Bayer CropScience

Document Title

Summary of the residues in or on treated products, food and feed for Iodosulfuron-methyl-sodium

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Data Requirements

EU Regulation 1107/2009 & EU Regulation 283/2013
Document MCA
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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Version history

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[1] Note how the amendments or additions are represented (italics/colour etc)

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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 iodosulfuron-methyl-sodium 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.

Iodosulfuron-methyl-sodium (AE F115008) is an herbicidal active substance. In the original dossier, submitted to Germany in 1999, residue trial data supported the use on cereals. In this Annex I Renewal ("AIR") dossier, only the "representative use" on cereals 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 iodosulfuron. A reasoned opinion on the review of the existing maximum residue levels (MRLs) for iodosulfuron was published in EFSA Journal 2012; 10(11):2974.

Report:	[redacted];2012;M-475538-01
Title:	Reasoned opinion on the review of the existing maximum residue levels (MRLs) for iodosulfuron according to Article 12 of Regulation (EC) No 396/2005
Report No:	M-475538-01-1
Document No:	M-475538-01-1
Guidelines:	**Article 12 of Regulation (EC) No 396/2005;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 the sum of iodosulfuron-methyl and its salts, expressed as iodosulfuron-methyl, proposed an MRL of 0.01 mg/kg on barley, maize, rye and wheat grain. A residue definition for enforcement and risk assessment in products of animal origin is not required. 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 6.1/04&05 – a storage stability study in wheat shoot and wheat straw performed to extend the storage period.
- KCA 6.1/06&07 – an extract of a method report is presented due to the fact that it contains data on the stability of iodosulfuron-methyl in sample extracts over time. [The study reports are also summarised in the relevant section of the methods].
- KCA 6.1/08 - an extract of an ILV report is presented due to the fact that it contains data on the stability of iodosulfuron-methyl 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. Although still not triggered, the poultry (KCA 6.2.2/01)

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metabolism study is summarised in this dossier for completeness. The cow metabolism study (KCA 6.2.3/01) is now required and presented.

- KCA 6.3.1/05 to 09. New residue trials have been performed to further support the representative formulation
- KCA 6.6.2/05. A rotational crop, performed to support registration in the US, is considered as supportive for the Annex I renewal, and is reported.

All the other studies were evaluated for the original approval of iodosulfuron-methyl-sodium and full study summarises are not provided.

CA 6.1 - Storage stability of residues

❖ **Stability of residues during storage of samples**

Original Annex II dossier

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.

Studies submitted and evaluated for the first inclusion of iodosulfuron-methyl-sodium on Annex I:

Report:	[redacted];[redacted];1998;M-181689-01
Title:	Stability of AE F115008 in wheat grain during deep freeze storage of 24 months
Report No:	C001041
Document No:	M-181689-01-1
Guidelines:	**Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted];[redacted];1998;M-181582-01
Title:	Stability of AE F115008 in wheat straw during deep freeze storage of 24 months (interim report) Code: AE F115008
Report No:	C000983
Document No(s):	M-181582-01-1
Guidelines:	**Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted];[redacted];1998;M-181587-01
Title:	Stability of AE F115008 in wheat shoot during deep freeze storage of 24 months (interim report) Code: AE F115008
Report No:	C000985
Document No(s):	M-181587-01-1
Guidelines:	**Deviation not specified**
GLP/GEP:	**yes**

"AIR3" process/ New studies submitted

Justification for including this report in this "AIR" dossier

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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 CA 6.1- 1 shows the overall maximum storage stability periods assessed.

Table CA 6.1- 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 (new study)
	Wheat Straw	Up to 28 months	M-192550-01-1 / C005716 (new study)
	Wheat Grain	Up to 24 months	M-181689-01-1 / C001041 (in original dossier)

Report:	[redacted]; [redacted];1999;M-192961-01
Title:	Stability of AE F115008 in wheat shoot during deep freeze storage of 26 months Code: AE F115008
Report No:	C005930
Document No:	M-192961-01-1
Guidelines:	**Deviation not specified**

Material and Methods

The study was designed to determine the stability of iodosulfuron-methyl-sodium (AE F115008) residues in wheat shoot during storage under deep freeze conditions for up to 26 months. Homogenised wheat shoot samples were fortified with iodosulfuron-methyl-sodium at 0.48 mg/kg and stored in a freezer at about -18 °C for up to 26 months. Control samples were stored under the same conditions to allow procedural recovery determination from freshly fortified samples.
Samples were taken for analysis at the day of fortification and after storage periods of 3, 6, 12, 18, and 26 months. Three stored fortified samples and two stored control samples were analysed at each storage interval. Three recoveries performed at 0.05 (n=1) and 0.50 mg/kg (n=2) were run concurrently to each storage interval. Samples were analysed according to the method AL120/96-0. The limit of quantification was 0.05 mg/kg. The procedure involves extraction of residues with methanol, purification by liquid / liquid partitioning under acidic conditions (subsequently with *n*-hexane, ethyl acetate, and toluene), clean-up on a RP18 cartridge, and HPLC/UV determination.

Findings

The average procedural recoveries from all storage intervals amounted to 89% (RSD of 6%) at 0.05 mg/kg and 80% (RSD of 12%) at 0.5 mg/kg. Table CA 6.1-2 summarises the storage recoveries of iodosulfuron-methyl-sodium (AE F115008) determined after the various storage intervals. In order to compensate for small variations in the analytical method efficiency, the storage recoveries were corrected by the concurrent procedural recoveries relevant to the fortification level of the stored samples. Both the uncorrected and corrected values are given. The results indicate that iodosulfuron-methyl-sodium (AE F115008) spiked to shoot samples remained stable throughout the 26 months of deep frozen storage.

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Table CA 6.1- 2: Storage stability of iodosulfuron-methyl-sodium in wheat shoot

Storage interval [months]	Concurrent recovery (a) [%]			Recovered residue in stored samples [%]				
				uncorrected				corrected (b)
	Individual		Mean	Individual			Mean	
0	95	87	91	84	89	85	86	95
3	73	73	73	61	49*	96	79	108
6	73	85	79	46**	89	86	88	111
12	64	69	67	80	64	67	70	104
18	89	73	81	57	79	63	66	82
26	88	86	87	82	80	59	74	85

a) Mean recovery from shoot samples freshly (each storage interval) fortified at 0.50 mg/kg.
b) To compensate for variations in the analytical method efficiency the recoveries from stored samples were corrected taking into account the concurrent procedural recovery from samples freshly fortified at 0.50 mg/kg.
*result not valid due to problems during work-up, not used for further calculation
**outlier as proved by DIXON statistical test, not used for further calculation

Conclusion

Residues of iodosulfuron-methyl-sodium in wheat shoot were shown to be stable upon deep freeze storage at ca. -18 °C for at least 26 months.

Report:	[redacted];1999;M-192550-01
Title:	Stability of AE F115008 in wheat straw during deep freeze storage of 28 months Code: AE F115008
Report No:	C005716
Document No:	M-192550-01-1
Guidelines:	**Deviation not specified**

Material and Methods

The study was designed to determine the stability of iodosulfuron-methyl-sodium (AE F115008) residues in wheat straw during storage under deep freeze conditions for up to 28 months. Homogenised wheat straw samples were fortified with iodosulfuron-methyl-sodium at 0.48 mg/kg and stored in a freezer at about -18 °C for up to 28 months. Control samples were stored under the same conditions to allow procedural recovery determination from freshly fortified samples.
Samples were taken for analysis at the day of fortification and after storage periods of 4, 6, 12, 18, 26, and 28 months. Three stored fortified samples, two stored control samples were analysed at each storage interval. Three recoveries performed at 0.05 (n=1) and 0.50 mg/kg (n=2) were run concurrently to each storage interval. Analyses were performed according to the method AL121/96-0 with a limit of quantification of 0.05 mg/kg. The procedure involves extraction of residues with methanol, purification by liquid / liquid partitioning under acidic conditions (subsequently with *n*-hexane and ethyl acetate), clean-up on a RP18 cartridge, and HPLC/UV determination.

Findings

The average procedural recoveries from all storage intervals amounted to 82% (RSD of 16%) at 0.05 mg/kg and 80% (RSD of 14%) at 0.5 mg/kg. Table CA 6.1-3 summarises the storage recoveries of iodosulfuron-methyl-sodium (AE F115008) determined after the various storage intervals. In order to compensate for small variations in the analytical method efficiency, the storage recoveries were

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corrected by the concurrent procedural recoveries relevant to the fortification level of the stored samples. The results indicate that iodosulfuron-methyl-sodium (AE F115008) spiked to straw samples remained stable throughout the 28 months of deep-frozen storage.

