Document Title

Summary of the residues in or on treated products, food and feed for Foramsulfuron

PUBLIC VERSION

Data Requirements

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Section 6: Residues in or on treated products, food and feed

According to the guidance document SANCO 10181/2013, for

preparing dossiers for the approval of a chemical active substance

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Bayer CropScience

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

[1] Changes will be presented according to the approach to showing revisions and version history as outlined in SANCO/10180/2013 Chapter 4 How to revise an Assessment Report

Table of Contents

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

This document contains only summaries of studies, which were not available at the time of the first Annex I inclusion of foramsulfuron and were therefore not evaluated during the first EU review of this compound. In order to facilitate discrimination between new and original information, the old information is written in grey letters. All studies, which were already submitted by Bayer for the first Annex I inclusion, are contained in the Monograph, its Addenda and in the original (baseline) dossier provided by Bayer CropScience and are not summarised in this document.

Foramsulfuron (AE F130360) is a herbicidal active substance. In the original dossier, submitted to Germany in 2000, residue trial data supported the use on corn. In this Annex I Renewal ("AIR") dossier, only the "safe use" on corn will be presented.

According to Article 12 of Regulation (EC) No 396/2005, the European Food Safety Authority (EFSA) has reviewed the Maximum Residue Levels (MRLs) currently established at European level for the pesticide active substance foramsulfuron. A reasoned opinion on the review of the existing maximum residue levels (MRLs) for foramsulfuron was published in EFSA Journal 2012; 10(11):2962.

Report:	KCA Section 6 /01; [redacted]; 2012; M-466418-01
Title:	Reasoned opinion on the review of the existing maximum residue levels (MRLs) for foramsulfuron according to Article 12 of Regulation (EC) No 396/2005
Report No:	M-466418-01-1
Document No:	M-466418-01-1
Guidelines:	**Regulation (EC) No 1107/2009; not specified**
GLP/GEP:	**n.a.**

EFSA evaluated the plant and animal metabolism studies, the residue studies and concluded that these were all acceptable. The GAPs evaluated cover the GAPs presented for the re-approval. EFSA defined the residue definition for enforcement and risk assessment in cereals as parent foramsulfuron, proposed an MRL of 0.01 mg/kg on maize grain, proposed the residue definition for enforcement and risk assessment in products of animal origin as foramsulfuron and recommended MRLs on animal commodities at the LOQ of 0.01 mg/kg. The consumer risk assessment according to the EFSA PRIMo model showed there was no concern.

In this renewal dossier new studies have been submitted for several data points:

- KCA 6.1/02 – a storage stability study in corn performed to extend the storage period.
- KCA 6.1/03 – an extract of a method report is presented due to the fact that it contains data on the stability of foramsulfuron (and a metabolite) in sample extracts over time. [The study report is also summarised in the relevant section of the methods].
- KCA 6.1/04 - an extract of an ILV report is presented due to the fact that it contains data on the stability of foramsulfuron (and a metabolite) in sample extracts over time. [The study report is also summarised in the relevant section of the methods].
- In the original EU dossier animal metabolism studies were not submitted and were not considered to be required / triggered. However, a cow and a poultry study are listed as studies in the Review Report as studies relied upon but not summarised in the DAR. Although still not triggered, the poultry (KCA 6.2.2/01) and cow (KCA 6.2.3/01) metabolism studies are summarised in this dossier for completeness as recommended by the RMS.
- KCA 6.6.1/02 – a summary of a rotational crop study performed for the registration of foramsulfuron in the USA.

All the other studies were evaluated for the original approval of foramsulfuron and full study summarises are not provided.

CA 6.1 Storage stability of residues

Stability of residues during storage of samples

Studies submitted and evaluated for the original inclusion of foramsulfuron on Annex I:
In the original dossier, a study was submitted to evaluate the storage stability of foramsulfuron in corn matrices (forage, stover and grain).

Report:	[redacted];2000;M-238478-01
Title:	Stability of AE F130360 and AE F153745 residues in corn (forage, stover and grain) during frozen storage, USA, 1998 (minimum storage interval of 209 days). AE F130360 00 1B99 0001; AE F153745 00 1B99 0001
Report No:	B002750
Document No(s):	Report includes Trial Nos.: CF98R004 M-238478-01-2
Guidelines:	**USEPA (=EPA): OPPTS 860.1380;Deviation not specified**
GLP/GEP:	**yes**

It was concluded that the compound is stable in deep-frozen samples over periods of 468, 209 and 243 days in corn grain, stover and forage, respectively. The analytes were found to be stable upon deep-freeze storage for the durations studied.

"AIR3" process/ New studies submitted

Justification for including this report in the "AIR" dossier

Since the Annex I inclusion, a new study with longer storage periods covered (minimum of 616 days) was generated. Table 6.1- 1 shows the maximum storage stability periods assessed.

Table 6.1- 1: Summary of storage stability of foramsulfuron and metabolite AE F153745 in maize matrices

Analytes	Plant matrix	Stability	Storage conditions	Reference
Foramsulfuron and AE F153745	Corn, Grain	Up to 866 days	-10 to -20 °C	M-238787-01-1 KCA 6.1/02
	Corn, Forage	Up to 616 days		
	Corn, Stover	Up to 620 days		

Report:	[redacted];2001;M-238787-01
Title:	Stability of AE F130360 and AE F153745 Residues in Corn (forage, stover and grain) During Frozen Storage, USA, 1998 (Minimum Storage Interval of 616 Days)
Report No:	B003134
Document No(s):	Report includes Trial Nos.: CF98R004 M-238787-01-1
Guidelines:	**USEPA (=EPA): 860.1380;Deviation not specified**
GLP/GEP:	**yes**

Material and Methods

This study was initiated to establish the stability of foramsulfuron (AE F130360) and its metabolite AE F153745 in corn forage, stover and grain during frozen storage for a period of over two years. This report presents data obtained at 866, 616 and 620 days of frozen storage, for grain, forage and stover, respectively.

Pre-weighed samples of forage, stover and grain were fortified, separately, with foramsulfuron and AE F153745, and then placed in frozen storage. Samples were withdrawn from frozen storage at different intervals, and analysed for the appropriate analyte. Extractable residues of foramsulfuron and AE F153745 were removed from the crop matrix by blending with aqueous acetonitrile. After filtration, the extract was concentrated in vacuo to a reduced volume. The aqueous/organic extract was transferred to a separation funnel and washed with hexane. The extract was then cleaned up via SPE column chromatography and analysed by HPLC/MS.

Findings

The half-life of each analyte was calculated by estimating the best-fit line of a first order kinetic model. The mean recoveries of foramsulfuron and AE F153745 from freshly fortified samples were 79% and 91%, respectively. The respective standard deviations were 25% and 12%.

Table 6.1- 2: Storage stability of foramsulfuron and metabolite AE F153745 in corn/maize matrices

Matrix Maize/corn	Storage interval [days]	Recoveries Foramsulfuron [%]				Recoveries AE F153745 [%]			
		Individual			Mean	Individual			Mean
Grain	0	62	62	56	60	76	74	67	72
	259	72	62	16*	67	65	75	61	70
	330	116	101	126	114	58	49	66	58
	468	48	115	83	82	143	101	135	126
	866	60	67	60	62	86	84	82	84
Forage	1	79	75	87	80	70	87	73	77
	71	95	114	106	105	83	79	78	80
	209	58	58	58	58	81	91	87	86
	243	74	67	70	70	-	-	-	-
	616	52	62	66	60	86	85	91	87
Stover	1	47	65	57	56	78	77	76	77
	72	95	85	93	91	62	60	58	60
	209	68	60	66	65	81	76	82	80
	620	73	62	65	67	90	89	85	88

* Outlier

Validation and linearity data are not presented in this storage stability study but are available in the analytical method already submitted in the original dossier and evaluated at EU level (Document M-238558-02-1; KCA 4.2/06).

