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Document Title

Summary of the residues in or on treated products, food and feed
iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 g/L)

Data Requirements

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

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

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Version history

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

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

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

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 iodosulfuron-methyl-sodium was described for cereal matrices (shoot, straw and grain). The results of the respective studies indicated that the compound is stable in deep-frozen samples over periods of 24 months in wheat grain and 18 months in wheat shoot and wheat straw. The analytes were found to be stable upon deep-freeze storage for the durations studied.

Since Annex I inclusion, two new studies have been generated with longer storage periods covered (26 months in wheat shoot and 28 months in wheat straw).

Table CP 8- 1 shows the maximum storage stability periods assessed.

Table CP 8- 1: Summary of storage stability of iodosulfuron-methyl-sodium (AE F115008) in cereal matrices

Active substance	Plant matrix	Stability	Reference
Iodosulfuron-methyl-sodium	Wheat Shoot	Up to 26 months	M-192961-01-1 / C005930
	Wheat Straw	Up to 28 months	M-192550-01-1 / C005716
	Wheat Grain	Up to 24 months	M-181689-01-1 / C001041

Stability of residues in samples extracts

During the development of the enforcement method 01360 (Report MR-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. 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.

During the development of the Independent Lab Validation, the stability was tested after storage of the final samples in the dark at a temperature between 2 – 8°C over three to thirteen days. 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

In the original Annex II dossier, the behavior and metabolism of iodosulfuron-methyl-sodium was investigated in cereals only.

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

Group	Crop	Label position	Application and sampling details				Reference
			Method F or G (a)	Rate (kg as/ha)	No	Sampling (DAT)	
Cereals	Wheat	2-^{14}C-triazinyl	Foliar, F	20 g/ha + safener (b)	1	Forage: 3, 7, 22 Hay: 35 Mature: 49 Harvest: 77	M-182772-01-1
		U-^{14}C-phenyl	Foliar, G	20 g/ha + safener (b)	1	Forage: 0, 20, 23, 28 Hay: 43 Harvest: 87	M-148037-01-1

(a): Outdoor/field application (F) or glasshouse/protected/indoor application (G)
(b): The safener used is mefenpyr diethyl at ratio 3/1

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

Metabolism in animals

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.
However, a poultry metabolism study was nevertheless conducted to satisfy formal requirements in the course of an anticipated registration of the active substance iodosulfuron-methyl-sodium in the USA.

The calculated dietary burdens do not exceed the trigger value of 0.004 mg/kg bw/day for poultry, cattle and swine. It is slightly exceeded for sheep lambs only. Therefore, a livestock metabolism study could be required.
A dairy cow metabolism study was conducted to satisfy formal requirements in the course of an anticipated registration of iodosulfuron-methyl-sodium in the USA.

Both studies are presented in the active substance dossier.

A pig metabolism study was not conducted, since metabolism followed comparable pathways in all other tested species (rat, dog, hen and cow).
Since no residues above 0.01 mg/kg were found in cereal grain and no accumulation is to be expected in tissues (log Pow < 3), the fish metabolism study is not required.

Residue trials (supervised field trials)

Cereals
Iodosulfuron-methyl-sodium is a herbicide from the substance class of sulfonylureas developed for the use in cereals. Like other sulfonylureas it acts systemically by inhibition of acetohydroxy acid synthase (AHAS). Iodosulfuron-methyl-sodium was included in Annex I to Directive 91/414/EEC by Commission Directive 2003/84/EC of 25 September 2003.
Application takes place once per season in spring or autumn. The residue trials were made in spring in order to cover the shortest pre-harvest interval (PHI). The critical GAP for iodosulfuron-methyl-

sodium consists of one treatment in cereal, in spring at a maximum rate of 10 g a.i./ha and at growth stages up to BBCH 32 (end of tillering, node 2 at least 2 cm above node 1). To increase its selectivity, the product contains the safener mefenpyr-diethyl (maximum rate of 30 g/L). The safener has no herbicidal activity; it decreases the sensitivity of the treated crop to the sulfonylurea active substances allowing efficient weed control without phytotoxicity to the treated crop.

