

FINAL REGISTRATION REPORT

Part B

Section 10

Assessment of the relevance of metabolites in groundwater

Detailed summary of the risk assessment

Product code: SHA 4100 A

Product name: HIFEN

Chemical active substance:

Thifensulfuron-methyl, 750 g/kg

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

Applicant: SHARDA Cropchem Ltd.

Submission date: September 2023

MS Finalisation date: March 2024, February 2025, March 2025,

February 2026

Version history

When	What
March 2024	zRMS assessment
July 2024	Applicant update
February 2025	The final Registration Report.
March 2025	Corrected of final Registration Report.
February 2026	Corrected nr. 2 of final Registration Report.

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10 Relevance of metabolites in groundwater

10.1 General information

The metabolites IN-V7160 and IN-A5546 are predicted to occur in groundwater at concentrations below 0.1 µg/L (see dRR Part B8. Chapter 8.8). Assessment of the relevance of these metabolites according to the stepwise procedure of the EC guidance document SANCO/221/2000 –rev.11 is therefore not required.

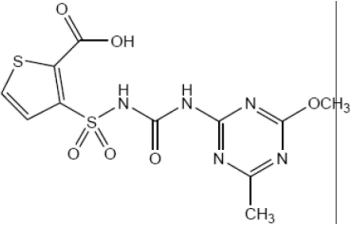
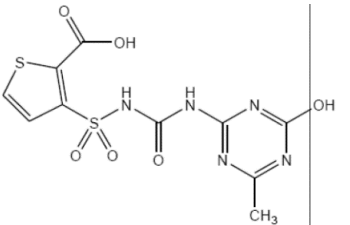
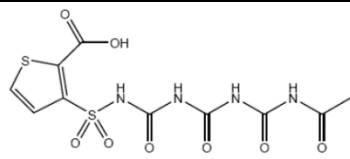
The non toxicologically relevant metabolites IN-L9225, IN-JZ789, 2-acid-3-triuret, IN-L9223, IN-A4098 and IN-W8268 are predicted to occur in groundwater at concentrations above 0.1 µg/L (see dRR Part B.8, Chapter 8.8). Assessment of the relevance of these metabolites according to the stepwise procedure of the EC guidance document SANCO/221/2000 –rev.11 is therefore required.

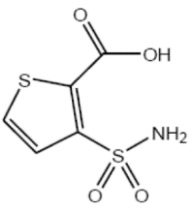
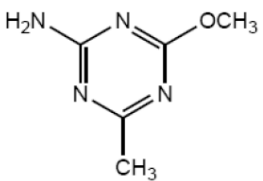
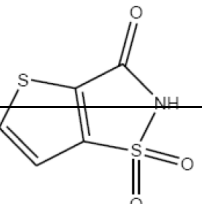
The relevance of the groundwater metabolites has already been assessed (see EFSA Journal 2015;13(7):4201 and confirmatory data (RAR 01 vol 1, appendix VI) and the conclusion is that metabolite IN-L9225 and IN-W8268 are not consider relevant according to the criterial laid down in the EC guidance document SANCO/221/2000 -rev.11.

The metabolites IN-JZ789, 2-acid-3-triuret, IN-L9223, IN-A4098 are ‘not relevant’ groundwater metabolites, but still pending the final decision on EU level.

General information on the metabolites is provided in Table 10.1-1. The impact of the relevance assessment on whether a particular GAP use leads to acceptable risk or not is presented in the summary of the cGAP evaluation in chapter 8.8 of the dRR Part B, Section 8 (Environmental fate and behaviour).