Conclusion

A half-life of approximately 12 years for foramsulfuron in grain was estimated. No decline of foramsulfuron and AE F153745 could be observed in any other matrix. Inspection of the results show that there is no significant decline in recovery of the aged samples in any of the three matrices over a period of 866 days, 616 days and 620 days for grain, forage and stover, respectively. One may therefore conclude that both analytes exhibited good stability during frozen storage in corn raw agricultural commodities over the periods tested.

The longest period of time for which samples from field residue trials presented or summarised in this dossier were stored prior to analysis is given in Table 6.1- 3. All the maximum storage periods of samples are covered by the storage stability data.

Table 6.1- 3: Maximum storage period of samples from supervised field trials

Compound	Crop	Sample material	Maximum storage period (days)	Duration Covered (days)
Foramsulfuron and AE F153745	Maize	Green material	556	616
		Shoot	527	
		Rest of plant	477	620
		Ear	475	866
		kernel	429	

Stability of residues in samples extracts

The storage stability of pesticide residues in sample extracts is generally checked during the development of the applicable analytical residue methods. Moreover, the relevant information on the stability in the final or any intermediate step can be derived from the fortification experiments performed during method validation. If the recoveries in fortified samples are within the acceptable range of 70 - 110%, stability is considered as sufficiently proven. Additionally every analytical batch contains at least one concurrent recovery, which is handled and stored in parallel to residue samples. Therefore, the acceptability of the concurrent recoveries demonstrates the stability of samples during the work up procedure.

"AIR3" process/ New studies submitted

EFSA recently published their reasoned opinion on the existing MRLs for foramsulfuron, a copy of their report is provided in this dossier (KCA 6/01). EFSA concluded that a confirmatory method for enforcement of residues in maize grain and forage was required. During the development of the enforcement method [method number 01360 (Report AIR-13/007)] for the determination of amidosulfuron, metsulfuron-methyl, iodosulfuron-methyl-sodium, mesosulfuron-methyl and foramsulfuron in samples from plant origin by HPLC-MS/MS, the stability in final plant extracts was checked for the tested sample materials over a period of 16 to 43 days. In addition in the Independent Laboratory Validation (ILV) the stability in extracts was rechecked over a shorter time period. The stability results from both studies are summarised below. Full details of the method and the ILV are presented in the method section (Section 4) of the active substance dossier ([redacted] 2013; M-455564-01-1; KCA 4.2/20 and [redacted]; 2013; M-470160-01-1; KCA 4.2/21).

Report:	[redacted];[redacted];2013;M-455564-01
Title:	Analytical method 01360 for the determination of amidosulfuron, metsulfuron-methyl, iodosulfuron-methyl-sodium, mesosulfuron-methyl, and foramsulfuron in samples from plant origin by HPLC-MS/MS
Report No:	MR-13/007
Document No:	M-455564-01-1
Guidelines:	**Regulation (EC) No 1107/2009 of the European Parliament and the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC** **Guidance document on residue analytical methods, SANCO/825/00/rev. 8.1, European Commission, Directorate General Health and Consumer Protection 16/11/2010** **US EPA Residue Chemistry Test Guideline OCSPP 860.1340: Residue Analytical Method** **OECD Guideline, ENV/JM/MONO (2007) 17, Aug 13, 2007;not applicable**
GLP/GEP:	**yes**

Material and Methods

Stability of residues in sample extracts was studied in sugar beet body, sugar beet leaf, lemon fruit, oilseed rape and cereal straw (0.1 mg/kg). The following table shows the recoveries comparing initial day of analysis and analysis after storage of the final extracts at 4°C ± 3°C under dark conditions over the given periods. To check the stability after storage freshly prepared matrix standards were prepared and analysed together with the aged recovery samples.

Findings

Foramsulfuron was stable for all matrices under the tested conditions.

Table 6.1- 4: Stability of Foramsulfuron in Plant Extracts, Quantifier Mass Transition

Sample Material	Fortification Level [mg/kg]		Recovery Rates [%]					Mean
Sugar beet, body	0.1	Day 0 (initial analysis)	101	92	94	100	99	
		43 days reanalysis	97	92	90	94	95	
		deviation day 0/43 days	4.0	0.0	4.3	6.0	4.0	3.7
Sugar beet, leaf	0.1	Day 0 (initial analysis)	84	89	89	93	89	
		43 days reanalysis	84	81	87	87	82	
		deviation day 0/43 days	0.0	9.0	2.2	6.5	7.9	5.1
Lemon, fruit	0.1	Day 0 (initial analysis)	97	91	92	88	93	
		16 days reanalysis	105	104	93	94	97	
		deviation day 0/16 days	8.2	14.3	1.1	6.8	4.3	6.9
Oilseed Rape	0.1	Day 0 (initial analysis)	96	97	100	95	96	
		38 days reanalysis	81	79	80	79	81	
		deviation day 0/38 days	15.6	18.6	20.0	16.8	15.6	17.3
Cereals Straw	0.1	Day 0 (initial analysis)	78	77	76	72	74	
		30 days reanalysis	103	105	105	98	96	
		deviation day 0/30 days	32.1	36.4	38.2	36.1	29.7	34.5

Conclusion

The results for all sulfonylureas suggest that samples should be analysed as soon as possible after preparation, because not all analytes are stable in final plant extracts. This is not surprising when considering the hydrolytical data of sulfonylureas.

Report:	[redacted];2013;M-470160-01
Title:	Independent lab validation of BCS method 01360 for the determination of residues of amidosulfuron, metsulfuron-methyl, iodosulfuron-methyl-sodium, mesosulfuron-methyl and foramsulfuron in samples from plant origin by HPLC-MS/MS
Report No:	2013/0060/01
Document No:	M-470160-01-1
Guidelines:	**REGULATION (EC) No 1107/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC.** **European Commission Guidance Document for Generating and Reporting Methods of Analysis in Support of Pre-Registration data Requirements for Annex II (part A, Section 4) and Annex III (part A, section 5) of directive 91/414, SANCO/3029/99.** **Guidance document on residue analytical methods; SANCO/825/00 rev. 8.1, European Commission, Directorate General Health and Consumer Protection; 2010-11-16.** **OECD Guidance Document on Pesticide Residue analytical Methods; ENV/JM/Mono(2007); 2007-08-13** **US-EPA Residue Chemistry Test Guideline OCSPP 860.1340: Residue Analytical Method;not applicable**
GLP/GEP:	**yes**

Stability was tested after storage of the final samples in the dark at a temperature between 2 – 8°C over three to thirteen days. The following tables show the measurements comparing initial day of analysis and analysis after storage of the final samples in the dark at a temperature between 2 – 8°C over the given periods. Calibration was conducted with freshly prepared matrix standards at initial analysis and for analysis after storage.

Table 6.1- 5 : Stability of Foramsulfuron in Plant Extracts, Quantifier Mass Transition.

Sample Material	Fortification Level [mg/kg]	Date of analysis	Concentration [ng/ml]			Mean deviation [%]*
Sugar beet, body	0.1	2013-08-28	10.30	9.60	9.90	7
		2013-09-10	9.56	9.55	9.94	
Sugar beet, leaf	0.1	2013-08-29	9.63	8.92	9.32	23
		2013-09-09	7.23	7.06	7.09	
Lemon, fruit	0.1	2013-09-06	8.76	8.55	8.65	-77
		2013-09-09	2.07	1.90	1.94	
Oilseed Rape	0.1	2013-09-02	10.30	10.30	10.40	69
		2013-09-09	3.32	3.25	3.18	
Cereals Straw	0.1	2013-09-04	7.80	7.96	7.33	11
		2013-09-09	8.65	8.74	8.18	

* Mean deviation [%] between initial analysis and days of reanalysis

Conclusion
Significant deviations between initial and re-analysis were observed especially for the matrices lemon fruit and oilseed rape. Therefore the analysis of the samples should be conducted within 1 day.

CA 6.2 Metabolism, distribution and expression of residues

CA 6.2.1 Plants

Original dossier
In the original dossier, the behaviour and metabolism of foramsulfuron was only investigated in corn because foramsulfuron was not intended for use in any other crop. In these studies, foramsulfuron was radiolabelled with 14C in two different positions as presented in figure 6.2.1-1 below.