Table CP 8-3: Use pattern (GAPs) for the spray application of iodosulfuron-methyl-sodium containing formulations on cereals in Europe (Northern and Southern regions)

Crop	Member state or country	F / G or I	Formulation Conc. of as	Pests or group of pests controlled	Growth stage	Number	Water (L/ha)	Application (g as/ha)	PHI
Winter cereals (Barley, wheat, durum, rye, spelt, triticale) Spring cereals (Barley, wheat, triticale)	Europe North / South	F	OD 100 g/kg iodosulfuron-methyl-sodium + 300 g/kg mefenpyr-diethyl	Grass weed species and dicot weed species	BBCH 12-32 End winter, beginning of spring	1 per season	100-400	7.5-10 g iodosulfuron-methyl-sodium + 22.5-30 g mefenpyr-diethyl	Covered by the normal vegetation period between last application and harvest

A total of 14 supplementary trials were performed since Annex I inclusion.

<u>Northern Europe</u>: six residue trials were conducted with a 400OD formulation. The formulations were applied once at growth stage 32 to 43. Residues of iodosulfuron-methyl-sodium in shoot ranged from 0.08 to 0.31 mg/kg at the day of the application. Residues of iodosulfuron-methyl-sodium at harvest were always lower than the respective LOQ at harvest (LOQ grain: 0.01 mg/kg and LOQ straw: 0.05 mg/kg).

<u>Southern Europe</u>: eight residue trials were conducted with two different formulation types (20WG with addition of the adjuvant Biopower and 400OD). The formulations were applied once at growth stage BBCH 32 to 33. Residues of iodosulfuron-methyl-sodium in shoot ranged from < 0.05 to 0.58 mg/kg at the day of the application and were always lower than the LOQ (LOQ shoot: 0.05 mg/kg) at intermediate growth stage (13 days after the application). Residues of iodosulfuron-methyl-sodium at harvest were always lower than the respective LOQ at harvest (LOQ grain: 0.01 mg/kg and LOQ straw: 0.05 mg/kg).

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 iodosulfuron-methyl-sodium. A reasoned Opinion on the review of the existing maximum residue levels (MRLs) for iodosulfuron-methyl-sodium was published in EFSA Journal 2012; 10(11):2974.

Livestock 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 iodosulfuron-methyl-sodium in cereals according to the recommended GAP is not likely to result in significant residues in any of these commodities. Furthermore, livestock metabolism studies showed that iodosulfuron-methyl-sodium do not accumulate in eggs, milk or edible tissues. The calculated dietary burdens do not exceed the trigger value of 0.004 mg/kg bw/day for poultry, cattle and swine. It is slightly exceeded for sheep lambs only. Therefore, no livestock feeding studies to investigate the residue levels of iodosulfuron-methyl-sodium in food of animal origin are required.

Effects of processing

Metabolism studies conducted with iodosulfuron-methyl-sodium at an application rate of 20 g a.s./ha in cereals showed residues of 0.006 - 0.011 mg/kg TRR (total radioactive residue) in the edible agricultural commodity grain.

In the field residue trials, no residues of iodosulfuron-methyl-sodium above 0.01 mg/kg (Limit of quantification) were found in grain at the exaggerated application rate of 15 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.

Furthermore iodosulfuron-methyl-sodium is of low toxicity.

Therefore, no processing study is required to investigate the residues of iodosulfuron-methyl-sodium in processed cereal commodities.

Studies for Residues in Representative Succeeding Crops

Nature of residues

A confined rotational crop study was submitted in the original EU dossier.