Table 10.1-1: General information on the metabolite(s)

Name of active substance	Metabolite name and code	Structural/molecular formula	Trigger for relevance assessment	
Thifensulfuron-methyl	IN-L9225		Max PEC _{gw} Based on:	0.573 µg/L Okehampton PEARL scenario
	IN-JZ789		Max PEC _{gw} Based on:	1.122 µg/L Jokionen PEARL scenario
	2-acid-3-triuret		Max PEC _{gw} Based on:	0.283 µg/L Hamburg PEARL scenario

Name of active substance	Metabolite name and code	Structural/molecular formula	Trigger for relevance assessment	
	IN-L9223		Max PEC _{gw} Based on:	3.174 µg/L Jokionen PEARL scenario
	IN-A4098		Max PEC _{gw} Based on:	0.279 µg/L Hamburg PEARL scenario
	~~IN-W8268~~		~~Max PEC_{gw} Based on:~~	~~0.343 µg/L Jokionen PEARL scenario~~

10.2 Relevance assessment of IN-L9225

Comments of ZRMs:	According to the available toxicological data, the metabolite IN-L9225 is considered not genotoxic. It has lower or equal toxicity as the parent substance (28-d rat study) and has no pesticidal activity. The parent substance is not classified in regards to mammalian toxicology. The maximum PEC_{gw} of IN-L9225 (acc. to the application rate presented in the GAP table) amounts to 0.573 µg/L. Since the predicted max. PEC_{gw} value is below the upper limit for metabolites (≥ 0.75 µg/L), the consumer risk calculation for this metabolite is not required. Conclusions: Taking into account the toxicological data, the metabolite IN-L9225 is considered toxicologically non-relevant. The use of SHA 4100 A (HIFEN) according to the list of intended uses presented in GAP Table, causes no risk for health of the adults, toddlers and infants.
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Summary:

The relevance of the groundwater metabolite IN-L9225 has already been assessed (see EFSA Journal 2015;13(7):4201 and confirmatory data (RAR 01 vol 1, appendix VI) and the conclusion is that metabolite IN-L9225 is 'not relevant' groundwater metabolite.

A summary of the relevance assessment is given in Table 10.2-1 and the corresponding studies are listed in the corresponding sections.

Table 10.2-1: Summary of the relevance assessment for IN-L9225

	Assessment step		Result of assessment	
	STEP 1		Metabolite of no concern?	No
fication of ground water contam-	STEP 2		Max PEC _{gw}	0.573 µg/L
			Based on	Okehampton PEARL scenario
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;	None
			Classification of parent	None
			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: not applicable

10.2.1 STEP 1: Exclusion of degradation products of no concern

IN-L9225 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

PEC_{gw} calculations after leaching from soil for IN-L9225 were performed (see Part B, Section 8, chapter 8.8). The uses for which concentrations of IN-L9225 were considered to exceed 0.1 µg/L are listed in Table 10.2-1. Details are given in Part B, Section 8, chapter 8.8.

10.2.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.2.3.1 STEP 3, Stage 1: screening for biological activity

The metabolite IN-L9225 has been evaluated in the peer review in view of the Annex I inclusion of Thifensulfuron-methyl. The metabolites has no biological activity as compared to the parent compound (EFSA Journal 2015;13(7):4201).

10.2.3.2 STEP 3, Stage 2: screening for genotoxicity

IN-L9225 was screened for genotoxic activity by the following data package of *in vitro* genotoxicity studies: Ames test, gene mutation test with mammalian cells, a chromosome aberration test and a micronucleus test. IN-L9225 was non-genotoxic as shown by a negative Ames test, negative gene mutation test with mammalian cells, negative chromosome aberration test and negative micronucleus test. IN-L9225 is con-

sidered not relevant and is further evaluated in Stage 3.

The studies were reviewed at EU level and they are summarized in part B, Section 6.

10.2.3.3 STEP 3, Stage 3: screening for toxicity

The parent, Thifensulfuron-methyl, to IN-L9225 is not classified as acutely or chronically toxic or very toxic, nor for reproductive toxicity, nor as a carcinogen. There are no reasons to expect that IN-L9225 may be toxic or highly toxic. However, acute and chronic toxicity was reviewed at EU level and they summarized in part B Section 6. Metabolite IN-L9225 is not considered relevant and is further evaluated in Step 4.