Table CA 6.1-3: Storage stability of iodosulfuron-methyl-sodium in wheat straw

Storage interval [months]	Concurrent recovery (a) [%]			Recovered residue in stored samples [%]				
				uncorrected				
	Individual		Mean	Individual			Mean	corrected (b)
0	94	89	92	68	72	75	72	78
4	94	81	88	73	70	80	74	84
6	80	69	75	62	70	66	66	88
12	91	91	91	81	83	82	82	90
18	64	83	74	72	75	78	75	101
26	63	75	69	63	59	28*	61	88
28	72	67	70	67	66	71	68	97

a) Mean recovery from straw samples freshly (each storage interval) fortified at 0.50 mg/kg
b) To compensate for variations in the analytical method efficiency the recoveries from stored samples were corrected taking into account the concurrent procedural recovery from samples freshly fortified at 0.50 mg/kg
*outlier as proved by DIXON statistical test, not used for further calculation

Conclusion

Residues of iodosulfuron-methyl-sodium in wheat straw were shown to be stable upon deep freeze storage at ca. -18 °C for at least 28 months.

Overall conclusion

The storage stabilities of iodosulfuron-methyl-sodium were carried out in different cereal matrices (wheat shoot, straw and grain). The results of these studies demonstrate that the compounds are stable in the tested plant commodities for the tested periods. For wheat grain and straw, these cover the longest period of time for which samples from supplementary field residue trials presented or summarised in this dossier were stored prior to analysis. For wheat shoot, this period is slightly exceeded. This slight exceedance is not considered as relevant as 26 months of storage stability can be considered relevant for a storage period of 27.2 months. These time periods are given in table CA 6.1-4.

Table CA 6.1- 4: Maximum storage time of the crop samples before analysis and maximum storage stability

Compound	Commodity	Duration covered	Maximum storage
Iodosulfuron-methyl-sodium	Wheat Grain	24 months	16 months (481 days)
	Wheat Straw	28 months	23.3 months (699 days)
	Wheat Shoot	26 months	27.2 months (818 days)

- **Stability of residues in samples extracts**

"AIR3" process/ New studies submitted

Testing the stability of iodosulfuron-methyl-sodium residues in sample extracts was not considered necessary since extracts were either used within the day of their generation and/or procedural recoveries were included in the residue analysis. Also, stability of residues in sample extracts from the

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metabolism study in plants was investigated as part of the study and found to be satisfactory. However, during the work on some method of analysis, additional storage stability data have been collected. They are reported here.

- During the validation of a new analytical method utilising LC-MS/MS for sulfonylureas, a short storage stability study of sample extracts was conducted for iodosulfuron-methyl-sodium (KCA 4.2/16; [redacted], O.; M-226888-01-1). This method was used for the analysis of 2003 and 2004 residue trials. The extract stability data are presented below.

Report:	[redacted]; [redacted];2004;M-226888-01
Title:	Modification M001 to method 00815 for the determination of residues of amidosulfuron, iodosulfuron-methyl-sodium including metabolite metsulfuron-methyl, foramsulfuron and mesosulfuron-methyl in/on flax and wheat matrices by HPLC-MS/MS
Report No:	00815/M001
Document No(s):	M-226888-01-1
Guidelines:	**Deviation not specified**

Material and Methods

Stability of residues in sample extracts was studied in wheat grain (0.01 mg/kg and 0.1 mg/kg), in wheat green material (0.05 mg/kg and 0.5 mg/kg), and in flax grain (0.01 mg/kg and 0.1 mg/kg). After initial analysis, the analytical solutions were stored in a refrigerator and reanalysed after 2 weeks. Storage conditions were the same as those used for analytical solutions (in a refrigerator at 4°C ± 3°C).

Findings

Stability tests showed all analytes were stable in solvent for at least 2 months and in matrix solutions for at least 2 weeks when refrigerated at 4°C ± 3°C. Please refer to Table CA 6.1- 5.

Table CA 6.1- 5: Storage stability of iodosulfuron-methyl-sodium (AE F115008) in sample extracts

Crop	Sample Material	Number of days	Fortification Level [mg/kg]	Recovery [%] Individual					Mean	Sample number	RSD [%]
Wheat	Grain	0	0.01	88	92	101	98	93	94	5	5.4
	Grain	0	0.10	97	90	92	96	97	94	5	3.4
	Grain	14	0.01	93	80	106	102	91	94	5	10.8
	Grain	14	0.10	98	87	92	92	95	93	5	4.4
Wheat	Green Material	0	0.05	92	88	92	92	92	91	5	2.0
	Green Material	0	0.5	89	91	89	87	89	89	5	1.6
	Green Material	14	0.05	98	92	92	95	96	95	5	2.8
	Green Material	14	0.5	90	95	92	92	92	92	5	1.9
Flax	Grain	0	0.01	94	92	91	88	81	89	5	5.7
	Grain	0	0.10	92	97	96	91	96	94	5	2.9
	Grain	14	0.01	92	87	89	90	77	87	5	6.8
	Grain	14	0.10	88	91	88	88	93	90	5	2.6

Conclusion

This investigation showed that iodosulfuron-methyl-sodium is stable in representative matrix solutions for at least two weeks under refrigerated conditions.

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- During the development of the enforcement method 01360 (Report MR-13/007) for the determination of iodosulfuron-methyl-sodium, and other sulfonylureas 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 (KCA 4.2/19 [redacted], S.; [redacted], C.; M-455564-01-1) and it has also been checked during the Independent Lab Validation over a period of 3 to 13 days (KCA 4.2/20 [redacted], S.; M-470160-01-1). The results are presented below and the studies are detailed in the Analytical Methods section.

Report:	[redacted];[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 samples at 4°C ± 3°C under dark conditions over the given periods. To check the stability after freshly prepared matrix standards were prepared and analyzed together with the aged recovery samples.

Findings
Iodosulfuron-methyl was not stable for all matrices at the given conditions. In sugar beet, body and leaf, a significant decrease could be observed, in lemon fruit and oil rape seed an increase was observed, which can be a result of different matrix effects in fresh matrix standards compared to old recovery samples.

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Table CA 6.1- 6: Stability of Iodosulfuron-methyl in Plant Extracts, Quantifier Mass Transition

Sample Material	Fortification Level [mg/kg]		Recovery Rates [%]					Mean
Sugar beet, body	0.1	Day 0 (initial analysis)	108	106	106	112	102	
		43 days reanalysis	72	75	74	74	72	
		deviation day 0/43 days	33.3	29.2	30.2	33.9	29.4	31.2
Sugar beet, leaf	0.1	Day 0 (initial analysis)	97	103	104	102	99	
		43 days reanalysis	67	67	68	68	66	
		deviation day 0/43 days	30.9	35.0	34.6	33.3	33.3	33.4
Lemon, fruit	0.1	Day 0 (initial analysis)	116	119	115	117	117	
		16 days reanalysis	128	133	126	132	124	
		deviation day 0/16 days	10.3	11.8	9.6	12.8	6.0	10.1
Oilseed Rape	0.1	Day 0 (initial analysis)	96	98	99	101	98	
		38 days reanalysis	149	136	143	145	146	
		deviation day 0/38 days	55.2	38.8	44.4	43.6	49.0	6.2
Cereals Straw	0.1	Day 0 (initial analysis)	113	109	110	102	104	
		30 days reanalysis	116	113	134	107	110	
		deviation day 0/30 days	2.7	3.7	21.8	4.9	5.8	7.8

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.

Report:	[redacted];[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(s):	M-470160-01-1
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**
GLP:	**yes**

Material and Methods

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. The following table shows the measurements comparing initial day of analysis and analysis after storage of the final

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samples over the given periods. Calibration was conducted with freshly prepared matrix standards at initial analysis and for analysis after storage.

Findings

Table CA 6.1- 7: Stability of iodosulfuron-methyl 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	10.70	9.52	10.70	13
		2013-09-10	10.90	12.00	11.80	
Sugar beet, leaf	0.1	2013-08-29	10.90	9.36	9.30	2
		2013-09-09	10.50	9.61	9.92	
Lemon, fruit	0.1	2013-09-06	9.85	9.42	10.16	-47
		2013-09-09	5.32	5.00	5.34	
Oilseed Rape	0.1	2013-09-02	10.70	10.80	10.90	-66
		2013-09-09	3.78	3.56	3.62	
Cereals Straw	0.1	2013-09-04	8.76	8.98	8.92	-3
		2013-09-09	8.69	8.76	8.38	

* 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 has to be conducted within 1 day.

CA 6.2 -Metabolism, distribution and expression of residues

CA 6.2.1 – Plants

Original Annex II dossier
In the original Annex II dossier, the behavior and metabolism of iodosulfuron-methyl-sodium was investigated in cereals only because iodosulfuron-methyl-sodium was not intended for use in other crops.
In these metabolism studies iodosulfuron-methyl-sodium was radiolabelled with ^{14}C in the 2-^{14}C-triazinyl position and in the U-^{14}C-phenyl position.

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Table CA 6.2-1: 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 (KCA 6.2.1/01)
		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 (KCA 6.2.1/02)

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

The metabolism of iodosulfuron-methyl-sodium in wheat was investigated at the exaggerated rate of 20 g as/ha. In order to avoid phytotoxicity the radiolabelled active substance (either U-phenyl-^{14}C-label or 2-^{14}C-triazinyl-label) was applied in combination with the safener mefenpyr-diethyl. The total radioactive residues at harvest were low, 0.57 mg/kg in straw and 0.01 mg/kg in grain. The principal extractable residue in straw was the parent compound iodosulfuron-methyl-sodium in both test series (phenyl- and triazinyl-labelled). Characterisation of the very low residues in grain indicated that the individual concentrations of the parent compound and its metabolites are considerably below 0.01 mg/kg under field conditions.