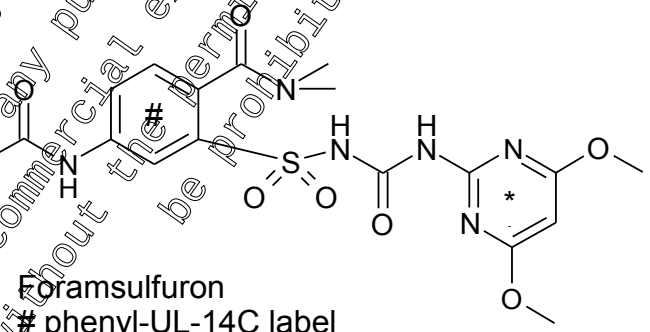

Figure 6.2.1-1: Label positions of foramsulfuron

2-^{14}C-pyrimidinyl-labelled AE F130360 (outdoor) or U-^{14}C-phenyl-labelled AE F130360 (glasshouse), formulated as water dispersible granules (WG), were applied by spraying to corn plants in the 7 leaves unfolded to 1st node visible stages (BBCH 17 to 31) with application rates of 60 and 240 g a.s./ha (maximum label rate is 60 g/ha). The non-radioactive safener isoxadifen-ethyl was included at a ratio of 1:1 with foramsulfuron. This safener has also been included in all residue trials performed on corn reviewed under the scope of Annex I inclusion.

Samples of raw agricultural commodities, including forage, stover and grain, were harvested and analysed. In general, low residues were detected in plant samples. At the immature forage stage, the maximum total radioactive residue (TRR) from the 240 g/ha treatment ranged from 0.894 to 1.661 mg-equiv./kg. At harvest, a maximum TRR of 1.874 to 1.945 mg-equiv./kg was found in stover, while the grain residue was very low, at 0.004 to 0.010 mg-equiv./kg. The principal extractable residue for forage, stover and grain was the parent compound. Two metabolites resulting from the cleavage of the sulfonylurea bridge, namely AE F153745 and AE F092944, were found in the extractable residue of forage and stover. Another metabolite, resulting from the cleavage of the formamide moiety was also found (in very small amounts) in forage and stover. The major metabolite detected in plants (AE F153745) was also identified in rat metabolism studies. The minor metabolite AE F130619 was also identified in rat metabolism studies.

It was concluded that the submitted studies gave sufficient information to propose a definition of residue for risk assessment in plant materials, as foramsulfuron. This was also recently confirmed by EFSA in their recent (2012) reasoned opinion for the MRLs of foramsulfuron.

Studies submitted and evaluated for the inclusion of foramsulfuron on Annex I:

Report:	[redacted];2000;M-185906-01
Title:	Metabolism of (U-^{14}C-phenyl)-AE F130360 and (2-14C-pyrimidyl)-AE F130360 in corn grown under field conditions Code: AE F130360
Report No:	C003293
Document No(s):	Report includes Trial Nos.: 512CF M-185906-01-1
Guidelines:	**USEPA (=EPA): OPPTS 860.1300;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted];2000;M-196292-01
Title:	Discussions on the different methods of evaluating growth stages of maize
Report No:	C007621
Document No:	M-196292-01-1
Guidelines:	**Deviation not specified**
GLP/GEP:	**no**

"AIR3" process

The data from the original submission is regarded as being sufficient. As no new uses have been developed subsequent to the first submission, and as corn – the AIR3 "safe use" – has already been tested, no new studies are presented for the Annex I Renewal.

CA 6.2.2 Poultry

In the original review for foramsulfuron at EU level it is stated in the DAR that animal metabolism studies were not triggered and were thus not required. However, during the EU evaluation a study on poultry (conducted in 1999 for North America) was submitted and evaluated and is included in the Foramsulfuron Review Report (Appendix III) as a study which was submitted during the evaluation period but which was not cited in the draft assessment report. In addition this study was reviewed by the RMS Germany who provided an evaluation report during the MRL consultation for Member States (2012). The characteristics of the study were presented by EFSA during their recent evaluation of the existing MRLs for foramsulfuron (EFSA Journal 2012; 10 (11):2962). Since this study was considered as part of the first EU review a full study summary would normally not be provided for the renewal process however since the study is not summarised in the DAR the RMS requested that a study summary be provided for completeness. No review or peer review of this study is required.

In this summary the dietary burden has been calculated according to current requirements and this is provided below. It can be seen that under the current requirements the calculated dietary burdens for different groups of poultry do not exceed the trigger value of 0.004 mg/kg bw/day.

Dietary burden calculation

Foramsulfuron is authorised on corn which might be fed to poultry. The median and maximum dietary burdens were therefore calculated for different groups of livestock using the OECD model.

Table 6.2.2- 6: Input values for the dietary burden calculation

Commodity	Dietary burden	
	Input value (mg/kg)	Comment
Risk assessment residue definition: foramsulfuron		
Maize silage	0.05	Highest residue
Maize grain	0.01	Median residue

Table 6.2.2- 7: Results of the dietary burden calculation according to OECD model

	Residue level in total feed dry matter (mg/kg)	Residue intake (mk/kg bw/day)
Poultry broiler	0.008	0.001
Poultry – layer	0.020	0.001
Poultry - turkey	0.006	0

The calculated dietary burdens for different groups of poultry do not exceed the trigger value of 0.004 mg/kg bw/day. Therefore, no poultry metabolism studies are required.

As previously mentioned a study summary has been provided at the request of the RMS – the study box and summary are provided in grey text to show that this study is not considered to be a new study for the re-approval process and is present in the baseline dossier. The poultry metabolism study has already been evaluated by RMS Germany in 2012 and it has been reported in the reasoned opinion on the review of the existing maximum residue levels (MRLs) for foramsulfuron according to Article 12 of Regulation (EC)No 396/2005 (EFSA Journal 2012;10(11):2962).

The study was designed to investigate the distribution, magnitude and nature of AE F130360 residues in the edible tissues and eggs of a laying hen following oral administration of foramsulfuron. This study showed that foramsulfuron was rapidly absorbed and excreted and that radioactivity in major organs was very low.

Report:	[redacted];;1999;M-191323-01
Title:	AE F130360: Poultry - Metabolism and nature of the residues in the eggs and edible tissues in the laying hen
Report No:	C005081
Document No(s):	Report includes Trial Nos.: Tox96080 M-191323-01-1
Guidelines:	**EU (=EEC): 96/68/EEC; USEPA (=EPA): OPPTS 860.1300;Deviation not specified**
GLP/GEP:	**yes**

Materials and Methods
Six laying hens were orally dosed with [^{14}C]-AE F130360 at 1.50 mg per bird per day for fourteen consecutive days. The dose was equivalent to approximately 10 ppm in the diet.

The characteristics of the study are reported in Table 6.2.23.

Table 6.2.2- 8: Summary of available metabolism study in poultry

Group	**Species**	**Label position**	**No of animals**	**Application details**		**Sample details**	
				Rate (mg/kg bw per day)	Duration (days)	Commodity	Time
Laying poultry	Hens	^{14}C-phenyl	6	0.75*	14	Eggs	Twice daily
						Excreta	Daily
						Tissues	After sacrifice

* Dose corresponding to 10 mg/kg DM feed

Excreta and cage washings were collected daily and eggs were collected twice daily. At necropsy liver, renal and subcutaneous fat, skin, skeletal muscle and undeveloped eggs were removed for the determination of the distribution and magnitude of [^{14}C]-AE F130360 residues. All collected samples were analysed to determine the residues of [^{14}C]-AE F130360 and its metabolites.

Findings
In egg yolks and whites, residues of AE F130360 were very low but detectable 24 hours after the initial dose administration. Residue levels in yolks continued to rise until reaching a plateau by day 10 of dosing at a concentration of 0.018 ± 0.005 mg equivalents/kg tissue. Residue levels in egg whites were an order of magnitude lower, with a maximum concentration of 0.007 and 0.006 mg equivalents/kg tissue seen on days 2-3 and 8 of dosing. In undeveloped eggs, the mean concentration of AE F130360 derived residue was 0.012 ±0.004 mg equivalents/kg.