10.2.4 STEP 4: Exposure assessment – threshold of concern approach

PEC_{gw} calculations for IN-L9225 are < 0.75 µg/L.

IN-L9225 is not considered to exceed the toxicological threshold of concern as defined in EC guidance document SANCO/221/2000 –rev.11.

10.2.5 STEP 5: Refined risk assessment

PEC_{gw} calculations for IN-L9225 are < 0.75 µg/L and a refined risk assessment at Step 5 is therefore not required.

10.3 Relevance assessment of IN-JZ789

Comments of ZRMs:	According to the available toxicological data, the metabolite IN-JZ789 is considered not genotoxic.		
	The parent substance is not classified in regards to mammalian toxicology.		
	The maximum PEC _{gw} of IN-JZ789 (acc. to the application rate presented in the GAP table) amounts to 1.122 µg/L.		
	Since the predicted max. PEC _{gw} value is above the upper limit for metabolites (≥0.75 µg/L), the consumer risk calculation for this metabolite is required. Acc. to EFSA Journal 2015;13(7):4201, <u>the reference value of the parent substance might be applied to the metabolite IN-JZ789</u> . The results of risk calculations are presented in the table below (using new default body weight values ¹).		
		Exposure (µg/kg b.w./d)	% ADI (parent substance)
Adults (70 ¹ /60 ² kg b.w.)	0.032/0.037	0.32/0.37	
Toddlers (12 ¹ /10 ² kg b.w.)	0.094/0.112	0.94/1.12	
Infants (5 ^{1,2} kg b.w.)	0.17	1.67	
Conclusions:			
Taking into account the toxicological data, the metabolite IN-JZ789 is considered			

	toxicologically non-relevant. The results of consumer risk calculations indicate that the use of SHA 4100 A (HIFEN) according to the list of intended uses presented in GAP Table, causes no risk for health of the adults, toddlers and infants. Conclusions: Taking into account all the data presented above, the level of exposure to the metabolite IN-L9223 is acceptable for consumers, when product SHA 4100 A (HIFEN) is used in accordance with the list of intended uses presented in the GAP Table. ¹According to EFSA Journal 2012;10(3):2579, Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured data. ²WHO Guidelines for drinking-water quality: fourth edition incorporating the first addendum, 2022
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Summary:

The relevance of the groundwater metabolite IN-JZ789 has already been assessed (see EFSA Journal 2015;13(7):4201 and confirmatory data (RAR 01 vol 1, appendix VI). The conclusion is that metabolite IN-JZ789 is ‘not relevant’ groundwater metabolite, but still pending the final decision on EU level.

A summary of the relevance assessment is given in Table 10.2-1 and the corresponding studies are listed in the corresponding sections.

Table 10.3-1: Summary of the relevance assessment for IN-JZ789

	Assessment step		Result of assessment	
	STEP 1		Metabolite of no concern?	no
Quantification of groundwater contamination	STEP 2		Max PEC _{gw}	1.122 µg/L
			Based on	Jokionen PEARL scenario
Hazard assessment	STEP 3	Stage 1	Biological activity comparable to the parent?	Not available
		Stage 2	Genotoxic properties of metabolite	Non-genotoxic
		Stage 3	Toxic properties of metabolite;	No data available
			Classification of parent	None
			Classification of metabolite	No data available
Consumer health risk assessment	STEP 4		Estimated consumer exposure via drinking water and other sources; threshold of concern approach	Not acceptable (> 0.75 µg/L)
	STEP 5		Refined risk assessment	acceptable

	Predicted exposure (% of ADI)	1.68% of ADI
	ADI based on	Parent ADI

10.3.1 STEP 1: Exclusion of degradation products of no concern

IN-JZ789 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 IN-JZ789 were performed (see Part B, Section 8, chapter 8.8). The uses for which concentrations of IN-JZ789 were considered to exceed 0.1 µg/L are listed in Table 10.2-1. Details are given in Part B, Section 8, chapter 8.8.

