4, and 6.6.3; MRL evaluations cf. IIA 6.7.2)

● MRLs reflect the sum of BYI 02960 and DFA, expressed in parent equivalents.

Commodity	Harmonized MRL Proposal (mg/kg)
PLANT matrices	
Citrus fruit	3.0
Tree nuts	0.15
Pome fruit	1.5
Grapes	3.0
Blueberries	4.0
Prickly pear	0.7
Root vegetables	0.3
Bulb vegetables	0.8††
Tomatoes/eggplants	3.0
Peppers	1.0
Chili peppers	3.0
Cucumbers/zucchini	1.0/1.5*
Watermelons	1.0
Sweet corn/maize	0.4 (4.0††)†
Brassica vegetables	0.3
Lettuces/spinach	7.0/9.0*
Endive (scarole)	0.3
Legume vegetables	2.0
Stem vegetables	0.6 (general) 40 (celery)
Pulses - dry beans - dry peas	10.0†† (general)

Commodity	Harmonized MRL Proposal (mg/kg)	
Oilseeds - peanuts - soybean - cotton	0.8†† (general) 4.0 (soybean) 0.9 (cotton)	
Potatoes (tuber veg.)	1.5††	
Hops	20	
Coffee	2.0	
Cereals - barley - corn/maize - sorghum - wheat	4.0 (general) 4.0†† (corn)	
ANIMAL matrices		
eggs	0.5††	(0.3) ‡
poultry meat (muscle)	0.8††	(0.5) ‡
poultry fat	0.3††	(0.2) ‡
poultry liver/offal	1.0††	(0.5) ‡
milk	0.3	(0.3) ‡
bovine meat (muscle)	1.0	(1.0) ‡
bovine fat	0.5	(0.5) ‡
bovine liver	2.0	(n.a.) ‡
bovine kidney	2.0	(n.a.) ‡
other bovine offal	2.0	(2.0) ‡

* proposal depends on whether or not the OECD calculator is used for EU data.
** to be delivered
† proposal depends on whether sweet corn is covered by EU rotational crop value for "cereals" or not
†† these values are based on a re-evaluation of the data subsequent to the original GJR submission, incorporating all EU rotational crop data which became available later (using an extrapolation from the EU use pattern to the Australian use pattern as well as the envisaged Australian soil accumulation factor).
‡ values based on Australian feeding calculations, but not considering rotational crops – as shown in the original submission
n.a. not applicable (no MRLs are set in Australia for these commodities)

On the basis of the MRLs (as well other data, such as STMRs and peeling factors), **dietary risk assessments** were conducted. In an evaluation of the <u>chronic</u> dietary risk, the TMDI, calculated according to the EFSA PRIMo model on the basis of MRLs, amounted to between 19.4% (PL general population) and 126.5% (WHO Cluster Diet B) of the ADI. Because three ADI usage values in these evaluations were above 100%, a further, more refined risk assessment was required. In the NEDI/IEDI calculation, ADI exhaustion ranged from 3.2% (PL general population) to 23.4% (WHO

Cluster Diet B). As all values were well below 100%, the use of BYI 02960 does not pose a chronic risk to consumers if used according to the GAPs as described in this dossier.

As for the *acute* dietary risk, IESTI calculations (using proposed MRLs instead of HRs) indicated that the maximum contribution to the ARfD is approx. 84% for sweet corn (children, IESTI 1 calculation), and thus far below 100%. The second-highest value is for potatoes, at approx. 66%. Despite using the most conservative approach for the assessment of the acute risk, it is evident that no acute risk for consumers will arise from the uses of BYI 02960 as presented in this dossier.

IIA 6.11.2 Reasonable grounds in support of the petition

Bayer CropScience is requesting registration of BYI 02960 as an insecticide for several uses. In this Annex II dossier, only the so-called "safe uses" are described (lettuce and hops). Further data on other crops will be submitted in a separate document later in 2012.

To support this registration Bayer CropScience has evaluated the risk associated with registration on these crops. The hazard of the compound was assessed by the conduct of toxicology studies with BYI 02960 (acute, short-term and chronic) as well as respective toxicology studies with selected metabolites. Exposure to BYI 02960 residues was evaluated by the conduct of plant (primary and confined rotational crops) and animal metabolism studies to define the residues of concern followed by the conduct of field residue studies on primary and succeeding crops and feeding studies to define the magnitude of residue in food and feed items. Acute and chronic dietary exposure assessments according to the EFSA PRIMo model (revision 2) have shown that total human dietary exposure to BYI 02960 represents only a small portion of the acute and chronic reference doses even when calculating with the most conservative approaches. Occupational exposure assessments have shown acceptable Margins of Exposure for all use practices.

Therefore, there is reasonable certainty that no harm will result from the use of BYI 02960 when it is used according to the label.