Levels of AE F130360 residues and/or its metabolites in the edible tissue of the hen were low, with the highest concentration seen in liver (0.023 ± 0.01 mg equivalents/kg). Residues in all other tissues were an order of magnitude lower at less than 0.005 mg equivalents/kg.

Following the administration of the first dose of [^{14}C]-AE F130360, elimination was rapid with 71.28 ± 4.03% of the administered dose recovered within the first twenty four hours of dosing. The overall mean daily recovery was 83.63 ± 5.00% over the fourteen day study period.
The major components of the radioactive residue were extracted and characterised in liver, egg yolk and excreta and were found to be parent compound (AE F130360) and the cleavage product (AE F153745). Small amounts of polar and unknown material were also found to be present.

Table 6.2.2- : Isolation and identification/characterisation of the residue in the tissue and excreta

Tissue	Residue level (ppm)	% total residue extracted	% total ^{14}C residue identified/characterised			
			AE F130360	AE F153745	Polar material	unknown
Egg yolk day 10	0.018	63.24	11.46	-	2.38	1.50
Egg yolk day 14	0.014	49.29	-	36.25	-	-
Egg white	0.005	NA	NA	NA	NA	NA
Liver	0.023	55.33	7.32	4.54	9.33	19.18
Muscle	0.003	NA	-			-
Renal fat	0.001	NA	-		-	
Subcutaneous fat	0.003	NA		-	-	
Skin	0.003	NA	-	-	-	-
Undeveloped eggs	0.012	NA	-			-
Excreta (6F; day 1)	1.797	93.37	41.34	29.37	2.00	10.49

NA = not analysed

Conclusion

Following administration of [^{14} C]-AE F130360 at a dose rate equivalent to 10 ppm in the diet for 14 consecutive days, residue levels were detectable in all edible tissues between 0.001 and 0.023 mg equivalents AE F130360/kg tissue, although only liver and egg yolk contained residues above 0.010 ppm. Identification of residues in liver and egg yolk showed the residue to be comprised of parent compound (AE F130360) and cleavage product (AE F153745) together with some polar and unknown material. These two compounds have also been identified as major metabolites in the rat.
Elimination of radioactivity in the excreta was rapid (>70% of the dose on day 1) and was found to be mainly composed by unchanged parent together with some cleavage product indicating that AE F130360 is either poorly absorbed or rapidly cleared. There was little systemic distribution of this compound since all tissue residues examined were very low.

CA 6.2.3 Lactating ruminants

In the original review for foramsulfuron at EU level it is stated in the DAR that animal metabolism studies were not triggered and were thus not required. However, during the EU evaluation a study on ruminants (performed in 1999 for North America) was submitted and evaluated and is included in the Foramsulfuron Review Report (Appendix III) as a study which was submitted during the evaluation period but which was not cited in the draft assessment report. In addition this study was reviewed by the RMS Germany who provided an evaluation report during the consultation for Member States (2012). The characteristics of the study were presented by EFSA during their recent evaluation of the existing MRLs for foramsulfuron (EFSA Journal 2012; 10 (11):2962). Since this study was considered as part of the first EU review a full study summary would normally not be provided for the renewal process however since the study is not summarised in the DAR the RMS requested that a study summary be provided for completeness. No review or peer review of this study is required.

In this summary the dietary burden has been calculated according to current requirements and this is provided below. It can be seen that under the current requirements the calculated dietary burdens for different groups of livestock do not exceed the trigger value of 0.004 mg/kg bw/day.

Dietary burden calculation

Foramsulfuron is authorized on corn which might be fed to livestock. The median and maximum dietary burdens were therefore calculated for different groups of livestock using the OECD model.

Table 6.2.3- 9: Input values for the dietary burden calculation

Commodity	Dietary burden	
	Input value (mg/kg)	Comment
Risk assessment residue definition: foramsulfuron		
Maize silage	0.05	Highest residue
Maize grain	0.01	Median residue

Table 6.2.3- 10: Results of the dietary burden calculation according to OECD model

	Residue level in total feed dry matter (mg/kg)	Residue intake (mk/kg bw/day)
Cattle – beef	0.102	0.003
Cattle – dairy	0.078	0.003
Sheep – rams/ewes	0.003	0
Sheep - lambs	0.041	0.002
Swine – breeding	0.033	0.001
Swine – finishing	0.008	0

The calculated dietary burdens for different groups of livestock do not exceed the trigger value of 0.004 mg/kg bw/day. Therefore, no livestock metabolism study is required. Nevertheless, a metabolism ruminant study had been conducted in 1999 for North America.

As previously mentioned a study summary has been provided at the request of the RMS – the study box and summary are provided in grey text to show that this study is not considered to be a new study for the re-approval process and is present in the baseline dossier. The ruminant metabolism study has already been evaluated by RMS Germany in 2012 and it has been reported in the reasoned opinion on the review of the existing maximum residue levels (MRLs) for foramsulfuron according to Article 12 of Regulation (EC)No 396/2005 (EFSA Journal 2012;10(11):2962).

The present study was designed to investigate the distribution, elimination, magnitude and nature of the AE F130360 residues in the edible tissues and milk of a dairy cow following oral administration. The study in ruminants showed that foramsulfuron was rapidly absorbed and excreted and radioactivity in major organs was very low.

Report:	[redacted];;1999;M-191251-01
Title:	Cow - metabolism, distribution and nature of the residues in milk and edible tissues AE F130360 Code: AE F130360 00 ZE
Report No:	C005046
Document No(s):	Report includes Trial Nos.: TOX6079 M-191251-01-1
Guidelines:	**EU (=EEC): 91/414/EEC; USEPA (=EPA): OPPTS 860.1300;Deviation not specified**
GLP/GEP:	**yes**

A dairy cow was orally dosed with [^{14}C]-AE F130360 with a single mean daily dose of 187.42 mg, equivalent to 0.389 mg/kg body weight, for seven consecutive days. The dose was equivalent to approximately 6.7 times the maximum expected exposure following dietary ingestion and equivalent to 15.99 ppm in the diet. The characteristics of the study are reported in Table 6.2.3- 11.

Table 6.2.3- 11: Summary of available metabolism study in lactating ruminant

Group	Species	Label position	No of animal	Application details		Sample details	
				Rate (mg/kg bw per day)	Duration (days)	Commodity	Time
Lactating ruminants	Cow	^{14}C-phenyl	1	0.389*	7	Milk and blood	Twice daily
						Urine and faeces	Daily
						Tissues	After sacrifice

* Dose corresponding to 16 mg/kg DM feed

Urine and faeces were collected daily; milk and blood were collected twice daily. At necropsy, 166 hours after initial dose, and approximately 22 hours after final dose, liver, kidney heart, lungs, renal fat, subcutaneous fat, omental fat, muscle (psoas, loin and hindquarter), rumen, abomasal fluid and bile were sampled and the radioactivity present quantified. Identification of metabolite residues was carried out in all edible tissues namely liver, kidney, muscle, fat and milk, and the metabolic profile of urine was also determined.

Findings

Residues of AE F130360 (0.001 ppm) were detected in milk at 6 hours post initial dose. The concentration of radioactive residues remained low and reached a plateau of only 0.006 ppm at 120 hours post initial dose.

The concentration of residues of AE F130360 and/or its metabolites were also generally low. The highest residue levels were found in the kidney at 0.036 mg equivalents/kg, followed by the liver at 0.025 mg equivalents/kg. Residues in fat were between 0.010 and 0.024 mg equivalents/kg and the lowest residue levels were found in the muscle (0.004 mg equivalents/kg) and milk (0.006 mg equivalents/kg).

Following the first dose of [^{14}C]-AE F130360, 36.31% of the administered dose was recovered within the first twenty hours of dosing, in urine and faeces. The mean daily recovery in faeces was 75.22 ± 26.35% and 6.59 ± 2.01% in urine, giving a mean total daily recovery in excreta of 81.81%.

Isolation and identification of the residues in the tissues is summarised below.

