FINAL REGISTRATION REPORT

Part B

Section 10

Assessment of the relevance of metabolites in groundwater

Detailed summary of the risk assessment

Product code: JME-HER 12 OD

Product name(s): -

Chemical active substance:

iodosulfuron-methyl-sodium, 2 g/L

mesosulfuron-methyl, 10 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: Pestila Sp. z o.o.

Submission date: December 2023, revision: April 2024

MS Finalisation date: 03/10/2024

Version history

When	What
January 2024	Dossier sent for evaluation
04.2024	Update of dRR on evaluator's request
July 2024	zRMS finalised evaluation
October 2024	Final version prepared by zRMS after Commenting period

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zRMS comments:
The text highlighted in grey was provided by the evaluator.

10 Relevance of metabolites in groundwater

zRMS's comment	**Iodosulfuron-methyl-sodium:** PECgw values for all active substance metabolites are below the trigger value of 0.1 µg/L. **Mesosulfuron-methyl:** PECgw values for active substance metabolites AE F160459, AE F160460, AE F147447 and BCS-CV14885 are above the trigger value of 0.1 µg/L. JME-HER 12 OD was considered equivalent/comparable to already registered Atlantis 12 OD, therefore the unprotected toxicological studies and relevance of metabolites assessment performed for Atlantis 12 OD is acceptable. Toxicological data on the metabolites of mesosulfuron-methyl with the potential to reach the groundwater in concentrations above 0.1 µg/L have been already reviewed during the EU peer review process. Data has been accepted based on EU peer review.

Introduction

This is the application for registration of a plant protection product under working name JME-HER 12 OD according to Article 33 and Article 34 of Regulation 1107/2009. JME-HER 12 OD is an oil dispersion formulation, containing 2 g/L of iodosulfuron-methyl-sodium and 10 g/L of mesosulfuron-methyl to be used as an herbicide to protect cereals.

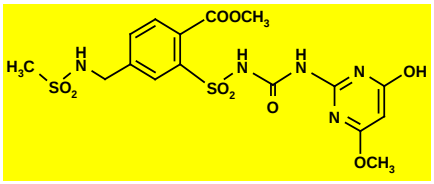
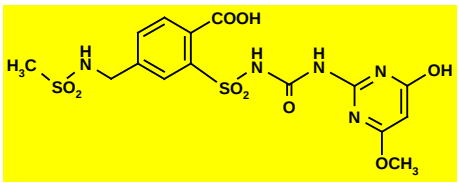
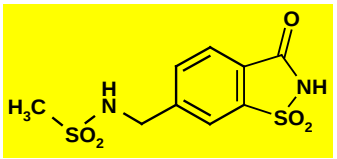
In respect to the above and taking into account Polish requirements for the applications for registration of a plant protection products according to Article 33 based on Article 34 of Regulation 1107/2009 applicant do not provide additional data and apply for using unprotected data of Atlantis 12 OD.

This document has been prepared by copying the summary of information included in the Atlantis 12 OD renewal Registration Report (zRMS: Poland, MS finalisation: 12/02019). The information and studies used in this document are not protected in accordance with Art. 59 Reg. 1107/2009 and can be used for purpose of JME-HER 12 OD registration.

10.1 General information

The 80th percentiles of the predicted annual average leachate concentrations of active substances and metabolites were below 0.1 µg/L except metabolites AE F160459, AE F160460, AE F147447 and BCS-CV14885 for which PECgw were greater than the regulatory threshold in some scenarios with a maximum of 0.391 µg/L (Jokionen). Nevertheless, these metabolites are considered non-relevant according to Sanco/221/2000 - rev.10 - final and have been evaluated in the RAR of mesosulfuron-methyl. No further evaluation is required.

Table 10.1-1: General information on the metabolites of mesosulfuron-methyl

Name of active substance	***Metabolite name and code***	***Structural/molecular formula***	***Trigger for relevance assessment***	
Mesosulfuron-methyl	*AE F160459*		*Max PEC_{gw}* *Based on:*	0.141 µg/L 12 g a.s/ha to winter cereals, PEARL Tier 1 simulation, scenario Hamburg
Mesosulfuron-methyl	*AE F160460*		*Max PEC_{gw}* *Based on:*	0.195 µg/L 12 g a.s/ha to winter cereals, PEARL Tier 1 simulation, scenario Hamburg
Mesosulfuron-methyl	*AE F147447*		*Max PEC_{gw}* *Based on:*	0.257 µg/L 12 g a.s/ha to winter cereals, PEARL Tier 1 simulation, scenario Jokioinen.
Mesosulfuron-methyl	*BCS-CV14885*		*Max PEC_{gw}* *Based on:*	0.391 µg/L 12 g a.s/ha to winter cereals, PEARL Tier 1 simulation, scenario Jokioinen

10.2 Relevance assessment of ~~metabolite 1~~ *AE F160459, metabolite of mesosulfuron-methyl*

Summary:

The relevance of groundwater metabolite AE F160459 has already been assessed and accepted at EU level (see EFSA conclusion Section 4, and List of Endpoints for mesosulfuron-methyl). Metabolite AE F160459 is <u>not</u> considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10. A summary of the relevance assessment is provided in Table 10.2-1.