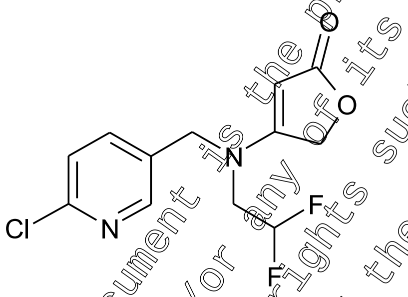
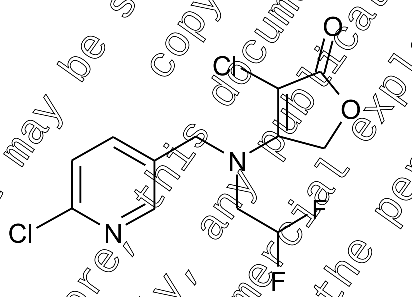
Adequate MRLs have been proposed for all food and feed items and Bayer CropScience requests establishment of these MRLs.

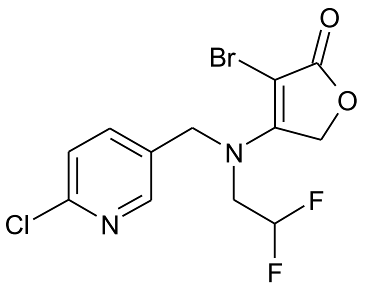
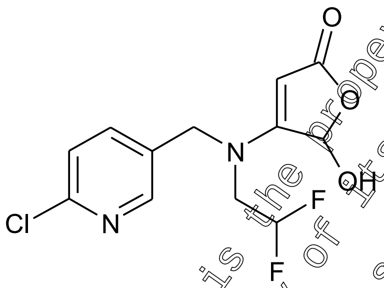
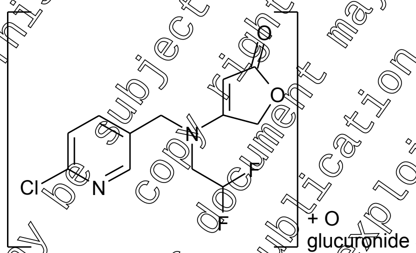
List of metabolites

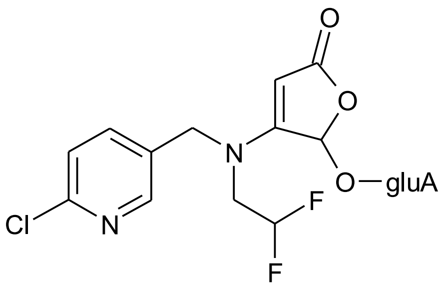
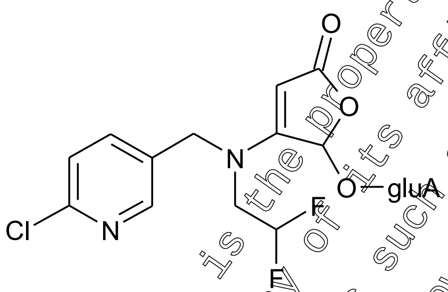
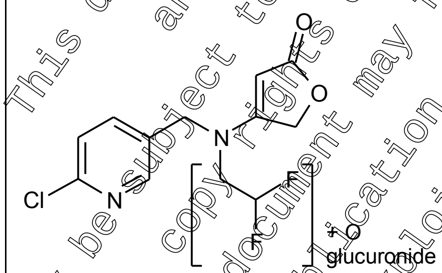
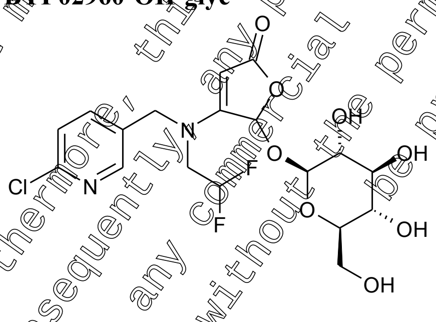
In the original study reports on BYI 02960 the metabolites are sometimes named by different synonyms. In order to present a common basis for the evaluation of the active substance and its degradation products a complete list of metabolites is presented.

