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Document Title

Summary of the residues in or on treated products, food and feed foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5 g/L)

Data Requirements

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

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

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Bayer CropScience

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Version history

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

[1] Amendments or additions are presented using the approach outlined in SANCO/10180 Chapter 4: How to revise an Assessment Report.

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

In this summary no new studies/information is provided that is not already included in the active substance dossier. A brief summary of the key data has been provided below for completeness.

Stability of residues

Stability of residues during storage of samples

In the original Annex II dossier, the storage stability of foramsulfuron was described for corn matrices (forage, stover and grain). The results of the respective studies indicated that the compound is stable in deep-frozen samples over periods of 468 days, 209 days 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. Since Annex I inclusion, a new study has been generated with longer storage periods covered (minimum of 616 days). Table 8- 1 shows the maximum storage stability periods assessed.

Table 8- 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	KCA 6.1 M-238787-01-1
	Corn, Forage	Up to 616 days		
	Corn, Stover	Up to 620 days		

All the maximum storage periods of samples are covered by the storage stability data.

Table 8- 2: Maximum storage period of samples from supervised field trials

Compound	Crop	Sample material	Maximum storage period (days)	Duration Covered (days)	Reference
Foramsulfuron and AE F153745	Maize	Green material	556	616	KCA 6.1 M-238787-01-1
		Shoot	527		
		Rest of plant	477	620	
		Ear	475	866	
		kernel	429		

Stability of residues in sample 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 the fortified samples are within the acceptable range of 70 - 110%, stability is considered as sufficiently proven. Additionally every analytical batch does contain at least one concurrent recovery which is handled and stored in parallel to the residue samples. So the acceptability of the concurrent recoveries demonstrates the stability of the samples during the work up procedure.

During the development of the enforcement method 01360 (KCA 4.2 /20; M-455564-01-1) 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. The results 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.

Stability was also tested during the Independent Lab Validation (KCA 4.2/21; M-470160-01-1) 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. Significant deviations between initial and re-analysis were observed especially for the matrices lemon fruit and oilseed rape. Therefore the analysis of the samples has to be conducted within 1 day.

Studies on metabolism in plants or livestock

Metabolism in plants

Metabolism of foramsulfuron was investigated for foliar application on cereals (maize) using ^{14}C-phenyl and ^{14}C-pyrimidine labelled foramsulfuron. The characteristics of these studies are summarised in Table 8- 3.

Table 8- 3: Summary of plant metabolism studies

Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G[a]	Rate (kg a.s./ha)	No	Sampling (DAT)	Remarks	
Cereals	Maize	^{14}C-phenyl	Foliar (BBCH 17-31)[b]	0.06 (1N) / 0.24 (4N)	1	Immature plant: 0, 14, 27, 42 Forage: 60 Stover and grain: 77	Foramsulfuron formulated with safener isoxadifen ethyl (1:1)	KCA 6.2.1/01 M-185906-01
		^{14}C-pyrimidyl				Immature plant: 0, 14, 42 Forage: 85 Stover and grain: 106		

(a): Outdoor/field application (F) or glasshouse/protected/indoor application (G)
(b): F or G not stated

It was concluded that the submitted studies give sufficient information to propose a definition of the residue for risk assessment in plant materials, as foramsulfuron.

Metabolism in livestock

No animal metabolism data was required at the time of the original EU dossier submission.

Poultry

Although not required, the RMS Finland recommended including the poultry study in the AIR3 submission. This allows the study to be peer reviewed and thus covered in case triggered by any future

uses of foramsulfuron. It 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, magnitude and nature of the AE F130360 residues in the edible tissues and eggs of a laying hen following oral administration. Metabolism study in poultry showed that foramsulfuron was rapidly absorbed and excreted and radioactivity in major organs was very low.

The characteristics of the study are reported in Table.

Table 8- 4 : Summary of available metabolism study in poultry

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

* Dose corresponding to 10 mg/kg DM feed

Ruminant

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. Metabolism study in ruminants showed that foramsulfuron was rapidly absorbed and excreted and radioactivity in major organs was very low.

The characteristics of the study are reported in Table 8- 5.

Table 8- 5 : 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 feaces	Daily
						Tissues	After sacrifice

* Dose corresponding to 16 mg/kg DM feed

The 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.

No additional metabolism studies were performed on pig.

Residue trials (supervised field trials)

Maize

Foramsulfuron (AE F130360) is an herbicidal active substance. In the Annex II dossier submitted in 2000 for Annex I inclusion, the use of the compound was supported in corn for the same formulation Equip OD.

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.

Table 8- 6: Comparison of intended and critical EU GAPs

Crop	Type of GAP	Number of applications	Application rate per treatment	Interval between application	Growth stage at last application	PHI (days)
Maize	PROFile EU N	1	60 g/ha	-	BBCH 18	-
	PROFile EU S	1	60 g/ha	-	BBCH 18	-
	EU (DAR)	1	60 g/ha	-	BBCH 16	-
	Intended EU N and S	1	60 g/ha	-	BBCH 18	-

Original II dossier
To clarify the residue behavior of foramsulfuron in corn, a total of 47 trials were conducted in corn with different formulations.