This agreed assessment is also applicable for the GAP and groundwater scenarios considered in this dRR, as predicted metabolite concentrations were always < 0.75 µg/L.

Table 10.2-1: Summary of the relevance assessment for AE F160459

	Assessment step		***Result of assessment***	
	Non-relevance EU-agreed?		*Yes*	*EFSA Journal 2016;14(10):4584*
	STEP 1		*Metabolite of no concern?*	*no*
Quantification of groundwater contamination	*STEP 2*		*Max PEC_{gw}*	0.141 µg/L
			Based on	12 g a.s/ha to winter cereals, PEARL Tier 1 simulation, scenario Hamburg
Hazard assessment	*STEP 3*	*Stage 1*	*Biological activity comparable to the parent?*	*no*
		Stage 2	*Genotoxic properties of metabolite*	*non-genotoxic*
		Stage 3	*Toxic properties of metabolite;*	
			Classification of parent	*No classification and labelling required with respect to toxicological profile*
			Classification of metabolite	*None*
Consumer health risk assessment	*STEP 4*		*Estimated consumer exposure via drinking water and other sources; threshold of concern approach*	*acceptable (<0.75 µg/L)*
	STEP 5		*Refined risk assessment*	*N/A**
			Predicted exposure (% of ADI)	*N/A**
			ADI based on	*N/A**

* *N/A: not applicable*

10.2.1 STEP 1: Exclusion of degradation products of no concern

~~Not relevant.~~

AE F160459 does not meet the criteria for products of no concern as defined in step 1 of the guidance and therefore needs further assessment.

10.2.2 STEP 2: Quantification of potential groundwater contamination

~~Not relevant.~~

PEC_{gw} calculations after leaching from soil for AE F1604569 were performed, for details see Part B, Section 8, chapter 8.8. The overall maximum concentration of AE F160459 from all assessed uses and scenarios is listed in Table 10.2-1 above.

10.2.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.2.3.1 STEP 3, Stage 1: screening for biological activity

~~Not relevant.~~

Metabolite AE F160459 does not have comparable target activity as the parent active compound, as shown by biological screening data. AE F160459 is considered not relevant and is further evaluated in Stage 2.

The biological screening on the metabolite has been considered within the EU peer review process (cf. RAR of mesosulfuron-methyl Vol.1, Level 2, Section 2.11.3.1).

10.2.3.2 STEP 3, Stage 2: screening for genotoxicity

~~Not relevant.~~

AE F160459 was addressed for genotoxic activity by the following data package: read across from mesosulfuron-methyl and metabolite AE F160460 allowed to conclude that the metabolite AE F160459 is devoid of genotoxic potential. (EFSA conclusion, Section 2). AE F160459 is considered not relevant and is further evaluated in Stage 3.

The genotoxicity studies and read across argument have been evaluated within the EU peer review process (cf. RAR of mesosulfuron-methyl Vol.1, Level 2, Section 2.11.3.2). During the Pesticides Peer Review Meeting TC134 (31 May 2016), the experts agreed that no further genotoxicity testing is necessary for the metabolite AE F160459.

10.2.3.3 STEP 3, Stage 3: screening for toxicity

~~Not relevant.~~

Parent compound mesosulfuron-methyl is not classified as toxic or very toxic, and has no classification for reproductive toxicity or carcinogenic properties. Consequently, according to Guidance Document Sanco/221/2000, rev.10-final, 25/02/2003, further toxicity testing with the metabolites is not required based on these criteria.

10.2.4 STEP 4: Exposure assessment – threshold of concern approach

~~Not relevant.~~

The metabolite AE F160459 did not reach or exceed the threshold level of 0.75µg/L. No relevant further route of consumer exposure applies for this component (cf. RAR of mesosulfuron-methyl Vol.1, Level 2, Section 2.11.4).