It was concluded that the submitted studies give sufficient information to propose a definition of the residue, in plant materials, as sum of iodosulfuron-methyl and its salts, expressed as iodosulfuron-methyl.

Studies submitted and evaluated for the first inclusion of iodosulfuron-methyl-sodium on Annex I:

Report:	[redacted];1998;M-182772-01
Title:	Metabolism in wheat (Triticum aestivum) after treatment at a nominal rate of 1 x 20 g as/ha Triazinyl-^{14}C-AE F115008
Report No:	C001497
Document No:	M-182772-01-1
Guidelines:	**BBA: IV, 3-2; EU (=EEC): 91/414/EEC, work. doc. 1607/VI/97, rev. 1 ; USEPA (=EPA): Subdivision O, § 171-4 (a);Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted];1998;M-148037-01
Title:	Metabolism in wheat (Triticum aestivum) after single treatment at a nominal rate of 20 g as/ha U-phenyl-^{14}C-AE F115008
Report No:	A01671
Document No:	M-148037-01-1
Guidelines:	**BBA: Part IV, 3-2; EU (=EEC): Working doc. 1607/VI/97 rev 1; USEPA (=EPA): Subdiv. O, § 171-4;Deviation not specified**
GLP/GEP:	**yes**

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"AIR3" process

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 "safe use" – has already been tested, no new studies are presented for the Annex I Renewal.

CA 6.2.2 – Poultry

Original Annex II dossier

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

"AIR3" process/ New studies submitted

Justification for including this report in this "AIR" dossier

Dietary burden calculation

Iodosulfuron-methyl-sodium is authorised on cereals 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 CA 6.2.2- 1: Input values for the dietary burden calculation

Commodity	**Dietary burden**	
	Input value (mg/kg)	**Comment**
Risk assessment residue definition: sum of iodosulfuron-methyl and its salts, expressed as iodosulfuron-methyl		
Cereals forage	0.05	Highest residue
Cereals straw	0.05	Highest residue
Cereals grain	0.01	Median residue
Corn field, forage	0.05	Highest residue
Corn grain	0.01	Median residue
Wheat, milled by-products	0.08	Median residue

Table CA 6.2.2- 2: Results of the dietary burden calculation according to OECD model

	Residue level in total feed dry matter (mg/kg)	**Residue intake (mg/kg bw/day)**
Poultry broiler	0.026	0.002
Poultry – layer	0.046	0.003
Poultry – turkey	0.025	0.002

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.

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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.

A short summary of this study is given here for completeness:

Report:	[redacted];[redacted];[redacted];1999;M-192269-01
Title:	Poultry - Metabolism, distribution and nature of the residues in eggs and edible tissues Code: (14C)-AE F115008
Report No:	C005548
Document No(s):	M-192269-01-1
Guidelines:	**EU (=EEC): 96/68 6.2; USEPA (=EPA): OPPTS 860.1300;Deviation not specified**
GLP/GEP:	**yes**

Material and Methods

Five laying hens were orally dosed with [phenyl-UL-^{14}C]AE F115008 at a mean daily dose of 1.47 mg per bird per day for fourteen consecutive days. The dose was equivalent to approximately 10 ppm in the diet. Excreta and cage washings were collected daily and eggs were collected twice daily. Eggs were divided into yolks and whites. At necropsy, liver, abdominal and subcutaneous fat, skin, skeletal muscle, undeveloped eggs and gastro-intestinal tract were removed for determination of the distribution and magnitude of [^{14}C]AE F115008. The residues of [^{14}C]AE F115008 and its metabolites were determined in the edible tissues.

Findings

In egg yolks and whites, residue levels of AE F115008 and its metabolites were detectable within 24 hours after the initial dose administration, with residue levels in egg yolks reaching a concentration of 0.022 ± 0.009 mg/kg at day 10 of dosing. The residue levels in egg whites were lower than those seen in egg yolks, with a plateau of 0.017 ± 0.014 mg/kg seen by days of dosing. In undeveloped eggs, the mean concentration of [^{14}C]AE F115008-derived residues was 0.019 ± 0.006 mg/kg. The concentration of AE F115008 and its metabolites in the edible tissues of the hen were low, with the highest concentration seen in the liver at 0.029 ± 0.024 mg/kg. Residues in skin were 0.014 ± 0.007 mg/kg. The residue levels in skeletal muscle and subcutaneous fat were 0.005 ± 0.002 mg/kg and 0.005 ± 0.001 mg/kg respectively. The residue in abdominal fat was 0.003 ± <0.001 mg/kg.
Following administration of the first dose of [^{14}C]AE F115008, elimination of the dosed radioactivity was rapid, with 90.04 ± 4.48% being recovered within 24 hours. The mean recovery of the administered dose in excreta and cage washes over 14 days was 91.96 ± 10.95%.
Isolation and identification/characterisation of the residues in the tissues and excreta was completed as summarised:

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Table CA 6.2.2- 3: Residues of iodosulfuron-methyl-sodium in eggs, tissues, and excreta of laying hens dosed 14 days with 10 ppm [phenyl-U-14C]AE F115008 in the diet

	Tissue residue				
	Egg Yolks*	Egg Whites**	Liver	Skin	Excreta
Total Residue Level (ppm)	0.021	0.016	0.029	0.014	
% extracted	61.73	77.70	73.99	48.92	98.96
Total % identified	19.92	50.16	39.00	34.01	81.52
% Identified as AE F115008	10.89	18.26	22.81	32.61	63.62
% Identified as AE F145741	1.54	13.14	5.48	1.40	8.66
% Identified as AE F114368	4.07	3.94	5.28	nd	2.87
% Identified as AE C627337	0.10	7.52	2.52	nd	1.15
% Identified as AE F143133	0.53	0.77	nd	nd	0.94
% Identified as AE F168532	2.79	nd	1.95	nd	4.28
% Identified as AE F161778	nd	CA 6.53	0.96	nd	nd
% Characterised as unknown metabolites	0.76	19.22	1.37	2.32	2.62
% Characterised as polar material	0.51	0.35	0.29	3.44	-
% Non-extracted	43.59	22.30	27.04	51.08	1.05
% Below limits of analysis	35.11	0.22	8.98	10.59	8.37

nd = not detected
* refers to analysis of eggs from day 12
** refers to analysis of eggs from day 4

As in other species tested (rat, dog, cow), unchanged parent substance represented the dominant residue in tissues and excreta. Metabolism of AE F115008 in the hen occurs by *O*-demethylation to AE F145741 and by hydroxylation to AE F168532. AE F145741 is dehalogenated to AE F161778. Both AE F145741 and AE F168532 lose the triazinyl group, possibly due to amidase activity to form AE F143628. The latter then loses the formamide group, again possibly due to amidases, to form AE F114368, which is in turn cyclised to AE F143133. Overall the metabolic profile is similar to that seen in the rat. Please refer to Figure CA 6.2.2-1.

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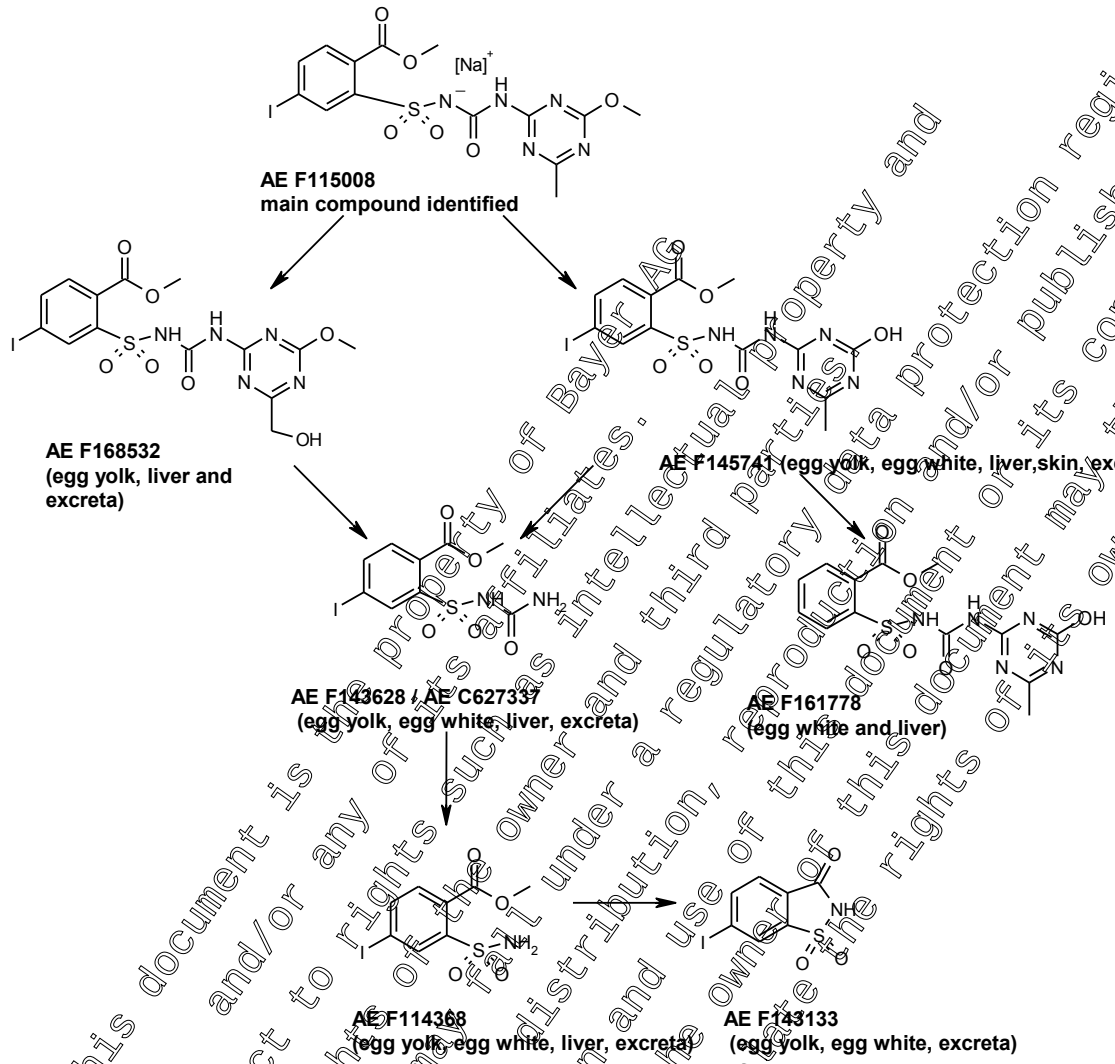