Table 6.2.3-4: Isolation and identification of the residues in lactating ruminant tissues

Tissue	Liver	Kidney	Muscle	Milk	Omental fat	Renal fat	Subcutaneous fat
Residue level (ppm)	0.025	0.036	0.004	0.006	0.013	0.024	0.010
% extracted	61.50	72.32	58.78	107.37	93.23	70.26	98.71
% identified/characterised	59.76	66.99	55.56	101.88	90.42	70.24	98.72
AE F130360	49.29	13.98	34.37	33.76	11.14	27.36	61.60
AE F153745	2.64	53.01	21.19	61.74	3.58	35.16	37.12
unknowns	7.83	-	-	6.38	75.70	7.72	-

Following dosing of [^{14}C]-AE F130360 at a dose rate equivalent to approximately 16 mg equivalents/kg in the diet for seven consecutive days (0.389 mg/kg body weight/day), residue levels were detectable in all edible tissues at concentrations which ranged between 0.004 to 0.036 mg equivalents/kg tissue. The major metabolites identified in all tissues were the parent compound

(AE F130360) and cleavage product (AE F153745). These two compounds have also been identified as major metabolites in the rat. The liver and omental fat contained small amounts of polar material (0.001 - 0.003 mg equivalents/kg) and unidentified metabolites less polar than the parent compound were seen in omental fat (0.006 mg equivalents/kg) and renal fat (0.001 mg equivalents/kg). These results indicate that AE F130360 is poorly absorbed and is largely eliminated as unchanged parent compound in the faeces. This compound is either cleared rapidly or undergoes little systemic distribution since the concentrations of tissue residues in the edible tissues were all low.

Based on these findings, EFSA concluded that the parent compound is a valid indicator in livestock, except for milk and kidney, where metabolite AE 153745 seems more appropriate. However, given the low dietary burdens calculated in the frame of the EFSA review, the relevant residue definition in products of animal origin is proposed as foramsulfuron, both for enforcement and risk assessment.

CA 6.2.4 Pigs

No additional metabolism studies were performed on pig.

CA 6.2.5 Fish

Since no residues above 0.01 mg/kg were found in corn grain and no accumulation is to be expected in tissues (log Pow < 3), the fish metabolism study is not required.

CA 6.3 Magnitude of residue trials in plants

Foramsulfuron (AE F130360) is a herbicidal active substance. In the original dossier submitted in 2000 for Annex I inclusion, the use of this compound was supported in corn. No new studies have since been conducted with foramsulfuron-containing formulations for use in European corn, which is the "safe use" crop supported in the AIR3 process.

CA 6.3.1 Corn

Original dossier

A short summary of the data evaluated for the first approval is provided. To evaluate the residue behaviour of foramsulfuron in corn, a total of 47 trials were conducted in corn with different formulations. The use pattern for corn, as shown in chapter 6.3 of the original dossier, is provided in table 6.3.1-1.

Table 6.3.1-1: Use patterns (GAPs) for the spray application of the formulation Equip in/on corn in Europe (northern and southern residue regions), as described in the 2000 dossier

Crop and/ or situation (a)	Member State or Country	Product name	F / G Or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	method, kind (f-h)	growth stage & season (j)	number min-max (k)	Interval between applications (min)	g as/hl min-max	water l/ha min-max	g as/ha min-max		
Corn, without sweet corn and seed production use	Europe North/South	Equip	F	Grassy weeds species and dicot. Weed species	Oily SD*	22.5g/L foramsulfuron +22.5 g/L isoxadifen-ethyl	Broad-cast High volume spraying	BBCH scale: 12-16	1 per season		15-60	100-400	45-60 g foramsulfuron + 45-60 g isoxadifen-ethyl	Is covered by the normal vegetative period between last application and harvest	
Corn, without sweet corn and seed production use	Europe North/South	Equip	F	Grassy weeds species and dicot. Weed species	Oily SD*	22.5g/L foramsulfuron +22.5 g/L isoxadifen-ethyl	Broad-cast High volume spraying	BBCH scale: 12-16	2 per season	7-14 days		100-400	30 g foramsulfuron + 30 g isoxadifen-ethyl followed by 30 g foramsulfuron + 30 g isoxadifen-		Split application in 7-14 days interval
Corn, without sweet corn and seed production use	Europe North/South	Equip	F	Grassy weeds species and dicot. Weed species	Oily SD*	22.5g/L foramsulfuron +22.5 g/L isoxadifen-ethyl	Broad-cast High volume spraying	BBCH scale: 12-16	2 per season	7-14 days		100-400	40 g foramsulfuron + 40 g isoxadifen-ethyl followed by 20 g foramsulfuron + 20 g isoxadifen		Split application in 7-14 days interval

*Formulation type now classified as an OD (oil dispersion)

(a) The EU and Codex classifications (both) should be used
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) e.g. biting and suckling insects, soil born insects, foliar fungi, weeds
(d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GIFAP Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants
(i) g/kg or g/l
(j) Growth stage at last treatment
(k) Indicate the minimum and maximum number of applications possible under practical use conditions
(l) PHI - Pre-harvest interval; n.a - not applicable
(m) Remarks: SI - intervals between applications (in days); Max. appl. rate/season (in g as/ha)

Residue trials in corn were performed in a representative selection of regions and localities in Europe. Various formulations were used in tank mix with a safener compound thus applying foramsulfuron according to usual practice. The trials therefore represent typical residue behaviour of foramsulfuron in corn under European conditions.

The **trial locations in Europe** were spread over main growing areas of the EU northern zone and EU southern zone in order to cover different soil and climatic conditions. The trials consisted of two treatments, one untreated and one treated plot. The rates generally exaggerated the maximum seasonal dose rate applied for the active substance in order to investigate the residue pattern. The application rate corresponded to two applications of 45 g a.s./ha or 60 g/ha of foramsulfuron at growth stage 12-14 then 16-18 for northern Europe and at growth stages 13-14 then growth stage 16-17 for southern Europe. Pre-harvest intervals (PHI) were depending on the period between treatment and maturity of the grain and thus defined by the conditions of use.

In **1997 and 1998**, a WG-formulation containing 50% (w/w) of foramsulfuron (AE F130360) was applied in tank mix with the safener isoxadifen-ethyl (AE F122006) formulated as a WG. In some of the trials in 1997 and all of the trials in 1998 the tank mix also contained the sulfonylurea herbicide iodosulfuron-methyl-sodium (AE F115008), formulated as a 20% WG (w/w). The application rate for the formulation was 2 times 0.09 kg/ha (equivalent to 2 times 45 g a.s./ha of foramsulfuron). The application rates of the 50% WG-formulation of isoxadifen-ethyl was 2 times 0.09 kg/ha (corresponding to 2 times 45 g/ha). The rate of the 20% WG-formulation of iodosulfuron-methyl-sodium was 2 times 0.015 kg/ha (equivalent to 2 times 3 g a.s./ha). The spray volume was 250 – 300 L/ha.

In **1998** and **1999**, an oil-flowable-formulation (AE F130360 01 1K05 A201 or A302) was applied. The application rates were 45 or 60 g a.s./ha.

Residues of foramsulfuron in shoots (forage) at the day of application ranged between 0.9 and 4.0 mg/kg. At the time of a second shoot (forage) sampling, the residues had already fallen below the limit of quantification (0.05 mg/kg). Foramsulfuron, when applied to corn according to GAP, does not lead to residues of foramsulfuron or metabolite AE F153745 in grain at or above the limit of quantification of 0.01 mg/kg at harvest. It was concluded that there were sufficient trials to support the GAP, and that there were no detectable residues of the parent substance (or metabolites) in crop parts to be used as feed or food. An MRL of 0.01 mg/kg was proposed in maize grain.

Studies submitted and evaluated for the inclusion of foramsulfuron on Annex I:
All the study reports listed below were provided for the first approval of foramsulfuron and are still considered to be acceptable.