10.2.5 STEP 5: Refined risk assessment

~~Not relevant.~~

As metabolite AE F160459 does not reach or exceed the threshold level of 0.75µg/L, a refined risk assessment is not necessary for this component (cf. RAR of mesosulfuron-methyl Vol.1, Level 2, Section 2.11.5).

10.3 Relevance assessment of AE F160460, metabolite of mesosulfuron-methyl

Summary:

The relevance of groundwater metabolite AE F160460 has already been assessed and accepted at EU level (see EFSA conclusion Section 4, and List of Endpoints for mesosulfuron-methyl). Metabolite AE F160460 is not considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10. A summary of the relevance assessment is provided in Table 10.3-1.

This agreed assessment is also applicable for the GAP and groundwater scenarios considered in this dRR, as predicted metabolite concentrations were always < 0.75 µg/L.

Table 10.3-1: Summary of the relevance assessment for AE F160460

	Assessment step		***Result of assessment***	
	Non-relevance EU-agreed?		*Yes*	*EFSA Journal 2016;14(10):4584*
	STEP 1		*Metabolite of no concern?*	*no*
Quantification of groundwater contamination	*STEP 2*		*Max PEC_{gw}*	0.195 µg/L
			Based on	12 g a.s/ha to winter cereals, PEARL Tier 1 simulation, scenario Hamburg.
Hazard assessment	*STEP 3*	*Stage 1*	*Biological activity comparable to the parent?*	*no*

		Stage 2	*Genotoxic properties of metabolite*	*non-genotoxic*
		Stage 3	*Toxic properties of metabolite;*	
			Classification of parent	*No classification and labelling required with respect to toxicological profile*
			Classification of metabolite	*None*
Consumer health risk assessment	*STEP 4*		*Estimated consumer exposure via drinking water and other sources; threshold of concern approach*	*acceptable (<0.75 µg/L)*
	STEP 5		*Refined risk assessment*	*N/A**
			Predicted exposure (% of ADI)	*N/A**
			ADI based on	*N/A**

* N/A*: not applicable*

10.3.1 STEP 1: Exclusion of degradation products of no concern

AE F160460 does not meet the criteria for products of no concern as defined in step 1 of the guidance and therefore needs further assessment.

10.3.2 STEP 2: Quantification of potential groundwater contamination

PEC_{gw} calculations after leaching from soil for AE F160460 were performed, for details see Part B, Section 8, chapter 8.8. The overall maximum concentration of AE F160460 from all assessed uses and scenarios is listed in Table 10.3-1.

10.3.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.3.3.1 STEP 3, Stage 1: screening for biological activity

Metabolite AE F160460 does not have comparable target activity as the parent active compound, as shown by biological screening data. AE F160460 is considered not relevant and is further evaluated in Stage 2.

The biological screening on the metabolite has been considered within the EU peer review process (cf. RAR of mesosulfuron-methyl Vol.1, Level 2, Section 2.11.3.1).

10.3.3.2 STEP 3, Stage 2: screening for genotoxicity

AE F160460 was addressed for genotoxic activity by the following data package of in vitro genotoxicity studies: Ames Test on Salmonella Typhimurium, Chromosomal aberrations in Chinese Hamster V79 cells, and Gene mutation (HPRT) in Chinese Hamster V79 cells. Negative results in all tests allowed to conclude that the metabolite AE F160460 is devoid of genotoxic potential. (EFSA conclusion, Section 2). AE F160460 is considered not relevant and is further evaluated in Stage 3.

The genotoxicity studies have been evaluated within the EU peer review process (cf. RAR of mesosulfuron-methyl Vol.1, Level 2, Section 2.11.3.2).

10.3.3.3 STEP 3, Stage 3: screening for toxicity

Parent compound mesosulfuron-methyl is not classified as toxic or very toxic, and has no classification for reproductive toxicity or carcinogenic properties. Consequently, according to Guidance Document Sanco/221/2000, rev.10-final, 25/02/2003, further toxicity testing with the metabolites is not required based on these criteria.

10.3.4 STEP 4: Exposure assessment – threshold of concern approach

The metabolite AE F160460 did not reach or exceed the threshold level of 0.75µg/L. No relevant further route of consumer exposure applies for this component (cf. RAR of mesosulfuron-methyl Vol.1, Level 2, Section 2.11.4).

10.3.5 STEP 5: Refined risk assessment

As metabolite AE F160460 does not reach or exceed the threshold level of 0.75µg/L, a refined risk assessment is not necessary for this component (cf. RAR of mesosulfuron-methyl Vol.1, Level 2, Section 2.11.5).