Figure CA 6.2.2- 1: Metabolic pathway of AE F115008 in poultry

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Conclusion

AE F115008 does not accumulate in eggs or edible tissues of the laying hen; the plateau residue level is low. The metabolite pattern observed is in good agreement with that of other species tested (rat, dog and cow). However, the major portion of AE F115008 is excreted as the unchanged parent substance.

CA 6.2.3 - Lactating ruminants

Original Annex II dossier

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

"AIR3" process/ New studies submitted

Justification for including this report in this "AIR" dossier

Dietary burden calculation

Iodosulfuron-methyl-sodium is authorised on cereals 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 CA 6.2.3- 1: Input values for the dietary burden calculation

Commodity	Dietary burden	
	Input value (mg/kg)	Comment
Risk assessment residue definition: sum of iodosulfuron-methyl and its salts, expressed as iodosulfuron-methyl		
Cereals forage	0.05	Highest residue
Cereals straw	0.05	Highest residue
Cereals grain	0.01	Median residue
Corn field, forage	0.05	Highest residue
Corn grain	0.01	Median residue
Wheat, milled by-products	0.08	Median residue

Table CA 6.2.3-2: 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	0.118	0.003
Cattle – dairy	0.103	0.004
Sheep – rams/ewes	0.121	0.004
Sheep - lambs	0.129	0.005
Swine – breeding	0.089	0.002
Swine – finishing	0.051	0.002

The calculated dietary burden is below or at the trigger value of 0.004 mg/kg bw/day for cattle and swine and for sheep lambs slightly above at 0.005 mg/kg bw/day. Therefore, a livestock metabolism study is required and presented below.

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. A short summary of this study is given here for completeness.

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Report:	[redacted]; [redacted];1999;M-192483-01
Title:	Ruminant - Metabolism, distribution and nature of residues in milk and edible tissues (14C) AE F115008 Code: AE F115008
Report No:	C005678
Document No(s):	M-192483-01-1
Guidelines:	EU: Council Directive 91/414/EEC Amended EU Commission Directive 96/68/EC USEPA: Residue Chemistry Test Guidelines OPPTS 860.1300 Nature of the Residue - Plant, Livestock
GLP/GEP:	**yes**

Material and Methods

A dairy cow was orally dosed with [phenyl-UL-^{14}C]AE F115008 with a single mean daily dose of 220.85 ± 0.49 mg (equivalent to 0.29 mg/kg body weight) for seven consecutive days. The dose administered was equivalent to 14.23 ppm in the diet.

Urine and faeces were collected daily and milk was collected twice daily. At necropsy (168 hours after initial dose and approximately 22 hours after final dose) liver, kidneys, heart, lungs, fat (renal, omental and subcutaneous), muscle (psoas, loin and hindquarter), rumen and abomasal fluid, gastro-intestinal contents and bile were sampled and quantified. Identification of the metabolite residues was carried out in milk and edible tissues, namely liver, kidney, omental fat and renal fat. Residue levels in omental fat were less than 0.01 mg equivalents/kg, however, analysis was performed as means of method development for analysis of renal fat. The metabolic profile of urine was also determined.

Findings

In milk, residue levels were detectable by 7 hours post administration of the initial dose, but remained at low concentrations throughout the study reaching a maximum concentration of 0.017 mg equivalents AE F115008/kg at 103 hours post-administration of the initial dose (on day 4). Tissue residues of AE F115008 and/or its metabolites approximately 22 hours after the final dose (day 7) were generally low. Highest residue levels were found in the kidney at 0.100 mg equivalents/kg, followed by the lungs at 0.067 mg equivalents/kg. Liver (0.061 mg equivalents/kg) and renal fat (0.022 mg equivalents/kg) showed the next highest residue levels, followed by heart and subcutaneous fat at 0.008 mg equivalents/kg. Residue levels in omental fat and muscle (loin, hindquarter and psoas) were lowest at 0.007, 0.002, 0.002 and 0.004 mg equivalents/kg respectively.

Following the first dose of [^{14}C]AE F115008, 61.36% of the dose was recovered in urine and 9.07% in faeces within the first twenty-four hours. The overall mean daily recovery in urine was 70.98 ± 9.33%, and 20.82 ± 9.30% in faeces, giving a total mean daily recovery in excreta of 91.79%. The main residue seen in the extracts of tissues was unchanged AE F115008. The isolation and identification of the residues in the tissues is summarised as follows:

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Table CA 6.2.3-3: Residues of iodosulfuron-methyl-sodium in tissues and milk of a dairy cow dosed 7 days with 14.23 ppm [phenyl-U-^{14}C]AE F115008 in the diet

	Tissue residue				
	Kidney	Liver	Renal Fat	Omental Fat	Milk*
Total Residue Level (ppm)	0.100	0.061	0.022	<0.009	0.017
% extracted	98.31	60.63	73.23	75.48	92.64
Total % identified / characterised	80.70	35.67	46.37	53.64	64.06
% Identified as AE F115008 **	2CA 6.45	23.88	9.83	18.94	15.12
% Identified as AE F145740	5.47	-	1.34	-	2.44
% Identified as AE F075736	9.91	-	2.02	-	-
% Identified as AE F145741	5.75	-	1.72	7.09	-
% Identified as AE F168532	0.96	-	-	0.55	-
% Identified as AE F161778	2.30	1.79	1.43	-	-
% Identified as AE F114368	0.38	Trace	-	-	-
% Identified as AE F143133	0.22	-	-	-	-
% Characterised as polar material	2.09	-	-	-	-
% Characterised as unknown metabolites	27.15	9.98	32.02	24.98	47.48
% Below levels requiring further analysis	13.67	13.10	12.06	10.93	0.64

- = not detected
* maximum value
** for some extracts as reconstituted minimum value (sum of hydrolytic artifacts upon sample clean-up)

Unchanged parent substance represented the dominant residue in tissues and excreta. Metabolism of AE F115008 in the dairy cow shows *O*-demethylation to AE F145741 and hydroxylation to AE F168532. AE F145741 is dehalogenated to AE F161778. Both AE F145741 and AE F168532 lose the triazinyl group to form AE C627337, which is then further metabolised to AE F114368 and eventually cyclised to AE F143133. Overall the metabolic profile is similar to that seen in the rat. Please refer to Figure CA 6.2.3-1.