10.3.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.3.3.1 STEP 3, Stage 1: screening for biological activity

The assessment of biological activity of IN-JZ789, according to EFSA and confirmatory data (RAR 01 vol 1, appendix VI) is still pending final decision on EU level.

10.3.3.2 STEP 3, Stage 2: screening for genotoxicity

IN-JZ789 was screened for genotoxic activity by the following data package of *in vitro* genotoxicity studies: AMES test and micronucleus test. IN-JZ789 was non-genotoxic as shown by a negative Ames test, negative micronucleus test. IN-JZ789 is considered not relevant and is further evaluated in Stage 3.

The studies were reviewed at EU level and they are summarized in part B, Section 6.

10.3.3.3 STEP 3, Stage 3: screening for toxicity

The parent, Thifensulfuron-methyl, to IN-JZ789 is not classified as acutely or chronically toxic or very toxic, nor for reproductive toxicity, nor as a carcinogen. There are no reasons to expect that IN-JZ789 may be toxic or highly toxic. IN-JZ789 has not been subject to targeted testing. IN-JZ789 is not considered relevant and is further evaluated in Step 4.

10.3.4 STEP 4: Exposure assessment – threshold of concern approach

The potential exposure to IN-JZ789 is > 0.75 µg/L but <10 µg/L. A further assessment in Step 5 is required.

10.3.5 STEP 5: Refined risk assessment

IN-JZ789 has a PEC_{gw} between 0.75 µg/L and 10 µg/L. A refined assessment of the potential toxicological significance including the selected ADI is presented here.

The consumer risk assessment demonstrates an acceptable risk.

The estimated safety margin including potential exposure via other routes besides drinking water for IN-JZ789 are 1.68% of ADI (infant), 1.12% of ADI (child), 0.38% of ADI (adult).

Justification for the selected ADI:

No acute or repeated dose toxicity studies are available for IN-JZ789. However, given the close structural similarity between Thifensulfuron methyl and IN-JZ789, a similar hazard profile is expected. Therefore, the ADI value set for the parent (0.01 mg/kg bw/d) can be used for the risk assessment of IN-JZ789.

Calculation of risk (% ADI) for 5-kg bottle-fed infant (consuming 0.75 l/day), for 10-kg child (consuming 1.0 l/day), for 60-kg adult (consuming 2.0 l/day):

	Max PEC _{gw} (µg/L)	Weight (kg)	Exposure (L/day)	TMDI (µg/kg bw/day)	ADI (µg/kg bw/day)	% ADI
Bottle fed infant	1.122	5	0.75	0.1683	10	1.68
Child		10	1	0.1122		1.12
Adult		60	2	0.0374		0.38

10.4 Relevance assessment of 2-acid-3-triuret

Comments of ZRMs:	Acc. to EFSA Journal 2015;13(7):4201, the toxicological data on the metabolite 2-acid-3-triuret is not available. The parent substance is not classified in regards to mammalian toxicology. The maximum PEC_{gw} of 2-acid-3-triuret (acc. to the application rate presented in the GAP table) amounts to 0.283 µg/L and is below the upper limit for metabolites (<0.75 µg/L).
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Summary:

The relevance of the groundwater metabolite 2-acid-3-triuret has already been assessed (see EFSA Journal 2015;13(7):4201 and confirmatory data (RAR 01 vol 1, appendix VI). The conclusion is that metabolite 2-acid-3-triuret is 'not relevant' groundwater metabolite, but still pending the final decision on EU level.

A summary of the relevance assessment is given in Table 10.2-1 and the corresponding studies are listed in the corresponding sections.

Table 10.4-1: Summary of the relevance assessment for 2-acid-3-triuret

	Assessment step		Result of assessment	
	STEP 1		Metabolite of no concern?	No
Quantification of groundwater contamination	STEP 2		Max PEC _{gw}	0.283 µg/L
			Based on	Hamburg PEARL scenario
Hazard assessment	STEP 3	Stage 1	Biological activity comparable to the parent?	No data available.