10.4 Relevance assessment of AE F147447, metabolite of mesosulfuron-methyl

Summary:

The relevance of groundwater metabolite AE F147447 has already been assessed and accepted at EU level (see EFSA conclusion Section 4, and List of Endpoints for mesosulfuron-methyl). Metabolite AE F147447 is <u>not</u> considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10. A summary of the relevance assessment is provided in Table 10.4-1.

This agreed assessment is also applicable for the GAP and groundwater scenarios considered in this dRR, as predicted metabolite concentrations were always < 0.75 µg/L.

Table 10.4-1: Summary of the relevance assessment for AE F147447

	Assessment step	***Result of assessment***	
	Non-relevance EU-agreed?	*Yes*	*Reference:* *EFSA conclusion and LoEP of mesosulfuron,* *EFSA Journal 2016;14(10):4584, Section 4 and Table 2;* *EFSA Journal 2016;14(10):4584*
	STEP 1	*Metabolite of no concern?*	*no*
Quantification	*STEP 2*	*Max PEC_{gw}*	0.257 µg/L

			Based on	12 g a.s/ha to winter cereals, PEARL Tier 1 simulation, scenario Jokioinen.
Hazard assessment	*STEP 3*	*Stage 1*	*Biological activity comparable to the parent?*	*no*
		Stage 2	*Genotoxic properties of metabolite*	*non-genotoxic*
		Stage 3	*Toxic properties of metabolite;*	
			Classification of parent	*No classification and labelling required with respect to toxicological profile*
			Classification of metabolite	*None*
Consumer health risk assessment	*STEP 4*		*Estimated consumer exposure via drinking water and other sources; threshold of concern approach*	*acceptable (<0.75 µg/L)*
	STEP 5		*Refined risk assessment*	*N/A**
			Predicted exposure (% of ADI)	*N/A**
			ADI based on	*N/A**

* N/A: not applicable

10.4.1 STEP 1: Exclusion of degradation products of no concern

AE F147447 does not meet the criteria for products of no concern as defined in step 1 of the guidance and therefore needs further assessment.

10.4.2 STEP 2: Quantification of potential groundwater contamination

PEC_{gw} calculations after leaching from soil for AE F147447 were performed, for details see Part B, Section 8, chapter 8.8. The overall maximum concentration of AE F147447 from all assessed uses and scenarios is listed in Table 10.4-1.

10.4.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.4.3.1 STEP 3, Stage 1: screening for biological activity

Metabolite AE F147447 does not have comparable target activity as the parent active compound, as shown by biological screening data. AE F147447 is considered not relevant and is further evaluated in Stage 2.

The biological screening on the metabolite has been considered within the EU peer review process (cf. RAR of mesosulfuron-methyl Vol.1, Level 2, Section 2.11.3.1).

10.4.3.2 STEP 3, Stage 2: screening for genotoxicity

AE F147447 was addressed for genotoxic activity by the following data package of in vitro genotoxicity studies: Ames Test on Salmonella Typhimurium, Chromosomal aberrations in Chinese Hamster V79 cells, and Gene mutation (HPRT) in Chinese Hamster V79 cells. Negative results in all tests allowed to conclude that the metabolite AE F147447 is devoid of genotoxic potential. (EFSA conclusion, Section 2). AE F147447 is considered not relevant and is further evaluated in Stage 3.

The genotoxicity studies have been evaluated within the EU peer review process (cf. RAR of mesosulfuron-methyl Vol.1, Level 2, Section 2.11.3.2).

10.4.3.3 STEP 3, Stage 3: screening for toxicity

Parent compound mesosulfuron-methyl is not classified as toxic or very toxic, and has no classification for reproductive toxicity or carcinogenic properties. Consequently, according to Guidance Document Sanco/221/2000, rev.10-final, 25/02/2003, further toxicity testing with the metabolites is not required based on these criteria.

10.4.4 STEP 4: Exposure assessment – threshold of concern approach

The metabolite AE F147447 did not reach or exceed the threshold level of 0.75µg/L. No relevant further route of consumer exposure applies for this component (cf. RAR of mesosulfuron-methyl Vol.1, Level 2, Section 2.11.4).

10.4.5 STEP 5: Refined risk assessment

As metabolite AE F147447 does not reach or exceed the threshold level of 0.75µg/L, a refined risk assessment is not necessary for this component (cf. RAR of mesosulfuron-methyl Vol.1, Level 2, Section 2.11.5).