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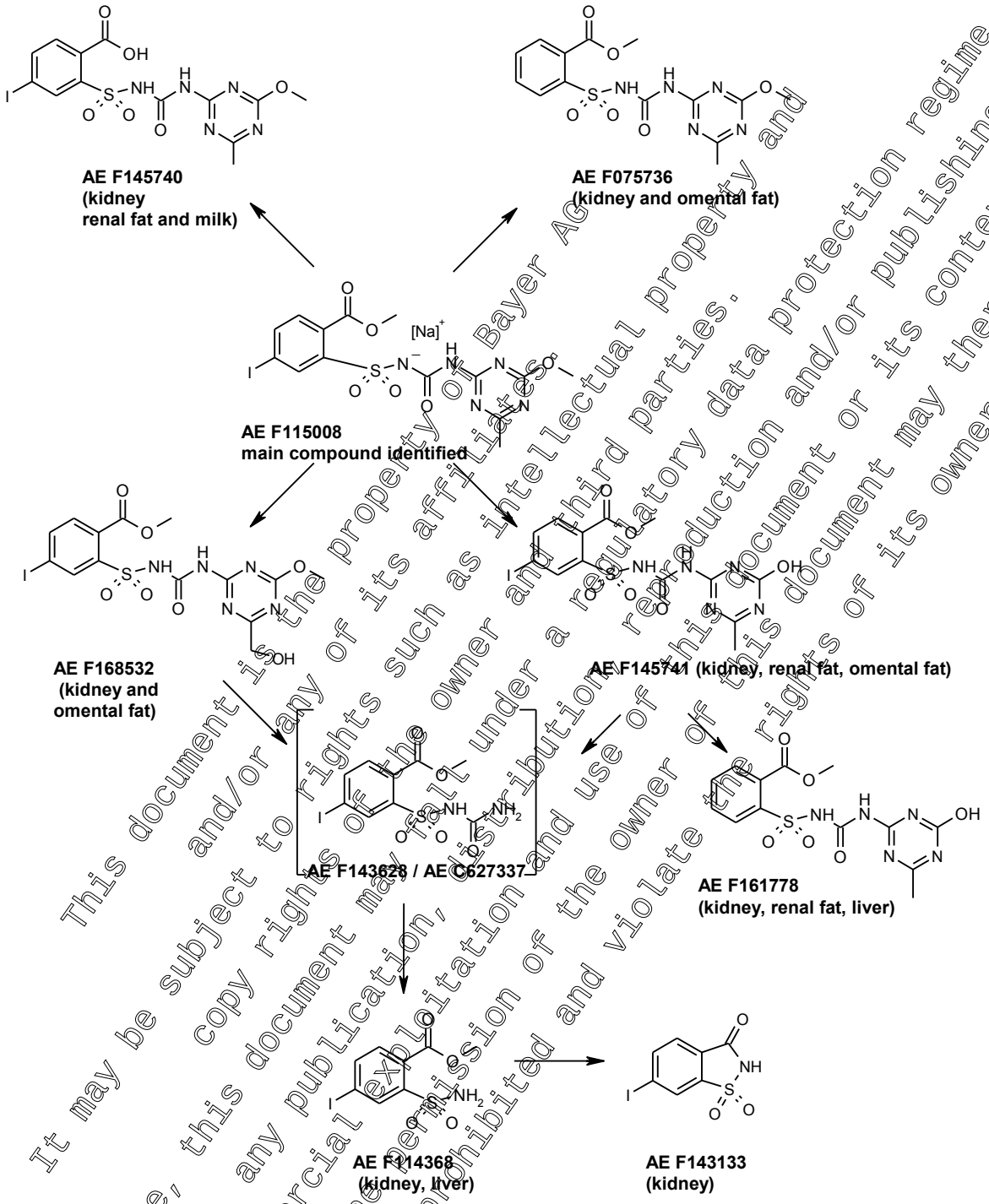

Figure CA 6.2.3-1: Metabolic pathway of AE F115008 in the dairy cow

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Conclusion

AE F115008 does not accumulate in milk or edible tissues of the dairy cow, the plateau residue level is low. The metabolite pattern observed is in good agreement with that of other species tested (rat, dog, hen). However, the major portion of AE F115008 is excreted as the unchanged parent substance.

CA 6.2.4 – Pigs

A pig metabolism study was not conducted, since metabolism followed comparable pathways in all other tested species (rat, dog, hen and cow).

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

Iodosulfuron-methyl-sodium (AE F115008) is a herbicidal active substance. In 1999, the original Annex II dossier was submitted to Germany. In that dossier, uses on cereals were supported with residue trial data.
Some new studies have since been conducted with iodosulfuron-methyl-sodium-containing formulations for use in European cereals, which is the "representative use" crop supported in the AIR3 process.

CA 6.3.1 - Cereals

Original Annex II dossier
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 two sulfonylurea active substances allowing efficient weed control without phytotoxicity to the treated crop.

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Table CA 6.3.1-1: Use patterns (GAPs) for the spray application of the formulation Hussar WG in/on cereals in Europe (northern and southern residue regions), as described in the 1999 dossier

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 rate (g as/ha)	PHI
Winter wheat, rye, triticale, summer wheat, spring barley, durum wheat	Europe North/South	F	WG 50 g/kg iodosulfuron-methyl-sodium + 150 g/kg mefenpyr-diethyl	Grass weed species and dicot weed species	BBCH 13-32 spring	1 per season	200-400	7.5-10 g iodosulfuron-methyl sodium + 22.5-30 g mefenpyr-diethyl	covered by the normal vegetation period between last application and harvest

Outdoor or field use (F), glasshouse application (G) or indoor application (I)

A total of 20 residue trials have been conducted in the vegetation periods of 1995 and 1996. The product was applied to winter wheat (Triticum aestivum and Triticum durum), summer barley (Hordeum vulgare) and winter rye (Secale cereale) once per season, at the 1.5-fold proposed rate (15 g iodosulfuron-methyl-sodium/ha) and shortest pre-harvest-interval (PHI). The trial locations were spread over main growing areas of the EU Northern zone and EU Southern zone in order to cover different soil and climatic conditions. Different growing regions were covered in Germany, northern and southern France, United Kindom, Italy and Spain. In all trials one plot left untreated for control and two plots were treated.

In the 1995 trials two different tank mixtures were applied:

- two WG formulations containing 20 % (w/w) of iodosulfuron-methyl-sodium and 15 % (w/w) of the safener mefenpyr each,
- a WG formulation containing 20 % (w/w) of iodosulfuron-methyl-sodium and an EC formulation with a content of 10 % (w/w) of the safener.

Application rates were 15 g iodosulfuron-methyl-sodium/ha and 45 or 47.7 g mefenpyr/ha once per growing season.

In 1996 trials were run using co-formulations:

- a WG formulation of 5 % iodosulfuron-methyl-sodium and 15 % of the safener mefenpyr,
- an EG formulation of 5 % iodosulfuron-methyl-sodium and 15 % of the safener.

Application rates were 15 g iodosulfuron-methyl-sodium/ha and 45 g mefenpyr/ha once per growing season. In each trial spray volume was 200 - 300 l/ha of water.

The applications for both treated plots were carried out at growth stage BBCH 39 (flag leaf stage) in nearly all trials, with the exception of 3 x 2 trials:

- Spain 1995 (2 trials: WG/WG), one application carried out at growth stage BBCH 51 (beginning of heading)
- United Kingdom 1996 (2 trials: EG/WG), at growth stage BBCH 53 (30 % of inflorescence emerged)
- Italy 1996 (2 trials: EG/WG), at growth stage BBCH 41 (flag leaf sheath extending, early boot).

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Each trial was performed on winter wheat.

Residues of iodosulfuron-methyl ~~-sodium~~ and its salts in shoot at the day of application (DAT 0) ranged between 0.10 and ~~0.50~~ 0.48 mg/kg. At the time of a second shoot sampling (DAT 10 - 28), the residues had already fallen below the limit of quantification of 0.05 mg/kg. Also in grain (LOQ = 0.01 mg/kg) and straw (LOQ <0.05 mg/kg) taken at harvest time at DAT 51 - 96 no residues could be determined. This residue pattern clearly allows an MRL proposal of 0.01 mg/kg which represents the validated LOQ for wheat grain.

Studies submitted and evaluated for the first inclusion of iodosulfuron-methyl-sodium on Annex I:

Report:	[redacted]; [redacted]; 1998; M-140498-01
Title:	AE F115008 00 WG20 A103 WG (wettable granule) 200 g/kg in tank mix with two different formulations of the safener AE F107892 (AE F107892 00 WG15 A101 and AE F107892 00 EG10 A102) Residue trial on wheat to determine residue decline of AE F115008 and AE F107892 following 1 application: European Union (northern zone)
Report No:	A56709
Document No:	M-140498-01-1
Guidelines:	**Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted]; [redacted]; 1998; M-140497-01
Title:	AE F115008 00 WG20 A103 WG (wettable granule) 200 g/kg in tank mix with two different formulations of the safener AE F107892 (AE F107892 00 WG15 A101 and AE F107892 00 EG10 A102) Residue trial on wheat to determine residue decline of AE F115008 and AE F107892 following 1 application: European Union (southern zone)
Report No:	A56708
Document No:	M-140497-01-1
Guidelines:	**Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted]; [redacted]; 1998; M-143213-02; Amended: 1999-06-11
Title:	AE F115008 and AE F107892 EG (emulsifiable granule) and WG (water dispersible granule) 50 and 150 g/kg Code: AE F115008 02 EG20 A401 and Code: AE F115008 02 WG20 A403 Residue trials on cereals with two different coformulations to determine residue decline of AE F115008 and AE F109872 following 1 application European Union (southern zone)
Report No:	A59542
Document No:	M-143213-02-1
Guidelines:	**BBA: Part IV, 3-6 (1990);Deviation not specified**
GLP/GEP:	**yes**

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Report:	[redacted];[redacted];1998;M-143212-01
Title:	AE F115008 and AE F107892 EG (emulsifiable granule) and WG (water dispersible granule) 50 and 150 g/kg Code: AE F115008 02 EG20 A401 and Code: AE F115008 02 WG20 A903 Residue trials on cereals with two different coformulations to determine a residue decline of AE F115008 and AE F107892 following 1 application European Union (Northern zone)
Report No:	A59541
Document No:	M-143212-01-1
Guidelines:	**BBA: Part IV, 3-6 (1990);Deviation not specified**
GLP/GEP:	**yes**

"AIR3" process/ New studies submitted

Table CA 6.3.1-2: 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.