Report:	[redacted];[redacted];[redacted];[redacted];1999;M-187968-01
Title:	Decline of residues in maize European Union (southern zone) 1997 AE F130360 and AE F122006 water dispersible granule 50 % w/w Code: AE F130360 00 WG50 A106, AE F122006 00 WG50 A202
Report No:	C004454
Document No:	M-187968-01-1
Guidelines:	**Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted];[redacted];[redacted];[redacted];1999;M-191238-01
Title:	Decline of residues in maize European Union (southern zone) 1997 AE F130360, AE F122006, AE F115008 water dispersible granule 50, 50, 20% w/w Code: AE F130360 00 WG50 A106, AE F122006 00 WG50 A202, AE F115008 00 WG20 A105
Report No:	C005041
Document No:	M-191238-01-1
Guidelines:	**EU (=EEC): 7029/VI/95 rev. 5;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted];[redacted];[redacted];[redacted];1999;M-185891-01
Title:	Decline of residues in maize European Union (northern zone) 1997 AE F130360 and AE F122006 water dispersible granule 50 % w/w Code: AE F130360 00 WG50 A106, AE F122006 00 WG50 A202
Report No:	C003280
Document No:	M-185891-01-1
Guidelines:	**Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted];[redacted];[redacted];[redacted];1999;M-191242-01
Title:	Decline of residues in maize European Union (northern zone) 1997 AE F130360, AE F122006, AE F115008 water dispersible granule 50, 50, 20% w/w Code: AE F130360 00 WG50 A106, AE F122006 00 WG50 A202, AE F 115008 00 WG20 A105
Report No:	C005042
Document No:	M-191242-01-1
Guidelines:	**EU (=EEC): 7029/VI/95 rev. 5;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted];[redacted];[redacted];[redacted];1999;M-192667-01
Title:	Decline of residues in maize European Union southern zone 1998 AE F130360, AE F122006, AE F115008 water dispersible granule 50, 50, 20 % w/w Code: AE F130360 00 WG50 A108, AE F122006 00 WG50 A203, AE F115008 00 WG20 A108
Report No:	C005800
Document No:	M-192667-01-1
Guidelines:	**EU (=EEC): 7029/VI/95 rev. 5 - 22/07/97;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted];[redacted];[redacted];[redacted];2000;M-193664-01
Title:	Decline of residues in maize European Union (northern and southern zone) 1998 AE F130360 and AE F122006 oil flowable (1K) 22.5 and 22.5 g/L Code: AE F130360 01 1K05 A201
Report No:	C006322
Document No:	M-193664-01-1
Guidelines:	**EU (=EEC): 7029/VI/95 rev.5 - 22/07/97;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted];[redacted];[redacted];[redacted];1999;M-192663-01
Title:	Decline of residues in maize European Union northern zone 1998 AE F130360, AE F122006, AE F115008 water dispersible granule 50, 50, 20 % w/w Code: AE F130360 00 WG50 A108, AE F122006 00 WG50 A203, AE F115008 00 WG20 A108
Report No:	C005799
Document No:	M-192663-01-1
Guidelines:	**EU (=EEC): 7029/VI/95 rev.5-22/7/97;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted];[redacted];[redacted];[redacted];2000;M-194328-01
Title:	Decline of residues in maize European Union (northern zone) 1999 AE F130360 and AE F122006 oil flowable (1K) 22.5 + 22.5 g/L Code: AE F130360 01 1K05 A302
Report No:	C006632
Document No:	M-194328-01-1
Guidelines:	**EU (=EEC): 7029/VI/95 rev. 5 - 22/07/97;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted];[redacted];[redacted];[redacted];2000;M-194325-01
Title:	Decline of residues in maize European Union (southern zone) 1999 AE F130360 and AE F122006 oil flowable (1K) 22.5 + 22.5 g/L Code: AE F130360 01 1K05 A302
Report No:	C006631
Document No:	M-194325-01-1
Guidelines:	**EU (=EEC): 7029/VI/95 rev. 5 - 22/07/97;Deviation not specified**
GLP/GEP:	**yes**

The following three studies are cited in the Review Report and are included here for completeness despite the fact that they are trials performed outside of Europe.

Report:	[redacted];[redacted];2000;M-238344-01
Title:	At harvest AE F130360 and isoxadifen-ethyl derived residues in field corn following applications of AE F130360 and/or isoxadifen-ethyl WDG at the maximum proposed rates and the shortest proposed PHI, USA and Canada, 1997
Report No:	B002604
Document No(s):	Report includes Trial Nos.: CF97R001 M-238344-01-1
Guidelines:	**USEPA (=EPA): OPPTS 860.1500;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted]d;[redacted];2000;M-238212-01
Title:	At harvest AE F130360 and isoxadifen-ethyl derived residues in field corn following applications of AE F130360 and/or isoxadifen-ethyl WDG at the maximum proposed rates and the shortest proposed PHI, USA and Canada, 1998: AE F130360 00 WG5
Report No:	B002465
Document No(s):	Report includes Trial Nos.: CF98R001 M-238212-01-1
Guidelines:	**USEPA (=EPA): OPPTS 860.1500;Deviation not specified**
GLP/GEP:	**yes**

No additional residue trials have been performed on corn since the Annex I inclusion. In the renewal dossier there are two key use patterns for the formulation, Equip OD. The first consists of a single application at a maximum rate of approx. 2.6 L per hectare at growth stage 12-18. The second consists of split application, two applications at a max rate of 1L per application between BBCH 12-18 with an interval of 7-14 days. The critical GAP is defined as the single application at approx. 2.6L per hectare (highlighted in grey in Table 6.3.1-2).

Table 6.3.1-2: Use pattern (GAPs) for the spray application of foramsulfuron containing formulations on corn in Europe (Northern and Southern regions)

Crop	Region	Application timing	Max a.s.rate of application	Max number of applications	PHI (days)	Remark
Corn	N-EU S-EU	BBCH 12-18	60 g/ha (1) 60 g/ha (2)	1		Single application of Equip OD at a maximum product rate of 2.6 L/ha
Corn	N-EU S-EU	BBCH 12-18	30 g/ha (1) 30 g/ha (2)	2		Split application of Equip OD.

Note: (1) Foramsulfuron (2) isoxadifen

We wish to support a use where the final application could be latest at a growth stage of BBCH 18 although some residue trials were performed at BBCH 16-17. Nevertheless, it should be noted that because the application is made very early in the growing season and the trials presented in the original dossier have much higher (one and a half or double) application rates, they cover the use supported in this dossier.

According to Article 12 of Regulation (EC) No 396/2005, the European Food Safety Authority (EFSA) has reviewed the Maximum Residue Levels (MRLs) currently established at European level for the pesticide active substance foramsulfuron. A reasoned Opinion on the review of the existing maximum residue levels (MRLs) for foramsulfuron was published in EFSA Journal 2012; 10(11):2962. To assess the magnitude of foramsulfuron residues resulting from critical GAPs chosen by EFSA (1-2x 60 g a.s./Ha; GS 12-18), all trials reported in the PROFile including residue trials evaluated in the framework of the peer review were considered. A sufficient number of trials complying with the GAP was reported by the RMS Germany for maize (grain and forage).

CA 6.4 Feeding studies

The cereal commodities likely to be fed to livestock consist of grain (which is fed to poultry, pigs and cattle) and straw (which is fed to cattle only). Use of foramsulfuron in maize according to the recommended GAP is not likely to result in significant residues in any of these commodities. Furthermore, livestock metabolism studies showed that foramsulfuron does not accumulate in eggs, milk or edible tissues. The calculated dietary burdens for different groups of livestock do not exceed

the trigger value of 0.004 mg/kg bw/day. Therefore, no livestock feeding studies are required to investigate the residue levels of foramsulfuron in food of animal origin.

The nature and magnitude of foramsulfuron residues in commodities of animal origin has been evaluated by EFSA. A reasoned opinion on the review of the existing maximum residue levels (MRLs) for foramsulfuron was published in EFSA Journal 2012; 10(11):2962). It was concluded that no livestock feeding study is needed.

CA 6.4.1 Poultry

No study was performed.

CA 6.4.2 Ruminants

No study was performed.