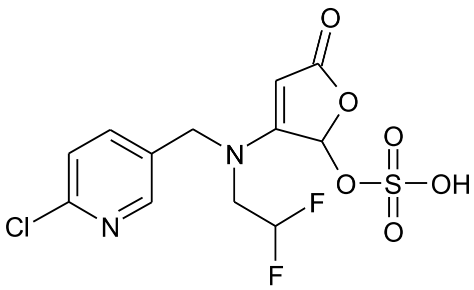
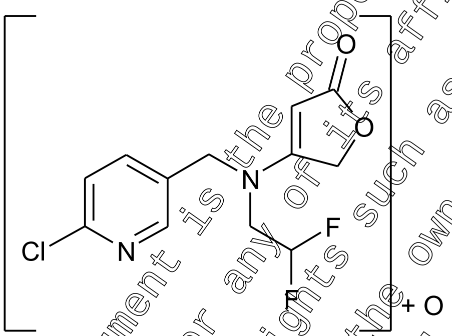
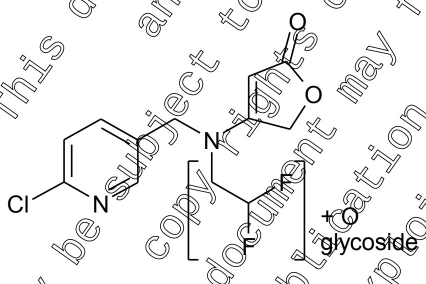
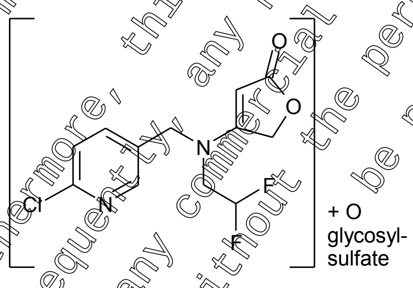
The following abbreviations were used:

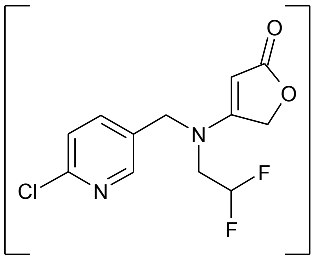
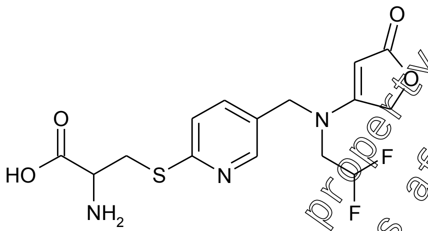
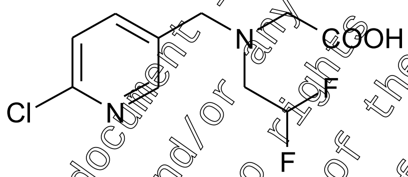
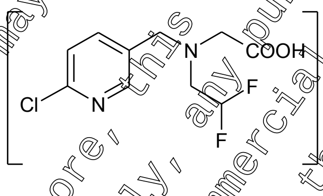
gluc = glucoside (conjugation with glucose)
glyc = glycoside (conjugation with a hexose)
gluA = glucuronide (conjugation with glucuronic acid)
OH = hydroxy
SA = sulfate

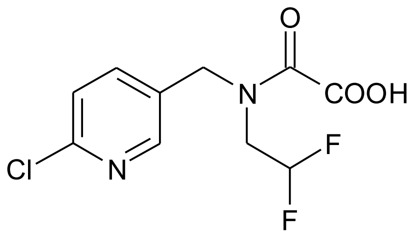
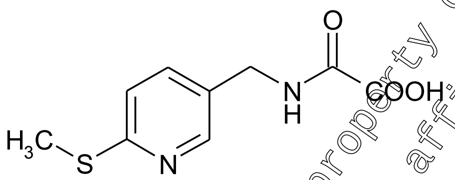
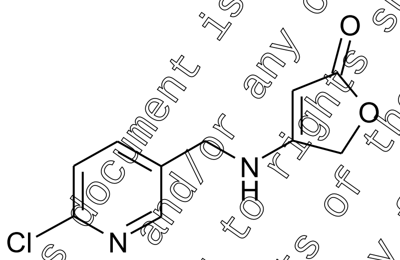
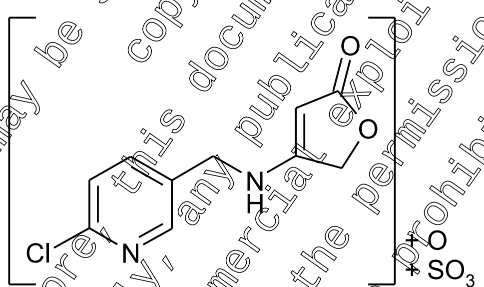
	Report name, Structure **IUPAC name** **CAS name, [CAS number]**	**Molecular formula** **molar mass** **Other names / codes**	**Occurrence**
a.s.	**BYF 02960 (parent compound)**  4-[[(6-chloropyridin-3-yl)methyl](2,2-difluoroethyl)amino]furan-2(5H)-one (IUPAC) 2(5H)-furanone, 4-[[(6-chloro-3-pyridinyl)methyl](2,2-difluoroethyl)amino]- (CAS) CAS-No.: 951659-40-8	$C_{12}H_{11}ClF_2N_2O_2$ 288.68 g/mol flupyradifurone	all matrices
M01	**BYI 02960-chloro**  3-chloro-4-{[(6-chloropyridin-3-yl)methyl](2,2-difluoroethyl)amino}furan-2(5H)-one	$C_{12}H_{10}Cl_2F_2N_2O_2$ 323.13 g/mol BCS-CD27046	Plant: rice cotton Swiss chard (CRC) turnips (CRC) wheat (CRC) (co-elution with BYI 02960-bromo) Environment: aerobic soil (minor)