The Residue Trial Tables can be found in the document below. They include the supplementary trials presented in this dossier in support of product iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400. During the completeness check done by Swedish Authorities, it has been identified that the expression of residues should be presented as iodosulfuron-methyl. The residue trial tables and this section 6 have been updated accordingly.

Report:	**KCA 6.3.1/05; [redacted], C.;2014**
Title:	Residue trial tables - Iodosulfuron-methyl-sodium - Annex I Renewal
Report No:	M-471100-02-1
Document No:	M-471100-02-1
Guidelines:	**EU Regulation 1107/2009 & EU Regulation 283/2013** **Document MCA** **Section 6: Residues in or on treated products, food and feed** **According to the guidance document, SANCO 10181/2013, for**

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	preparing dossiers for the approval of a chemical active substance;not specified
GLP/GEP:	**n.a.**

The formulations used in the supplementary residue trials are presented below:

Formulation name	Formulation type	Composition
AE F115008 02 WG20 B3 (adjuvant Biopower®) (a)	20WG: water dispersible granule	- 50 g/kg iodosulfuron-methyl-sodium, - 150 g/kg mefenpyr-diethyl
AE F115008 02 OD35 A1	400 OD: oil dispersion formulation	- 100 g/L iodosulfuron-methyl-sodium, - 300 g/L mefenpyr-diethyl
AE F115008 02 1L35 A2 (b)		

(a) Biopower® is an adjuvant used to improve the plant uptake of iodosulfuron-methyl-sodium and the safener.
(b) OD is the official code for oil dispersion formulations and replaces the previous expression "1L"

The number and distribution of residue trials are described in Table CA 6.3.1-3.

Table CA 6.3.1- 3: Number and distribution of new residue trials conducted per geographical region on cereals (wheat, barley, rye)

Formaulation Name	Climatic zone, Countries	Formulation type	Year / No. of trials	Reference Study number / Doc No.
Europe North				
AE F115008 02 1L35 A2	UK	400 OD	2003 / 1	RA-2751/03 (a) / M-230725-02-1
AE F115008 02 1L35 A2	Sweden	400 OD	2003 / 1	RA-2751/03 (a) / M-230725-02-1
AE F115008 02 OD35 A1	UK	400 OD	2003 / 1	RA-2615/03 (a) / M-231310-02-1
AE F115008 02 OD35 A1	Sweden	400 OD	2003 / 1	RA-2615/03 (a) / M-231310-02-1
AE F115008 02 OD35 A1	France	400 OD	2003 / 1	RA-2615/03 (a) / M-231310-02-1
AE F115008 02 OD35 A1	Germany	400 OD	2003 / 1	RA-2615/03 (a) / M-231310-02-1
Europe South				
AE F115008 02 WG20 B301	Italy	20WG	2001 / 4	01R713 (b) / M-210317-01-1
AE F115008 02 1L35 A2	Italy	400 OD	2003 / 2	RA-2616/03 (a) / M-231305-02-1
AE F115008 02 1L35 A2	Spain	400 OD	2003 / 1	RA-2616/03 (a) / M-231305-02-1
AE F115008 02 1L35 A2	France	400 OD	2003 / 1	RA-2616/03 (a) / M-231305-02-1

(a) Samples were analysed with the following analytical method: 00815/M001
(b) Samples were analysed with the following analytical method: EM F08/99-0

❖ **Comparability between the different formulations used in the supervised field trials**

To support the representative use, two types of formulations have been used: an OD (representative formulation) and a WG. No differences in terms of residues are expected applying the WG or the OD formulations. Actually, as an adjuvant (sodium lauryl ether sulfate, Biopower®) is added to the WG formulation as a tank mix, it is considered that the mixture applied is very close to an OD formulation.

Besides, supervised residue trials conducted with the OD and WG formulations following the use patterns described in Table CA 6.3.1-2 showed no measurable residues (see Tables CA 6.3.1-4 and CA 6.3.1- 5).

Report:	[redacted];2002;M-210317-01
Title:	Residues in wheat European Union (Southern zone) 2001 Biopower (R) Iodosulfuron-methyl-sodium (5 %) Mefenpyr-diethyl (15 %) Code: AE F115008 02 WG20 B301
Report No:	C020875
Document No:	M-210317-01-1
Guidelines:	**EU (=EEC): 7029/VI/95 rev.5 - 22/07/97;Deviation not specified**

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Report:	KCA 6.3.1 /07;[redacted], T.;2004;M-231305-01
Title:	Determination of residues of iodosulfuron-methyl-sodium and mefenpyr-diethyl in/on wheat following spray application of AE F115008 02 1L35 A2 400 OD in the field in italy, spain and southern france
Report No:	RA-2616/03
Document No(s):	M-231305-01-1
Guidelines:	**Deviation not specified**

Report:	[redacted];[redacted];2004;M-231310-02; Amended: 2007-01-16
Title:	Determination of residues of iodosulfuron-methyl-sodium and mefenpyr-diethyl in/on wheat following spray application of AE F115008 02 OD35 A1 400 OD and AE F115008 02 1L35 A2 400 OD in the field in sweden, germany, great britain and nothern
Report No:	RA-2615/03
Document No(s):	M-231310-02-1
Guidelines:	**Deviation not specified**

Report:	[redacted];2004;M-230725-02; Amended: 2007-01-16
Title:	Determination of residues of iodosulfuron-methyl-sodium and mefenpyr-diethyl in/on wheat following spray application of AE F115008 02 1L35 A2 (400 OD) in the field in Great Britain and Sweden
Report No:	RA-2751/03
Document No(s):	M-230725-02-1
Guidelines:	**Deviation not specified**

❖ **Storage stability**

Samples in the reported residue trials were kept deep-frozen for less than 27 months (please refer to CA 6.1 Storage stability studies were conducted in wheat grain, wheat straw and wheat shoot. The studies demonstrated stability up to 24-28 months for these three matrices (grain: 24 months, shoot: 26 months, straw: 28 months). Therefore analytical results are considered valid.

❖ **Northern Europe residue trials**

Test system

A total of 6 trials (see Table CA 6.3.1-3) were performed with the formulations AE F115008 02 OD35 A1 (OD formulation) and AE F115008 02 1L35 A2 (OD formulation). Iodosulfuron-methyl-sodium was applied to cereals (wheat) at a rate of 10 g a.s./ha in combination with the safener mefenpyr-diethyl. The applications were carried out from growth stages BBCH 32 (Node 2 at least 2 cm above node 1) to BBCH 43 (mid boot stage: flag leaf sheath just visibly swollen). Samples for analysis were taken at the day of application and at harvest (grain and straw).

Findings

Detailed results are shown in Table CA 6.3.1- 4. Residues of ~~parent~~ iodosulfuron-methyl~~-sodium~~ and its salts in shoots ranged between 0.08 mg/kg and ~~0.31~~ 0.30 mg/kg at the day of application. At harvest (70 to 90 days after application) residues in grain and straw were always less than the respective limits of quantification (grain: 0.01 mg/kg, straw: 0.05 mg/kg).

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Table CA 6.3.1- 4: Residue data for iodosulfuron-methyl-sodium (AE F115008), Northern Europe

Study Trial No. [a] Trial SubID GLP Year	Crop Variety	Country	Application					Residues		
			FL	No	g/ha (a.s.)	g/hL (a.s.)	GS	Portion analysed	PHI (days)	AE F115008* (mg/kg)
RA-2615/03 R 2003 0492 7 0492-03 GLP yes 2003	Wheat Isengren	Germany D-[redacted] Europe, North	400 OD (3)	1	10	3.5	32	Shoot Straw Grain	0 90 90	~~0.29~~ 0.28 <0.05 <0.01
RA-2615/03 R 2003 0494 3 0494-03 GLP yes 2003	Wheat Shawgo	France F-[redacted] Europe, North	400 OD (3)	1	10	4.0	32	Shoot Straw Grain	0 83 83	~~0.28~~ 0.27 <0.05 <0.01
RA-2615/03 R 2003 0493 5 0493-03 GLP yes 2003	Wheat Consort	United Kingdom GB-[redacted] Europe, North	400 OD (4)	1	10	5.0	39-43	Shoot Straw Grain	0 83 83	0.09 <0.05 <0.01
RA-2615/03 R 2003 0225 8 0225-03 GLP yes 2003	Wheat Kris	Sweden S-[redacted] Europe, North	400 OD (4)	1	10	3.3	39	Shoot Straw Grain	0 83 83	~~0.31~~ 0.30 <0.05 <0.01
RA-2751/03 R 2003 1136 2 1136-03 GLP yes 2003	Wheat Consort	United Kingdom GB-[redacted] Europe, North	400 OD (3)	1	10	5.0	39-43	Shoot Straw Grain	0 83 83	0.08 <0.05 <0.01
RA-2751/03 R 2003 1137 0 1137-03 GLP yes 2003	Wheat Kris	Sweden S-[redacted] Europe, North	400 OD (3)	1	10	3.3	39	Shoot Straw Grain	0 70 70	~~0.26~~ 0.25 <0.05 <0.01

FL = formulation, PHI = pre-harvest interval
[a] trial number as used in the Tier I tables,
(3) AE F115008 02 1L35 A2 (4) AE F115008 02 OD35 A1
* Sum of iodosulfuron-methyl and its salts expressed as iodosulfuron-methyl

❖ **Southern Europe residue trials**

Test system

A total of 8 supplementary trials (see Table CA 6.3.1-3) were performed with the formulations AE F115008 02 WG20 B301 (WG formulation containing the Biopower adjuvant) and AE F115008 02 1L35 A2 (OD formulation). Iodosulfuron-methyl-sodium was applied to cereals (wheat) at a rate of 10 g ai/ha in combination with the safener mefenpyr-diethyl. The applications were carried out at the growth stages BBCH 32 (Node 2 at least 2 cm above node 1) to 33 (node 3 at least 2 cm above node 2). Samples for analysis were taken at the day of application and at harvest (grain and straw). In some trials shoot samples were taken at intermediate growth stages.