10.5 Relevance assessment of BCS-CV14885, metabolite of mesosulfuron-methyl

Summary:

The relevance of groundwater metabolite BCS-CV14885 has already been assessed and accepted at EU level (see EFSA conclusion Section 4, and List of Endpoints for mesosulfuron-methyl). Metabolite BCS-CV14885 is not considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10. A summary of the relevance assessment is provided in Table 10.5-1.

This agreed assessment is also applicable for the GAP and groundwater scenarios considered in this dRR as predicted metabolite concentrations were always < 0.75 µg/L.

Table 10.5-1: Summary of the relevance assessment for BCS-CV14885

	Assessment step	***Result of assessment***

	Non-relevance EU-agreed?		*Yes*	*EFSA Journal 2016;14(10):4584*
	STEP 1		*Metabolite of no concern?*	*no*
Quantification of groundwater contamination	*STEP 2*		*Max PEC_{gw}*	0.391 µg/L
			Based on	12 g a.s/ha to winter cereals, PEARL Tier 1 simulation, scenario Jokioinen.
Hazard assessment	*STEP 3*	*Stage 1*	*Biological activity comparable to the parent?*	*no*
		Stage 2	*Genotoxic properties of metabolite*	*non-genotoxic*
		Stage 3	*Toxic properties of metabolite;*	
			Classification of parent	*No classification and labelling required with respect to toxicological profile*
			Classification of metabolite	*None*
Consumer health risk assessment	*STEP 4*		*Estimated consumer exposure via drinking water and other sources; threshold of concern approach*	*acceptable (<0.75 µg/L)*
	STEP 5		*Refined risk assessment*	*N/A**
			Predicted exposure (% of ADI)	*N/A**
			ADI based on	*N/A**

* N/A: not applicable

10.5.1 STEP 1: Exclusion of degradation products of no concern

BCS-CV14885 does not meet the criteria for products of no concern as defined in step 1 of the guidance and therefore needs further assessment.

10.5.2 STEP 2: Quantification of potential groundwater contamination

PEC_{gw} calculations after leaching from soil for BCS-CV14885 were performed, for details see Part B, Section 8, chapter 8.8. The overall maximum concentration of BCS-CV14885 from all assessed uses and scenarios is listed in Table 10.5-1.

10.5.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.5.3.1 STEP 3, Stage 1: screening for biological activity

Metabolite BCS-CV14885 does not have comparable target activity as the parent active compound, as shown by biological screening data. BCS-CV14885 is considered not relevant and is further evaluated in Stage 2.

The biological screening on the metabolite has been considered within the EU peer review process (cf. RAR of mesosulfuron-methyl Vol.1, Level 2, Section 2.11.3.1).

10.5.3.2 STEP 3, Stage 2: screening for genotoxicity

BCS-CV14885 was addressed for genotoxic activity by the following data package of in vitro genotoxicity studies: Ames Test on Salmonella Typhimurium, Chromosomal aberrations in Chinese Hamster V79 cells, and Gene mutation (HPRT) in Chinese Hamster V79 cells. Negative results in all tests allowed to conclude that the metabolite BCS-CV14885 is devoid of genotoxic potential. (EFSA conclusion, Section 2). BCS-CV14885 is considered not relevant and is further evaluated in Stage 3.

The genotoxicity studies have been evaluated within the EU peer review process (cf. RAR of mesosulfuron-methyl Vol.1, Level 2, Section 2.11.3.2).

10.5.3.3 STEP 3, Stage 3: screening for toxicity

Parent compound mesosulfuron-methyl is not classified as toxic or very toxic, and has no classification for reproductive toxicity or carcinogenic properties. Consequently, according to Guidance Document Sanco/221/2000, rev.10-final, 25/02/2003, further toxicity testing with the metabolites is not required based on these criteria.

10.5.4 STEP 4: Exposure assessment – threshold of concern approach

The metabolite BCS-CV14885 did not reach or exceed the threshold level of 0.75µg/L. No relevant further route of consumer exposure applies for this component (cf. RAR of mesosulfuron-methyl Vol.1, Level 2, Section 2.11.4).

10.5.5 STEP 5: Refined risk assessment

As metabolite BCS-CV14885 does not reach or exceed the threshold level of 0.75 µg/L, a refined risk assessment is not necessary for this component (cf. RAR of mesosulfuron-methyl Vol.1, Level 2, Section 2.11.5).

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
-	-	-	-	-	-

List of data submitted or referred to by the applicant and relied on, but already evaluated at EU peer review

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner

List of data submitted by the applicant and not relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner

List of data relied on not submitted by the applicant but necessary for evaluation

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner

Appendix 2 Additional information

Not relevant.