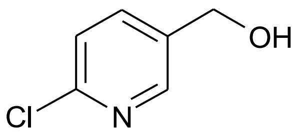
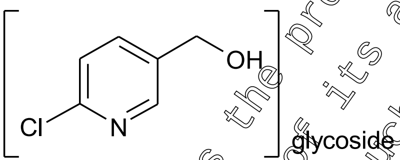
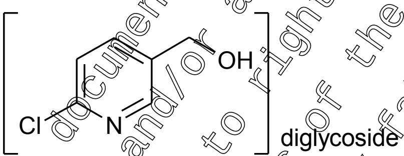
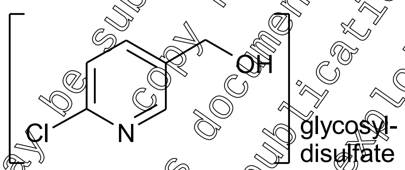
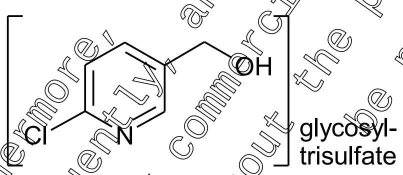
	Report name, Structure IUPAC name CAS name, [CAS number]	Molecular formula molar mass Other names / codes	Occurrence
M02	**BYI 02960-bromo**  3-bromo-4-{[(6-chloropyridin-3-yl)methyl](2,2-difluoroethyl)amino}furan-2(5H)-one	$C_{12} H_{10} Br Cl F_2 N_2 O_2$ 367.58 g/mol BCS-CD27042	Plant: rice cotton Swiss chard (CRC) turnips (CRC) wheat (CRC) (co-elution with BYI 02960-chloro)
M03	**BYI 02960-OH**  4-{[(6-chloropyridin-3-yl)methyl](2,2-difluoroethyl)amino}-5-hydroxyfuran-2(5H)-one	$C_{12} H_{11} Cl F_2 N_2 O3$ 304.68 g/mol BYI 02960-hydroxy BCS-CQ74364	Animal: rat lactating goat laying hen Plant: tomato potato apple cotton rice Swiss chard (CRC) turnips (CRC) wheat (CRC)
M04	**BYI 02960-OH-gluA (isomer 1)**  	$C_{18} H_{19} Cl F_2 N_2 O_9$ 480.81	Animal: rat lactating goat

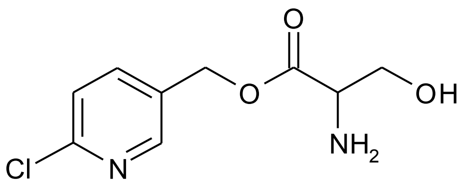
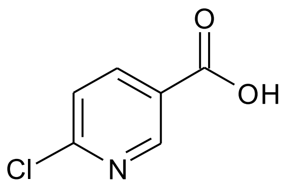
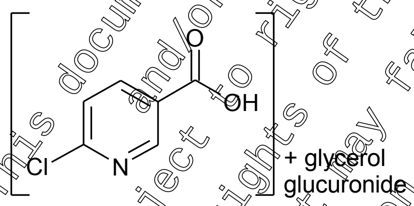
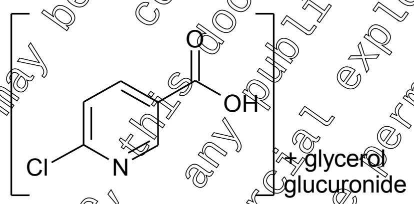
	Report name, Structure IUPAC name CAS name, [CAS number]	Molecular formula molar mass Other names / codes	Occurrence
M05	**BYI 02960-OH-gluA (isomer 2)**  3-{[(6-chloropyridin-3-yl) methyl](2,2-difluoroethyl) amino}-5-oxo-2,5-dihydrofuran-2-yl beta-D-glucopyranosiduronic acid	$C_{18} H_{19} Cl F_2 N_2 O_9$ 480.81	Animal: lactating goat
M06	**BYI 02960-OH-gluA (isomer 3)**  3-{[(6-chloropyridin-3-yl) methyl](2,2-difluoroethyl) amino}-5-oxo-2,5-dihydrofuran-2-yl beta-D-glucopyranosiduronic acid	$C_{18} H_{19} Cl F_2 N_2 O_9$ 480.81	Animal: rat lactating goat
M07	**BYI 02960-OH-gluA (isomer 4)** 	$C_{18} H_{19} Cl F_2 N_2 O_9$ 480.81	Animal: lactating goat
M08	**BYI 02960-OH-glyc**  3-{[(6-chloropyridin-3-yl)methyl](2,2-difluoroethyl)amino}-5-oxo-2,5-dihydrofuran-2-yl beta-D-glucopyranoside	$C_{18} H_{21} Cl F_2 N_2 O_8$ 466.83 g/mol BYI 02960-OH-gluc BCS-CR46036	Plant: tomato potato apple cotton (co-elution with BYI 02960-acetic acid) Swiss chard (CRC) turnips (CRC) wheat (CRC)