Findings

Please refer to Table CA 6.3.1-5 for detailed results. Residues of ~~parent~~ iodosulfuron-methyl~~-sodium~~ and its salts in shoots ranged between < 0.05 mg/kg and ~~0.58~~ 0.56 mg/kg at the day of application and declined to < 0.05 mg/kg by the second sampling (13 days after application). At harvest (50 to

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78 days after application) residues in grain and straw were always less than the respective limits of quantification (grain: 0.01 mg/kg, straw: 0.05 mg/kg). Iodosulfuron-methyl-sodium when applied to cereals according to GAP did not lead to residues in grain of parent compound at or above the limit of quantification.

Table CA 6.3.1- 5: Residue data for iodosulfuron-methyl-sodium (AE F115008), Southern Europe

Study Trial No. [a] Trial SubID GLP Year	Crop Variety	Country	Application					Residues		
			FL	No	g/ha (a.s.)	g/hL (a.s.)	GS	Portion analysed	PHI (days)	AE F115008* (mg/kg)
01R713 01R713-1 GLP yes 2001	Wheat, durum Simeto	Italy [redacted] Europe, South	20 WG (2)	1	10	3.4	32	Shoot Straw Grain	0 78 78	0.14 <0.05 <0.01
01R713 01R713-2 GLP yes 2001	Wheat, durum Ciccio	Italy [redacted] Europe, South	20 WG (2)	1	10	3.4	32	Shoot Shoot Straw Grain	0 13 61 61	<0.05 <0.05 <0.05 <0.01
01R713 01R713-3 GLP yes 2001	Wheat, durum Simeto	Italy [redacted] Europe, South	20 WG (2)	1	10	3.4	32	Shoot Shoot Straw Grain	0 13 61 61	<0.05 <0.05 <0.05 <0.01
01R713 01R713-4 GLP yes 2001	Wheat, durum Simeto	Italy [redacted] Europe, South	20 WG (2)	1	10	3.4	32	Shoot Shoot Straw Grain	0 13 74 74	~~0.58~~ 0.56 <0.05 <0.05 <0.01
RA-2616/03 R 2003 0226 6 0226-03 GLP yes 2003	Wheat, durum Rusticano	Italy, I-[redacted] Europe, South	400 OD (4)	1	10	3.3	32	Shoot Straw Grain	0 50 50	~~0.20~~ 0.19 <0.05 <0.01
RA-2616/03 R 2003 0489 7 0489-03 GLP yes 2003	Wheat, durum Arcangelo	Italy I-[redacted] Europe, South	400 OD (4)	1	10	3.3	32	Shoot Straw Grain	0 51 51	~~0.23~~ 0.22 <0.05 <0.01
RA-2616/03 R 2003 0490 0 0490-03 GLP yes 2003	Wheat, durum Bolido	Spain E-[redacted] Europe, South	400 OD (4)	1	10	3.3	32	Shoot Straw Grain	0 70 70	~~0.33~~ 0.32 <0.05 <0.01
RA-2616/03 R 2003 0491 9 0491-03 GLP yes 2003	Wheat, durum Joyaux	France F[redacted] Europe, South	400 OD (4)	1	10	3.3	32-33	Shoot Straw Grain	0 56 56	~~0.43~~ 0.41 <0.05 <0.01

FL = formulation, PHI = pre-harvest interval

[a] trial number as used in the Tier I tables

(2) AE F115008 02 WG20 B301

(4) AE F115008 02 NJ35 A2

* Sum of iodosulfuron-methyl and its salts expressed as iodosulfuron-methyl

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❖ Recoveries

During the sample analysis, recoveries in wheat shoot, wheat straw, and wheat grain, were performed. The data are presented in Table CA 6.3.1-6. These data demonstrate the method performance, accuracy, and robustness.

Table CA 6.3.1- 6: Recovery data for Iodosulfuron-methyl-sodium (AE F115008) in cereals

Study GLP Year	Crop	Portion analysed	a.s./metabolite	n	Fortification level (mg/kg) Min	Fortification level (mg/kg) Max	Recovery (%) Individual values	Recovery (%) Mean	Recovery (%) RSD
01R713 GLP yes 2001	Wheat	shoot	Iodosulfuron-methyl-sodium [a]	5	0.051	0.535	97 / 95 / 96 / 90 / 96	95	2.9
		straw	Iodosulfuron-methyl-sodium [a]	5	0.053	0.526	109 / 98	104	7.5
		grain	Iodosulfuron-methyl-sodium [a]	2	0.011	0.107	102 / 105	104	2.0
RA-2751/03 & RA-2615/03 & RA-2616/03 GLP yes 2003	Wheat	shoot	Iodosulfuron-methyl-sodium [a]	15	0.05	0.50	92 / 88 / 92 / 92 / 92 / 89 / 91 / 89 / 87 / 89 / 99 / 104 / 102 / 100 / 101	94	CA 6.1
		Straw	Iodosulfuron-methyl-sodium [a]	15	0.05	0.50	98 / 95 / 95 / 97 / 91 / 100 / 98 / 94 / 91 / 94 / 99 / 94 / 94 / 86 / 91	94	3.9
		Grain	Iodosulfuron-methyl-sodium [a]	15	0.01	0.10	88 / 92 / 101 / 98 / 93 / 96 / 101 / 97 / 102 / 99 / 97 / 90 / 92 / 96 / 97	96	4.3

[a] Final determination as: iodosulfuron-methyl; residues calculated as: iodosulfuron-methyl

❖ Conclusions

In addition to the 20 trials included in the original AII dossier showing residues of iodosulfuron-methyl-~~sodium~~ and its salts at harvest always lower than the respective LOQ (LOQ grain: 0.01 mg/kg and LOQ straw: 0.05 mg/kg), news trials have been performed that support the Hussar OD product.

Northern Europe: 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~~ and its salts in shoot ranged from 0.08 to ~~0.31~~ 0.30 mg/kg at the day of the application. Residues of iodosulfuron-methyl-~~sodium~~ and its salts at harvest were always lower than the respective LOQ (LOQ grain: 0.01 mg/kg and LOQ straw: 0.05 mg/kg).

Southern Europe: eight residue trials were conducted with two different formulation types (20WG + Biopower® and 400OD). The formulations were applied once at growth stage BBCH 32 to 33. Residues of iodosulfuron-methyl-~~sodium~~ and its salts in shoot ranged from < 0.05 to ~~0.58~~ 0.56 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~~ and its salts at harvest were always lower than the respective LOQ (LOQ grain: 0.01 mg/kg and LOQ straw: 0.05 mg/kg).

The overall residue data package (original EU dossier and new AIR dossier) does confirm that no differences in term of residues were noticeable with trials performed with the OD and the WG formulations, even when no adjuvant was added to the WG (original EU dossier). Thus the two formulations are equivalent from a residue stand-point.

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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.

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 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 only slightly exceeded for sheep lambs. Therefore, no livestock feeding studies to investigate the residue levels of iodosulfuron-methyl-sodium in food of animal origin are required.

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 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.

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

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 cereals.

CA 6.5.3 - Magnitude of residues in processed commodities

No studies were performed.

CA 6.6 - Residues in rotational crops

CA 6.6.1 - Metabolism in rotational crops

Original Annex II dossier

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.
According to soil degradation studies, DT90 values of iodosulfuron-methyl-sodium are expected to be lower than 49 days.
Nevertheless, metsulfuron-methyl was identified as a relevant soil metabolite and its DT90 values are expected to be between 26 and 190 days. Therefore a confined rotational crop study was submitted in the original EU dossier.

Table CA 6.6.1-1: 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

The first experiment (conducted as 3 separate studies) utilised carrots, spinach and wheat, each planted at intervals of 29, 120, and 365 days after treatment of the soil with 20 g/ha iodosulfuron-methyl-sodium (i.e. a twofold excess of the maximum labelled product use rate). Such overdosing allowed for

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at least some identification of the generally very low level residues, but led to damage due to phytotoxicity of the carrots and spinach in some experiments. Significant residues in rotational crops other than cereals are therefore not expected.
The TRR in cereal grains were found to be below 0.01 mg eq/kg at all plant-back intervals. In cereal straw, the TRR ranged between 0.1 and 0.5 mg eq/kg depending on the plant-back interval. However, the main metabolites identified were also identified in the primary crop metabolism (iodosulfuron triazin and iodosulfuron-demethyl-hydroxy-triazin) and the metabolic pattern for primary crops and rotational crops were concluded to be similar (Germany, 2000).