CA 6.4.3 Pigs

No study was performed.

CA 6.4.4 Fish

No study was performed.

CA 6.5 Effects of processing

Metabolism studies (KCA 6.2.1/01 and KCA 6.2.1/02) conducted with foramsulfuron at an exaggerated application rate of 240 g a.s./ha in corn showed residues of 0.004 to 0.010 mg/kg TRR (total radioactive residue) in the edible agricultural commodity corn grain, depending on the ^{14}C label used.

In the field residue trials, no foramsulfuron derived residues above 0.01 mg/kg (limit of quantification) for the active substance and 0.01 mg/kg for the principal metabolite AE F153745 were found in corn grain at the exaggerated application rate of up to 90 g a.s./ha. Consequently, no residues of the active substance or metabolites are to be expected at levels above the trigger value of 0.1 mg/kg under normal field conditions.

The active substance does not show a toxicological profile which gives any reason for concern. Furthermore, all significant metabolites occurring in the plant have also been identified in animals.

As no residues were found in corn grain at the exaggerated application rate of up to 90 g a.s./ha and the chronic exposure does not exceed 10 % of the ADI, no studies on the effects of processing on the nature of the residue were considered necessary.

CA 6.5.1 Nature of the residue

No studies on the effects of processing on the nature of the residue were performed.

CA 6.5.2 Distribution of the residue in peel and pulp

Not relevant for corn.

CA 6.5.3 Magnitude of residues in processed commodities

The following study was submitted and evaluated under the scope of the inclusion of foramsulfuron at European level. It was not summarised in the DAR but is present in the review report in the list of studies submitted during the evaluation but not summarised in the DAR. Processing studies are not triggered in the EU but the study was performed for the US and is included here for completeness since it was submitted of for the first approval.

Report:	[redacted];2000;M-238387-01
Title:	AE F130360 and isoxadifen-ethyl derived residues in field corn grain and processed corn commodities following applications of AE F130360 and AE F122006 WDG at an exaggerated rate and the shortest proposed PHI, USA, 1998
Report No:	B002651
Document No(s):	Report includes Trial Nos.: CF98R002 M-238387-01-1
Guidelines:	**USEPA (=EPA): OPPTS 860.1520;Deviation not specified**
GLP/GEP:	**yes**

CA 6.6 Residues in rotational crops

CA 6.6.1 Metabolism in rotational crops

All data submitted for metabolism in plants and succeeding/rotational crops were considered to be acceptable during the EU review. In the Inclusion Directive and the Review Report there were no areas of potential concern highlighted for plant metabolism. Even though a confined rotational crop study was not triggered a study was available and submitted/reviewed for the EU approval. A short summary of the study is provided.

Report:	[redacted];[redacted];[redacted];1999;M-185898-01
Title:	Uptake of residues of (U-phenyl-14C)-AE F130360 and (2-pyrimidyl-14C)-AE F130360 in soil by rotational crops under confined conditions
Report No:	C003287
Document No(s):	Report includes Trial Nos.: 516CF M-185898-01-1
Guidelines:	**USEPA (=EPA): OPPTS 860.1850;Deviation not specified**
GLP/GEP:	**yes**

Table 6.6.1-12: Summary of available metabolism studies in rotational crops

Crop group	Crop	Label position	Application and sampling details				
			Method F or G [(a)]	Rate (kg a.s./ha)	Sowing intervals (DAT)	Harvest intervals (DAT)	Remarks
Root and tuber vegetables	Radish	^{14}C-phenyl or ^{14}C-pyrimidyl	Soil, G	0.06 or 0.09 [(b)]	59 [(c)], 119, 269	nr	-
Pulses and oilseeds	Soya bean				30, 119, 269	nr	-
Cereals	Wheat				59 [(c)], 119, 269	nr	-

Nr: not reported
(a): outdoor/field application (F) or glasshouse/protected/indoor application (G)
(b): 0.06 kg/ha after 119 days of ageing and 0.09 kg/ha after 30 and 269 days of ageing
(c): wheat and radishes planted after 30 days were replanted after 59 days due to phytotoxic effects of the soil residues

^{14}C -labelled foramsulfuron was applied to bare soil at rates of 60 g a.s./ha (119 days of ageing) and 90 g a.s./ha (30 and 269 days of aging). Separate soil plots were treated with either [U-phenyl-^{14}C]-foramsulfuron or [2-pyrimidyl-^{14}C]- foramsulfuron. Rotational crops (radishes, wheat and soybeans) were planted at 30 days, 119 days and 269 days after treatment. Soybeans replaced leafy vegetables since this crop is commonly rotated with corn. Wheat and radishes planted after 30 days were replanted after 59 days due to phytotoxic effects of the soil residues. The uptake of radioactive residue into raw agricultural commodities planted in soil previously treated with labelled foramsulfuron after various ageing intervals was extremely low. Most crop residues were well below 0.01 ppm. No single metabolite was above the level of significance in any crop even after short rotation times of 30 or 59 days.

A reasoned opinion on the review of the existing maximum residue levels (MRLs) for foramsulfuron was published in EFSA Journal 2012; 10(11):2962. It was concluded that maize may be grown in rotation but, according to the soil degradation studies evaluated in the framework of the peer review, DT_{90} values of foramsulfuron are all expected to be lower than 51 days which is far below the trigger value of 100 days. According to the European guidelines on rotational crops, further investigation of residues in rotational crops is not required and relevant residues in these crops are not expected. Considering the low levels of residues found in succeeding crops, EFSA concluded that a specific residue definition for rotational crops is not required.

"AIR3" process

A study has been performed for the registration of foramsulfuron in the USA (60 g/ha), this study has been included for completeness. This test included plantback intervals of 7 days and 14 days for soybean (emergency plantback scenario). No AE F130360 derived residues, above the limits of quantification, (0.01 µg/g for parent and 0.02 µg/g for AE F153745 in seed, 0.05 µg/g for both compounds in forage and hay) were observed in any raw agricultural commodities from soybeans planted seven days after treatment of the bare plot.

Report:	[redacted] •; [redacted] ;2000;M-238450-01
Title:	At-harvest AE F130360 and AE F122006 derived residues in rotational crops planted after treatment of a bare plot with AE F130360 WDG and AE F 122006 WDG at selected applications rates and rotational intervals, USA, 1997; AE F130360 00 WG50
Report No:	B002716
Document No(s):	Report includes Trial Nos.: CF97R002 M-238450-01-1
Guidelines:	**USEPA (=EPA): OPPTS 860.1900;Deviation not specified**
GLP/GEP:	**yes**

Material and Methods

Two sites were established for the field phase of this study. The crops were cultivated under agricultural practices typical of the trial site regions. Each site comprised two untreated control plots (one each for wheat and soybeans) and three treated plots (one for wheat, two for soybeans). The treated plots for rotation to soybeans each received a single application of both compounds as a tank mix. The soybean plots were treated at a rate of 60 grams foramsulfuron and isoxadifen-ethyl per hectare. The first plot was treated 14 days prior to planting the soybeans and the second seven days before planting. The treated plot for rotating to wheat received two applications of both compounds as a tank mix. The first application to the wheat plot was timed to be consistent with 91 cm tall corn, the second with 122 cm tall corn. The first application was made at a rate of 60 grams active ingredient per hectare, the second at a rate of 30 grams active ingredient per hectare. This plot was planted to winter wheat at the normal time.

Samples of wheat (forage - fall and spring cuttings, hay, straw and grain) and soybean (forage, hay and seed) were collected at representative sampling times. All samples were frozen shortly after collection. Samples of soybean (forage, hay and seed) from the seven day replanting, were analyzed for AE F130360 parent compound and its metabolite AE F153745.

Findings

No AE F130360 derived residues, above the limits of quantitation, (0.01 µg/g for AE F130360 and 0.02 µg/g for AE F153745 in seed, 0.05 µg/g for both compounds in forage and hay) were observed in any raw agricultural commodities from soybeans planted seven days after treatment of the bare plot. The agricultural use of AE F130360 will therefore not lead to a significant carryover of soil residues into rotated crops.