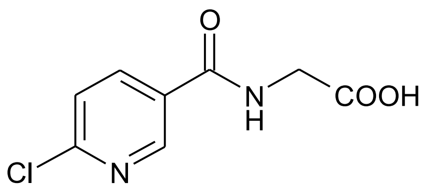
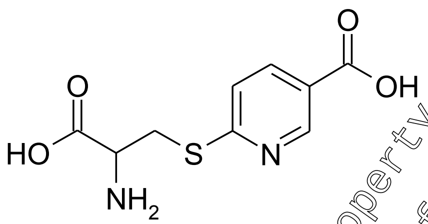
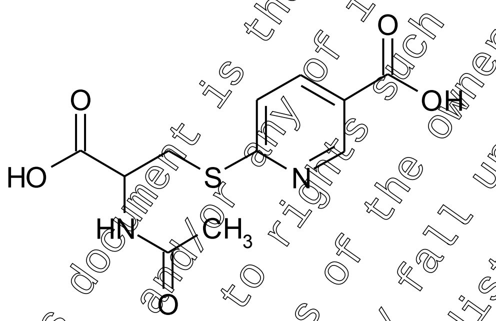
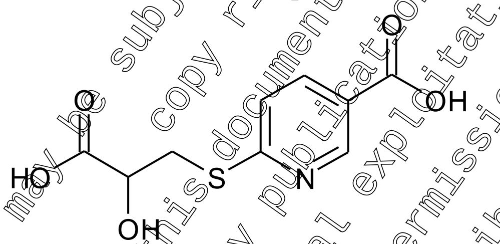
	Report name, Structure IUPAC name CAS name, [CAS number]	Molecular formula molar mass Other names / codes	Occurrence
M09	**BYI 02960-OH-SA**  3-{[(6-chloropyridin-3-yl)methyl](2,2-difluoroethyl)amino}-5-oxo-2,5-dihydrofuran-2-yl hydrogen sulfate	$C_{12}H_{11}ClF_2N_2O_6S$ 384.75 g/mol	Animal: rat laying hen
M10	**BYI 02960-iso-OH**  	$C_{12}H_{11}ClF_2N_2O_3$ 304.68 g/mol	Animal: rat lactating goat
M11	**BYI 02960-difluoroethyl-OH-glyc**  	$C_{18}H_{21}ClF_2N_2O_8$ 466.83 g/mol	Plant: apple
M12	**BYI 02960-OH-glyc-SA (isomer 1)**  	$C_{18}H_{21}ClF_2N_2O_{11}S$ 546.89 g/mol	Plant: Swiss chard (CRC) turnips (CRC)

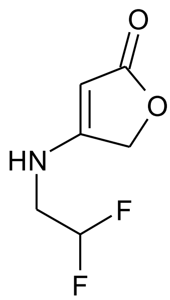
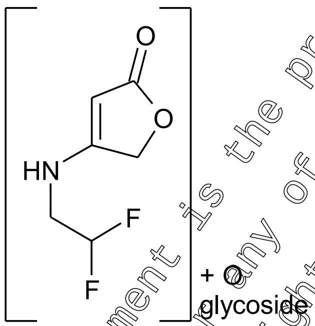
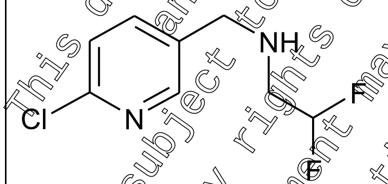
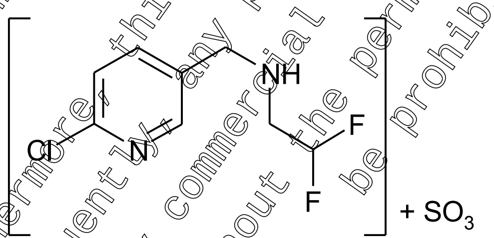
	Report name, Structure IUPAC name CAS name, [CAS number]	Molecular formula molar mass Other names / codes	Occurrence
M13	**BYI 02960-OH-glyc-SA (isomer 2)** 	$C_{18} H_{21} Cl F_2 N_2 O_{11} S$ 546.89 g/mol	Plant: Swiss chard (CRC) turnips (CRC) wheat (CRC)
M14	**BYI 02960-cysteine**  S-(5-{[(2,2-difluoroethyl)(5-oxo-2,5-dihydrofuran-3-yl)amino]methyl}pyridin-2-yl)cysteine	$C_{15} H_{17} F_2 N_3 O_4 S$ 373.38 g/mol	Animal: lacating goat
M15	**BYI 02960-acetic acid**  N-[(6-chloropyridin-3-yl)methyl]-N-(2,2-difluoroethyl)glycine	$C_{10} H_{11} Cl F_2 N_2 O_2$ 264.66 g/mol BCS-CQ74373	Plant: apple rice cotton (co-elution with BYI 02960-OH-glyc) Swiss chard (CRC) turnips (CRC) wheat (CRC) Animal: laying hen
M16	**BYI 02960-acetic acid-glyc** 	$C_{16} H_{21} Cl F_2 N_2 O_7$ 426.8 g/mol	Plant: apple rice cotton Swiss chard (CRC) turnips (CRC) wheat (CRC)