CA 6.6.2 - 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, provided that iodosulfuron is applied in compliance with the GAPs reported in Document D-1 of this dossier.

Specific plant back restrictions related to the use of iodosulfuron-methyl-sodium are therefore not required.

Studies submitted and evaluated for the first inclusion of iodosulfuron-methyl-sodium on Annex I:

Report:	[redacted];[redacted];1998;M-181318-01
Title:	Residues in rotated crops sown 29 days after application to bare soil at a rate of 20 g a.s./ha AE F115008-triazinyl 2-14C
Report No:	C000833
Document No:	M-181318-01-1
Guidelines:	**BBA: IV 3-10 (1988); EU (=EEC): working doc., appendix C rev.2 (97); USEPA (=EPA): OPPTS 860.1850 (1996);Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted];[redacted];[redacted];[redacted];1998;M-182667-01
Title:	Residues in rotated crops sown 120 days after application to bare soil at a rate of 20 g a.s./ha AE F115008-triazinyl 2-14C
Report No:	C004354
Document No:	M-182667-01-1
Guidelines:	**BBA: IV 3-10 (1988);Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted];[redacted];[redacted];[redacted];1998;M-182374-01
Title:	Residues in rotated crops sown 1 year after application to bare soil at a rate of 20 g a.s./ha AE F115008-triazinyl 2-14C
Report No:	C003331
Document No:	M-182374-01-1
Guidelines:	**BBA: IV 3-10 (1988); EU (=EEC): working doc., appendix C rev. 2 (97); USEPA (=EPA): Subd. N, § 166-1;Deviation not specified**
GLP/GEP:	**yes**

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Report:	[redacted];1998;M-182740-01
Title:	Selectivity thresholds for AE F115008 in various crops- ED10 values in soil
Report No:	C001481
Document No:	M-182740-01-1
Guidelines:	**Deviation not specified**
GLP/GEP:	**no**

"AIR3" process

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.

Report:	[redacted];[redacted];[redacted];1999;M-238341-01
Title:	Uptake of [14C]-AE F115008 residues from soil by rotational wheat, soybeans and sugarbeets under confined conditions
Report No:	B002595
Document No(s):	M-238341-01-1
Guidelines:	**USEPA (=EPA); 860.1850;Deviation not specified**
GLP/GEP:	**yes**

Material and Methods

Bare plots of sandy loam soil were treated with [2-^{14}C-triazinyl]-AE F115008 in formulated combination with the safener AE F122006 (isoxadifen-ethyl). In separate plots, soybeans were planted 7 and 14 days after treatment at 5.4 g ai/ha, sugarbeets were planted 60 days after treatment at 5.4 g ai/ha and wheat was planted 65 days after treatment at 8.1 g ai/ha. Untreated plots were used as controls. Crops were harvested from the treated and control plots at an immature stage, equivalent to a forage stage in soybeans and a late forage stage in wheat, and at maturity in all crops. At maturity, wheat was divided into straw (including hulls) and grain; sugarbeets were divided into roots and tops. The seeds were the only soybean raw agricultural commodity at maturity. Total radioactive residues in raw agricultural commodities (RACs) were determined by combustion analysis of ground material.

Findings

The total radioactive residues in all raw agricultural commodities in this study was significantly less than 0.01 µg a.s.-equiv./g (overview see Table CA 6.6.2-1). Control crops contained no significant radioactive residue (< 0.001 µg a.s.-equiv./g). In accordance with EPA guidance, no further characterization of residues was carried out.

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Table CA 6.6.2- 1: Summary of total radioactive residues (TRR) in rotated crops sown at different intervals after application of [triazinyl-2-14C]AE F115008 to bare soil

Raw Agricultural Commodity		Crop residue (TRR) in µg a.s.-equiv./g after plantback interval			
		7 days	14 days	60 days	65 days
Soybean	- Forage	0.003	0.003	-	-
	- Seed	0.003	0.003	-	-
Sugarbeet	- Tops	-	-	0.001	-
	- Root	-	-	<0.001	-
Wheat	-Forage	-	-	-	0.002
	-Straw	-	-	-	0.067
	-Grain	-	-	-	<0.001

'-' = not tested

Conclusion
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.

CA 6.7 - Proposed residue definitions and maximum residue levels

CA 6.7.1 - Proposed residue definitions

Original Annex II dossier
As presented in the original Annex II dossier for iodosulfuron-methyl-sodium, the proposed residue definition in plants, both for data collection and enforcement, was the sum of iodosulfuron-methyl and its salts, expressed as iodosulfuron-methyl.

Table CA 6.7.1- 1: Proposed residue definitions

Matrices	Residue definition		Reference
Food of plant origin	Risk assessment and Monitoring	iodosulfuron-methyl including its salts, expressed as iodosulfuron-methyl	Commission Directive 2005/48/EC of 23 August 2005
Food of animal origin	Risk assessment and Monitoring	None, as no residue anticipated	

"AIR3" process
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.

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Table CA 6.7.1- 2: 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	

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

Original Annex II dossier

For wheat (*Triticum aestivum* and *Triticum durum*), barley (*Hordeum vulgare*) and rye (*Secale cereale*), a total of 20 residue trials were conducted (10 in Northern Europe and 10 in Southern Europe) using different WG formulations. The application rate ranged from 10 to 15 g a.s./ha at growth stage BBCH 32 to BBCH 53. Pre-harvest intervals were between 50 and 96 days. In wheat grain and wheat straw, at harvest, residues were always lower than the respective LOQ (grain: 0.01 mg/kg and straw: 0.05 mg/kg). The maximum residue limits (MRLs) set for iodosulfuron-methyl-sodium were established taking into account the application scenarios considered in this document, all of which involve higher application rates and / or later treatments than the representative use pattern of iodosulfuron-methyl-sodium.

Table CA 6.7.2- 1: Existing EU MRLs

Commodity	Existing EU MRL (mg/kg)	Reference
Cereal grain	0.01	DAR

Studies submitted and evaluated for the first inclusion of iodosulfuron-methyl-sodium on Annex I:

Report:	[redacted];1998;M-182735-01
Title:	Determination of the maximum residue level (MRL) for AE F115008 in cereal grain (statement Code: AS F115008
Report No:	C001475
Document No:	M-182735-01-1
Guidelines:	**BBA - IV, 3-6 Jan. 1990; Deviation not specified**
GLP/GEP:	**no**

"AIR3" process

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.

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Table CA 6.7.2- 2: Current MRLs established by EFSA

Commodity	MRL (mg/kg)	Reference
Maize grain	0.01*	EFSA Journal 2012; 10(7):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

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

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.

Original Annex II dossier

Studies submitted and evaluated for the first inclusion of iodosulfuron-methyl-sodium on Annex I:

Report:	[redacted]; [redacted]; 1998; M-182735-01
Title:	Determination of the maximum residue level (MRL) for AE F115008 in cereal grain (statement) Code: AE F115008
Report No:	C081479
Document No:	M-182735-01-1
Guidelines:	**BBA: IV, 3-6 (Jan. 1990);Deviation not specified**
GLP/GEP:	**no**

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

Original Annex II dossier

The Acceptable Daily Intake (ADI) of 0.03 mg/kg body weight was established based on the rat 24-month carcinogenicity study with a safety factor of 100 (SANCO/10166/2003 (3 July 2003). No ARfD was allocated. On the basis of its toxicological profile, iodosulfuron-methyl-sodium is considered

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unlikely to present an acute hazard. The acute and short term oral toxicity of iodosulfuron-methyl-sodium is very low.

Calculation submitted and evaluated for the first inclusion of iodosulfuron-methyl-sodium on Annex I

Report:	[redacted];[redacted];1998;M-182742-01
Title:	TMDI estimation of dietary intake of AE F115008 from residues in cereals (statement) Code: AE F115008
Report No:	C001482
Document No:	M-182742-01-1
Guidelines:	**Deviation not specified**
GLP/GEP:	**no**

AIR3 process
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 CA 6.9-1.

Table CA 6.9- 1: input values used for TMDI calculation of iodosulfuron-methyl-sodium

Commodity	Chronic risk assessment		
	Input value (mg/kg)	Comment	Origin of the MRL
Maize grain	0.01*	Maize grain	EFSA Journal 2012; 10(11):2974
Barley grain	0.01*	Barley grain	
Rye grain	0.01*	Rye grain	
Wheat grain	0.01*	Wheat grain	

As shown in Table CA 6.9- 2, the highest TMDI calculated for iodosulfuron-methyl-sodium represented less than 1% of the ADI, which denotes considerable margins of safety.

Table CA 6.9- 2: Highest TMDI calculated for iodosulfuron-methyl-sodium according to the EFSA model

Compound	EFSA model Highest TMDI (%ADI)	Highest contributor	
		MS diet	Commodity / group of commodities
iodosulfuron-methyl-sodium	< 1%	WHO Cluster diet B	Cereals

CA 6.10 - Other studies

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

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

Iodosulfuron-methyl-sodium is applied on cereals early in the growing season (latest at BBCH 32) and no residues are expected in pollen and bee products.

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