There are no new/additional studies planned for metabolism in rotational crops.

CA 6.6.2 Magnitude of residues in rotational crops

The metabolism study on rotational crops has shown that no relevant residues at or above the LOQ of 0.01 mg/kg are expected in succeeding crops. Specific plant back restrictions related to the use of foramsulfuron are therefore not required.

CA 6.7 Proposed residue definitions and maximum residue levels

CA 6.7.1 Proposed residue definitions

As presented in the original dossier for foramsulfuron, the proposed residue definition in plants, both for data collection and enforcement, is the parent compound foramsulfuron itself.

Table 6.7.1- 1: European residue definitions

Matrices	Residue definition		Reference
Food of plant origin	Risk assessment and Monitoring	Foramsulfuron	DAR (01 April 2001)
Food of animal origin	Risk assessment and Monitoring	None, as no residue anticipated	

According to Article 12 of Regulation (EC) No 396/2005, the European Food Safety Authority (EFSA) has reviewed the Maximum Residue Levels (MRLs) currently established at European level for the pesticide active substance foramsulfuron. A reasoned opinion on the review of the existing maximum residue levels (MRLs) for foramsulfuron was published in EFSA Journal 2012; 10(11):2962). Considering the low levels of residues found in succeeding crops, EFSA concluded that a specific residue definition is not required. Given the low dietary burden calculated in the framework of the EFSA review, the relevant residue definition in products of animal origin was proposed as foramsulfuron, both for enforcement and risk assessment.

Table 6.7.1- 2: Current proposed residue definitions

Matrices	Residue definition		Reference
Food of plant origin	Risk assessment and Monitoring	Foramsulfuron	DAR (01 April 2001)
Food of animal origin	Risk assessment and Monitoring	Foramsulfuron	EFSA Journal 2012; 10(11):2962

CA 6.7.2 Proposed MRLs and justification of the acceptability of the levels proposed

As no residues above the analytical limit of quantification were detectable in any of the trials, a maximum residue level (MRL) of 0.01 mg/kg, expressed as parent substance, was proposed for foramsulfuron. This value was based on the evaluation of data packages submitted with the original dossier.

Table 6.7.2- 1: Existing EU MRLs

Commodity	Existing EU MRL (mg/kg)	Reference
Maize grain	0.01	Regulation (EC) No 149/2008 (29 January 2008)

According to the EFSA review, MRLs and risk assessment values for the relevant commodities in ruminants can be established at the LOQ level (0.01 mg/kg). For poultry and pigs, MRLs are not required because they are not expected to be exposed to significant levels of foramsulfuron residues.

Table 6.7.2- 2: Current MRLs established by EFSA

Commodity	MRL (mg/kg)	Reference
Maize grain	0.01* (a)	EFSA Journal 2012; 10(11):2962
Bovine meat, fat, liver, kidney	0.01*	
Sheep meat, fat, liver, kidney	0.01*	
Goat meat, fat, liver, kidney	0.01*	
Cattle, sheep, goat milk	0.01*	

* indicates that the MRL is set at the limit of analytical quantification
(a) Tentative MRL to be confirmed by a confirmatory method for enforcement in maize grain and forage (new enforcement method 01360 presented in Section 4)

CA 6.7.3 Proposed MRLs and justification of the acceptability of the levels proposed for imported products (import tolerance)

No import tolerances have been proposed in the EU or applied for in any EU Member State.

CA 6.8 Proposed safety intervals

The proposed safety intervals below are those evaluated during the first approval of foramsulfuron. No modifications/changes are required.

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

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

Re-entry period for man to crops, buildings or spaces treated:
Foramsulfuron is intended for use in maize. Re-entry in treated fields is generally not necessary. Therefore no re-entry period needs to be proposed for European product labels.

Withholding period (in days) for animal feedingstuffs:
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 feeding-stuff. Residues of foramsulfuron in corn grain were found to be below the limit of quantification (< 0.01 mg/kg) at harvest. Residues were also found to be below the limit of quantification (< 0.05 mg/kg) in green plants which might be used for silage. Due to the recommended application of products containing foramsulfuron, the withholding period is covered by the vegetation period of the crop.

Waiting period between the last applications and sowing or planting the crops to be protected:
Foramsulfuron is intended for use in corn. Treatment takes place post-emergence. Due to the selectivity of the herbicide, the crops to be protected are sufficiently resistant to its activity. Therefore no waiting period needs to be proposed. Replanting tests with application on bare soil have shown that the effects are few and also acceptable, when corn is planted 2 to 3 weeks after application. Even in emergency cases corn will not be sown less than 3 weeks after a previous treatment. Therefore no waiting period needs to be proposed for emergency replanting.

Waiting period between application and handling treated product:
Handling of treated crops is generally not required before harvest, which is always done mechanically. Thus, there is no need to define a waiting period between application and handling the treated corn commodities. It is covered by the vegetation period of the crop.

Waiting period between last applications and sowing or planting succeeding crops:
No measurable residues are expected in succeeding crops. Therefore there is no need to define a waiting period before sowing or planting succeeding crops.

CA 6.9 Estimation of the potential and actual exposure through diet and other sources

Acceptable Daily Intake (ADI) and Dietary Exposure Calculation

The Acceptable Daily Intake (ADI) of 0.5 mg/kg body weight was established based on the NOAEL in the rabbit developmental study with a safety factor of 100 (Commission Directive 2003/23/EC and SANCO/10324/2002). No ARfD was allocated. On the basis of its toxicological profile, foramsulfuron is considered unlikely to present an acute hazard. The acute and short term oral toxicity of foramsulfuron is very low. No specific effects were observed up to the limit dose.

Calculation submitted and evaluated for the inclusion of foramsulfuron on Annex I:

Report:	[redacted]; [redacted];2000;M-195132-01
Title:	TMDI estimation of dietary intake of AE F130360 from residues in maize (statement) Code: AE F130360
Report No:	C007058
Document No:	M-195132-01-1
Guidelines:	**Deviation not specified**
GLP/GEP:	**no**

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

According to Article 12 of Regulation (EC) No 396/2005, the European Food Safety Authority (EFSA) has reviewed the Maximum Residue Levels (MRLs) currently established at European level for the pesticide active substance foramsulfuron. A reasoned opinion on the review of the existing maximum residue levels (MRLs) for foramsulfuron was published in EFSA Journal 2012; 10(11):2962. EFSA concluded that for the use of foramsulfuron on maize grain and on maize forage some uncertainties remain due to the data gaps identified (confirmatory method required for enforcement of residues in maize grains and forage). However, EFSA concluded that when considering a tentative MRL in the exposure calculation it did not indicate a risk to consumers.

TMDI calculation was performed using the MRLs given in Table 6.9-1.

Table 6.9- 1 : input values used for TMDI calculation of foramsulfuron

Commodity	Chronic risk assessment		
	Input value (mg/kg)	Comment	Origin of the MRL
Maize grain	0.01*	Median residue (tentative) (a)	EFSA Journal 2012; 10(11):2962
Meat of ruminants	0.01*	Median residue	
Fat of ruminants	0.01*	Median residue	
Liver of ruminants	0.01*	Median residue	
Kidney of ruminants	0.01*	Median residue	
Milk of ruminants	0.01*	Median residue	

(a) confirmatory method required (see enforcement method 01360 in section 4)

As shown in Table 6.9- 2, the highest TMDI calculated for foramsulfuron represented less than 0.1% of the ADI, which denotes considerable margins of safety.

Table 6.9- 2: Highest TMDI calculated for foramsulfuron according to the EFSA model

Compound	EFSA model Highest TMDI (%ADI)	Highest contributor	
		MS diet	Commodity / group of commodities
Foramsulfuron	0.1%	NL Child	Cattle milk

CA 6.10 Other studies

The summary for the active substance sufficiently addresses aspects of the residue situation. Therefore, other special studies are not needed.

CA 6.10.1 Effect on the residue level in pollen and bee products

Foramsulfuron is applied on corn early in the growing season (latest at BBCH 18) and no residues are expected in pollen and bee products.