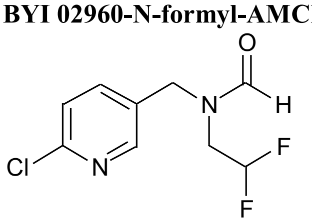
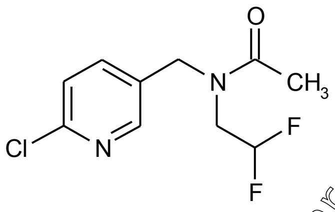
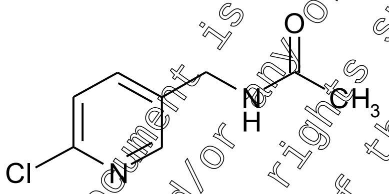
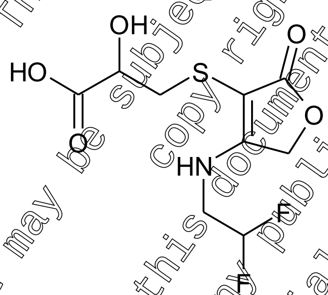
	Report name, Structure IUPAC name CAS name, [CAS number]	Molecular formula molar mass Other names / codes	Occurrence
M17	**BYI 02960-glyoxylic acid**  N-(6-chloropyridin-3-ylmethyl)-N-(2,2-difluoroethyl)oxamic acid	$C_{10} H_9 Cl F_2 N_2 O_3$ 278.64 g/mol BCS-CQ74372	Plant: rice cotton Swiss chard (CRC) turnips (CRC) wheat (CRC)
M18	**BYI 02960-methylthio-glyoxylic acid**  ({[6-(methylsulfanyl)pyridin-3-yl]methyl}amino)(oxo)acetic acid	$C_9 H_{10} N_2 O_3 S$ 278.64 g/mol	Animal: lactating goat
M19	**BYI 02960-des-difluoroethyl**  4-[(6-chloropyridin-3-ylmethyl)amino]furan-2(5H)-one	$C_{10} H_9 Cl N_2 O_2$ 224.65 g/mol BCS-AB49019	Animal: rat lactating goat laying hen Environment: Aerobic soil (minor)
M20	**BYI 02960-des-difluoroethyl-OH-SA** 	$C_{10} H_9 Cl N_2 O_6 S$ 320.71 g/mol	Animal: laying hen

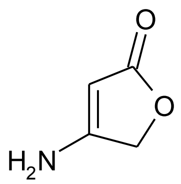
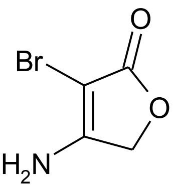
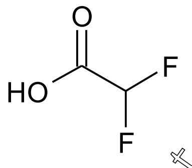
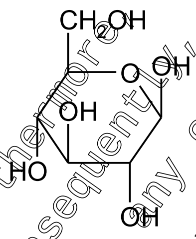
	Report name, Structure IUPAC name CAS name, [CAS number]	Molecular formula molar mass Other names / codes	Occurrence
M21	**BYI 02960-CHMP**  6-chloropyridin-3-ylmethanol (IUPAC) 3-pyridinemethanol, 6-chloro- (CAS) CAS-No.: 21543-49-7	C_6H_6ClNO 143.57 g/mol BCS-AA52175 6-CPA CPA (6-chloro-3-pyridyl)methanol BCS-AA52175 IM-0	Plant: tomato potato apple turnips (CRC) wheat (CRC)
M22	**BYI 02960-CHMP-glyc**  	$C_{12}H_{16}ClNO_6$ 305.72 g/mol	Plant: tomato potato apple
M23	**BYI 02960-CHMP-di-glyc**  	$C_{18}H_{26}ClNO_{11}$ 467.86 g/mol	Plant: tomato potato apple Swiss chard (CRC) turnips (CRC) wheat (CRC)
M24	**BYI 02960-CHMP-glyc-di-SA**  	$C_{12}H_{16}ClNO_{12}S_2$ 465.84 g/mol	Plant: Swiss chard (CRC)
M25	**BYI 02960-CHMP-glyc-tri-SA**  	$C_{12}H_{16}ClNO_{15}S_3$ 545.9 g/mol	Plant: Swiss chard (CRC)