Table CP-4: 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
Leafy vegetables	Spinach	^{14}C-triazinyl	Soil, F(b)	0.02	29, 120, 365	408	-
Root and tuber vegetables	Carrot					252, 454	-
Cereals	Wheat					99, 239, 464	-

(a): outdoor/field application (F) or glasshouse/protected/indoor application (G)
(b): or climatic chamber simulating outdoor conditions

Magnitude of residues in rotational crops

A reasoned opinion on the review of the existing maximum residue levels (MRLs) for iodosulfuron-methyl-sodium was published in EFSA Journal 2012; 10(11):2974. Based on the rotational field crop study, the individual metabolite fractions are not expected to exceed 0.05 mg/kg (=LOQ for cereal straw). Considering that it was carried out on a bare soil with twice the normal application rate and that the primary use of this active substance is authorised on cereal crops, it can be concluded that iodosulfuron residue levels in rotational commodities are not expected to exceed 0.01 mg/kg. Specific plant back restrictions related to the use of iodosulfuron-methyl-sodium are therefore not required.

A second experiment (single study) was performed later and consequently used lower application rates (5.4 – 8.1 g/ha). This test included plantback intervals of 7 days and 14 days for soybean (emergency plantback scenario), 60 days for sugarbeet, and 65 days for wheat (re-cropping scenario), to specifically support an envisaged registration of iodosulfuron-methyl-sodium in the USA. Extremely low residues of AE F115008 were transferred into rotated crops in all three tested crop rotation scenarios (emergency plantback of soybean 7 or 14 days after application of 5.4 g/ha AE F115008, plantback of sugarbeet 60 days after application of 5.4 g/ha AE F115008, plantback of wheat 65 days after application of 8.1 g/ha AE F115008). The agricultural use of AE F115008 will therefore not lead to a significant carryover of soil residues into rotated crops.

Proposed Residue Definition and Maximum Residue Levels

Proposed residue definition

According to Article 12 of Regulation (EC) No 396/2005, the European Food Safety Authority (EFSA) has reviewed the Maximum Residue Levels (MRLs) currently established at European level for the pesticide active substance iodosulfuron-methyl-sodium. A reasoned opinion on the review of the existing maximum residue levels (MRLs) for iodosulfuron-methyl-sodium was published in EFSA Journal 2012; 10(11):2974.

Table CP-5 : Current proposed residue definitions

Matrices	Residue definition		Reference
Food of plant origin	Risk assessment and Monitoring	sum of iodosulfuron-methyl and its salts, expressed as iodosulfuron-methyl	EFSA Journal 2012; 10(11):2974
Food of animal origin	Risk assessment and Monitoring	None, as no residue anticipated	

Proposed maximum residue levels (MRLs)
According to the EFSA review, MRLs for the animal commodities are not required because animals are not expected to be exposed to significant levels of residues.

Table CP 8-6 : Current MRLs established by EFSA

Commodity	MRL (mg/kg)	Reference
Maize grain	0.01*	EFSA Journal 2012; 10(11):2974
Barley grain	0.01*	
Rye grain	0.01*	
Wheat grain	0.01*	

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

Proposed Pre-Harvest Intervals, Re-Entry or Withholding Periods
It is not necessary to define a pre-harvest interval. Instead, the pre-harvest interval is given by the growing period between the growth stage at treatment and harvest.
The product is not intended for use in areas where livestock animals may be grazed. Therefore no re-entry period needs to be proposed.
The product is applied early post-emergence on very young plants. Thus, dermal exposure to persons entering a treated field is negligible. No use in buildings is intended. Therefore no re-entry period needs to be proposed for man.
Handling of treated cereals is generally not required before harvest, which is always done mechanically. Therefore there is no need to define a waiting period between application and handling of treated products.
The use of iodosulfuron-methyl-sodium in cereals is not likely to result in significant uptake of residues by succeeding crops. Thus, it is not necessary to set a waiting period between last application and sowing or planting succeeding crops.

Estimation of Exposure Through Diet and Other Means

TMDI calculations
In order to evaluate the potential chronic exposure to iodosulfuron-methyl-sodium 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.

TMDI calculation was performed using the MRLs given in Table CP 8-6.

The highest TMDI calculated for iodosulfuron-methyl-sodium represented less than 1% of the ADI, which denotes considerable margins of safety.