Corn kernels do not contain residues of foramsulfuron at or above the limit of quantification of 0.01 mg/kg after use as herbicide at a rate of 2 times 45 or 60 g/ha. Also no residues of the metabolite AE F153745 are found in corn kernels at harvest.

"AIR3" process
No additional residue trials were performed on corn since the Annex I inclusion.

There are two key use patterns for the formulation, Equip OD (FFN+IDF OD 45). 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 the table).

Table 8- 7: 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. Besides, no measurable residues of foramsulfuron could be found in any treated sample material under worst case application scenario than the intended GAP with FSN+IDF OD 45 product. Therefore, the trials already presented are deemed sufficient to cover the use of this product.

Livestock Feeding Studies

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 8-8: 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 8-11: 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	0.002
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
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 livestock do not exceed the trigger value of 0.004 mg/kg bw/day.

Use of foramsulfuron in maize according to the recommended GAP is not likely to result in significant residues (i.e. > 0.1 mg/kg) in any of these commodities. Furthermore livestock metabolism studies showed that foramsulfuron do not accumulate in eggs, milk or edible tissues. Therefore, no livestock feeding studies to investigate the residue levels of foramsulfuron in food of animal origin are required.

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.

Studies on Industrial Processing and/or Household Preparation

Quantifiable residues of foramsulfuron are not expected in maize grains and as the chronic exposure does not exceed 10 % of the ADI, there is no need to investigate the effect of industrial and/or household processing.

Studies for Residues in Representative Succeeding Crops

Nature of residues

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.

Nevertheless, a confined rotational crop study was submitted in the original EU dossier.

Table 8-12: 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)	Reference
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	KCA 6.6.1/01 M-185898-01-1
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

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.

Magnitude of residues

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.

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

Proposed Residue Definition and Maximum Residue Levels

Proposed residue definition

Table 8- 93: Residue definitions

	Definition	Conversion factor for enforcement to risk assessment	Source
Plant residue definition for monitoring	Foramsulfuron	-	EU regulation n° 149/2008
Plant residue definition for risk assessment	Foramsulfuron	-	DAR
Animal residue definition for monitoring	Foramsulfuron	-	EFSA journal 2012;10(11):2962
Animal residue definition for risk assessment	Foramsulfuron	-	EFSA journal 2012;10(11):2962
Other residue definitions (in processed commodities, …)	Not required	-	DAR, EFSA journal 2012;10(11):2962

Proposed maximum residue levels (MRLs)

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 Annex II dossier.

Table 8- 104: Proposed Maximum Residue Level?

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 8- 115:

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 (method 01360 presented in KCA Section 4)

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

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

Pre-harvest interval (in days) for each relevant crop
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.

Table 8- 12: Pre-harvest interval by crop

Crop (intended GAP)	PHI (days) or latest application growth stage (BBCH)
Maize (1 x 60 g a.s./ha)	BBCH 18

Re-entry period (in days) 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
Please refer to KCP 7.5 part of Mammalian Toxicology Section. 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 feedingstuff. 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 last application 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 application 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.

Estimation of Exposure Through Diet and Other Means

TMDI calculations
In order to evaluate the potential chronic exposure to foramsulfuron residues through the diet, the Theoretical Maximum Dietary Intakes (TMDI) was 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 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), but considering a tentative MRL in the exposure calculation did not indicate a risk to consumers.

TMDI calculation was performed using the MRLs given in the following table.

Table 8- 13: 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

The highest TMDI calculated for foramsulfuron represented less than 0.1% of the ADI, which denotes considerable margins of safety.

NEDI calculations
Not required.

NESTI calculations
No relevant, as no ARfD was set for foramsulfuron.

Consumer risk assessment conclusion
The proposed uses of foramsulfuron do not represent unacceptable acute and chronic risks for the consumer.

Summary and Evaluation of Residue Behaviour for foramsulfuron
The toxicological profile of foramsulfuron was evaluated at EU level, which resulted in the proposal of an ADI of 0.5 mg/kg bw/day that was considered in the frame of this evaluation. An ARfD was not deemed necessary.

Primary crop metabolism of active substance was sufficiently investigated to define residue for enforcement and risk assessment in crops under consideration.

Regarding the magnitude of residues in those crops, a sufficient number of residue trials are available to support all the intended GAPs in southern Europe. These data allowed to estimate the expected residue concentrations in the relevant plant commodities, and to confirm that no MRL exceedance will result from intended uses.

As residues of active substance do not exceed the trigger value of 0.1 mg/kg in treated crops, and the overall chronic exposure did not exceed 10% of the ADI, there is no need to investigate the effect of industrial and/or household processing.

Residues in succeeding crops have been sufficiently investigated; it is very unlikely that residues will be present in succeeding crops.

Considering dietary burden and based on the intended uses, no significant modification of the intake was calculated for livestock. MRLs in commodities of animal origin (0.01 mg/kg in ruminant commodities) were proposed by EFSA.

Chronic consumer exposure resulting from the uses proposed in the framework of this application was calculated. Based on EFSA PRIMo (rev2), chronic and acute exposures were considered as acceptable for all groups of consumers.