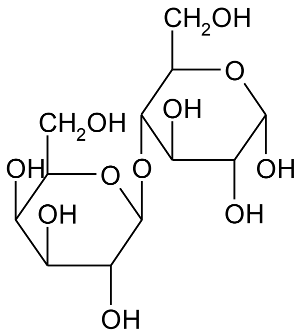
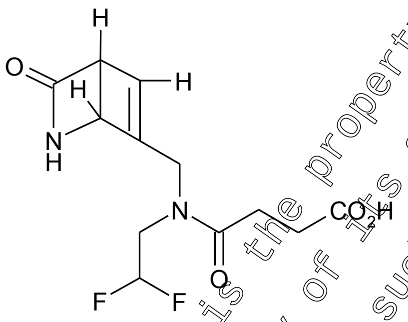
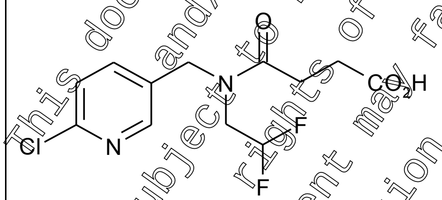
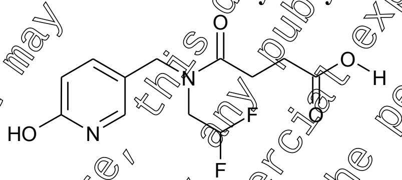
	Report name, Structure IUPAC name CAS name, [CAS number]	Molecular formula molar mass Other names / codes	Occurrence
M26	**BYI 02960-CHMP-serinate** 	$C_9 H_{11} Cl N_2 O_3$ 230.65 g/mol	Animal: laying hen
M27	**6-CNA**  6-chloronicotinic acid (IUPAC) CAS-No.: 5326-23-8	$C_6 H_4 Cl N O_2$ 157.56 g/mol 6-chloronicotinic acid IC-0 BYI 02960-6-CNA BCS-AA35572	Animal: rat laying hen Plant: tomato potato apple cotton rice Swiss chard (CRC) turnips (CRC) wheat (CRC) Environment Aerobic soil (major)
M28	**BYI 02960-6-CNA-glycerol-gluA (isomer 1)** 	$C_{15} H_{18} Cl N O_{10}$ 407.76 g/mol	Plant: potato (isomer was not assigned) wheat (CRC)
M29	**BYI 02960-6-CNA-glycerol-gluA (isomer 2 & 3)** 	$C_{15} H_{18} Cl N O_{10}$ 407.76 g/mol	Plant: wheat (CRC)

	Report name, Structure IUPAC name CAS name, [CAS number]	Molecular formula molar mass Other names / codes	Occurrence
M30	**BYI 02960-hippuric acid**  N-[(6-chloropyridin-3-yl)carbonyl]glycine	C8 H7 Cl N2 O3 214.61 g/mol	Animal: rat lactating goat
M31	**BYI 02960-cysteinyl-nicotinic acid**  6-[(2-amino-2-carboxyethyl)sulfanyl]nicotinic acid	C9 H10 N2 O4 S 242.26 g/mol	Animal: lactating goat
M32	**BYI 02960-acetyl-cysteinyl-nicotinic acid** 	C_{11} H_{12} N_2 O_5 S 284.29 g/mol	Animal: laying hen
M33	**BYI 02960-lactato-mercaptyl-nicotinic acid** 	C_9 H_9 N O_5 S 243.24 g/mol	Animal: laying hen

	Report name, Structure IUPAC name CAS name, [CAS number]	Molecular formula molar mass Other names / codes	Occurrence
M34	**BYI 02960-difluoroethyl-amino-furanone**  4-[(2,2-difluoroethyl)amino]furan-2(5H)-one	$C_6 H_7 F_2 N O_2$ 163.12 g/mol DFEAF BCS-CC98193	Plant: tomato potato apple Swiss chard (CRC) turnips (CRC) wheat (CRC) Animal: rat
M35	**BYI 02960-difluoroethyl-amino-furanone-OH-glyc** 	$C_{12} H_{17} F_2 N O_8$ 341.27 g/mol	Plant: Swiss chard (CRC) wheat (CRC)
M36	**BYI 02960-AMCP-difluoroethanamine**  N-[(6-chloropyridin-3-yl)methyl]-2,2-difluoroethanamine	$C_8 H_9 Cl F_2 N_2$ 206.62 g/mol BCS-AA10710	Plant: apple Animal: lactating goat
M37	**BYI 02960-AMCP-difluoroethanamine-SA** 	$C_8 H_9 Cl F_2 N_2 O_3 S$ 286.69 g/mol	Animal: laying hen

	Report name, Structure IUPAC name CAS name, [CAS number]	Molecular formula molar mass Other names / codes	Occurrence
M38	**BYI 02960-N-formyl-AMCP-difluoroethanamine**  N-[(6-chloropyridin-3-yl)methyl]-N-(2,2-difluoroethyl)formamide	$C_9 H_9 Cl F_2 N_2 O$ 234.63 g/mol	Plant: Swiss chard (CRC) turnips (CRC)
M39	**BYI 02960-N-acetyl-AMCP-difluoroethanamine**  N-[(6-chloropyridin-3-yl)methyl]-N-(2,2-difluoroethyl)acetamide	$C_{10} H_{11} Cl F_2 N_2 O$ 248.66 g/mol	Plant: Swiss chard (CRC) turnips (CRC)
M40	**BYI 02960-acetyl-AMCP** 	$C_8 H_9 Cl N_2 O$ 184.63 g/mol AMCP BYI 02960-AMCP	Animal: laying hen
M41	**BYI 02960-mercapto-lactic acid**  3-({4-[(2,2-difluoroethyl)amino]-2-oxo-2,5-dihydrofuran-3-yl}sulfanyl)-2-hydroxypropanoic acid	$C_9 H_{11} F_2 N O_5 S$ 283.25 g/mol	Plant: wheat (CRC)

	Report name, Structure IUPAC name CAS name, [CAS number]	Molecular formula molar mass Other names / codes	Occurrence
M42	**BYI 02960-amino-furanone**  4-aminofuran-2(5H)-one	$C_4 H_5 N O_2$ 99.09 g/mol	Plant: Swiss chard (CRC) turnips (CRC) wheat (CRC)
M43	**BYI 02960-bromo-amino-furanone**  4-amino-3-bromofuran-2(5H)-one	$C_4 H_4 Br N O_2$ 177.99 g/mol	Plant: wheat (CRC)
M44	**DFA**  difluoroacetic acid (IUPAC) Acetic acid, 2,2-difluoro- (CAS) CAS-No.: 381-73-7	$C_2 H_2 F_2 O_2$ 96.03 g/mol difluroacetic acid BYI 02960-DFA BYI 02960-difluoroacetic acid BYI 0260-Difluoro-acetic-acid BCS-AA56716	Animal: rat lactating goat laying hen Plant: tomato potato apple cotton rice Swiss chard (CRC) turnips (CRC) wheat (CRC) Environment aerobic soil (major) aerobic water/sediment (major)
M45	**Glucose (hexose)**  assumed structure D-glucose	$C_6 H_{12} O_6$ 180.16 g/mol glucose/carbohydrates D-glucose	Plant: tomato apple rice turnips (CRC) wheat (CRC)

	Report name, Structure IUPAC name CAS name, [CAS number]	Molecular formula molar mass Other names / codes	Occurrence
M46	**Lactose** 	$C_{10}H_{18}O_{11}$ 314.25 g/mol	Animal: lactating goat
M47	**BYI 02960-azabicyclosuccinamide**  4-{(2,2-difluoroethyl)[(3-oxo-2-azabicyclo[2.2.0]hex-5-en-6-yl)methyl]amino}-4-oxobutanoic acid (IUPAC)	$C_{12}H_{14}F_2N_2O_4$ 288.25 g/mol BCS-CS64875	Environment: water – aquatic photolysis (major)
M48	**BYI 02960-succinamide**  4-{[(6-chloropyridin-3-yl)methyl](2,2-difluoroethyl)amino}-4-oxobutanoic acid (IUPAC)	$C_{12}H_{13}ClF_2N_2O_3$ 306.69 g/mol BCS-CR74729	Environment: water – aquatic photolysis (major)
M49	**BYI 02960-deschlorohydroxysuccinamide**  4-{(2,2-difluoroethyl)[(6-hydroxypyridin-3-yl)methyl]amino}-4-oxobutanoic acid (IUPAC)	$C_{12}H_{14}F_2N_2O_4$ 288.25 g/mol DCHS	Environment: water – aquatic photolysis (minor)