Consumer health risk assessment		Stage 2	Genotoxic properties of metabolite	No data available.
		Stage 3	Toxic properties of metabolite;	No data available
			Classification of parent	None
			Classification of metabolite	No data available.
	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

2-acid-3-triuret 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 2-acid-3-triuret were performed (see Part B, Section 8, chapter 8.8). The uses for which concentrations of 2-acid-3-triuret were considered to exceed 0.1 µg/L are listed in Table 10.2-1. Details are given in Part B, Section 8, chapter 8.8.

10.4.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.4.3.1 STEP 3, Stage 1: screening for biological activity

The assessment of biological activity of 2-acid-3-triuret, according to EFSA and confirmatory data (RAR 01 vol 1, appendix VI) is still pending final decision on EU level.

10.4.3.2 STEP 3, Stage 2: screening for genotoxicity

The assessment of genotoxicity of 2-acid-3-triuret, according to EFSA and confirmatory data (RAR 01 vol 1, appendix VI) is still pending final decision on EU level.

10.4.3.3 STEP 3, Stage 3: screening for toxicity

The parent, Thifensulfuron-methyl, to 2-acid-3-triuret is not classified as acutely or chronically toxic or very toxic, nor for reproductive toxicity, nor as a carcinogen. There are no reasons to expect that 2-acid-3-triuret may be toxic or highly toxic. 2-acid-3-triuret has not been subject to targeted testing. 2-acid-3-triuret is not considered relevant and is further evaluated in Step 4.

10.4.4 STEP 4: Exposure assessment – threshold of concern approach

PEC_{gw} calculations for 2-acid-3-triuret are < 0.75 µg/L.

2-acid-3-triuret is not considered to exceed the toxicological threshold of concern as defined in EC guidance document SANCO/221/2000 –rev.11.

10.4.5 STEP 5: Refined risk assessment

PEC_{gw} calculations for 2-acid-3-triuret are < 0.75 µg/L and a refined risk assessment at Step 5 is therefore not required.

10.5 Relevance assessment of IN-L9223

Comments of ZRMs:	According to the available toxicological data, the metabolite IN-L9223 is considered non-genotoxic and has no pesticidal activity. However, the toxicological profile of this metabolite is incomplete for full consumer risk assessment and does not allow to establish the reference dose (data gap). The results generated with OECD QSAR toolbox indicate that IN-L9223 might be more toxic than the parent substance (predicted oral LD ₅₀ value) (RAR, Thifensulfuron-methyl - Volume 3, Annex B.6 : Toxicology and Metabolism).				
	The parent substance is not classified in regards to mammalian toxicology.				
	The maximum PEC _{gw} of IN-L9223 (acc. to the application rate presented in the GAP table) amounts to 3.174 µg/L.				
	Since the predicted max. PEC _{gw} value is above the upper limit for metabolites (≥0.75 µg/L), the consumer risk calculation for this metabolite is required.				
	Although <u>no reference dose has been established for this metabolite</u> , the consumer exposure resulting from drinking water was assessed using <u>maximum allowable concentration (MAC) based on 10% of thifensulfuron - methyl ADI value and the proportion of intake attributed to drinking water (20%)</u> . The results of risk calculations are presented in the table below:				
	MAC (µg/L) (based on 10% ADI, as conservative approach and proportion of intake attributable to drinking water)	Exposure (µg/kg b.w./d)	% of MAC	% ADI (parent substance)	
Adults (70 ¹ /60 ² kg b.w.)	70/60	0.09/0.11	4.5/5.3	0.9/1.1	
Toddlers (12 ¹ /10 ² kg b.w.)	24/20	0.4/0.42	13.2/15.9	4/4.2	
Infants (5 ^{1,2} kg b.w.)	13	0.48	24.4	4.8	
¹ According to EFSA Journal 2012;10(3):2579, Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured data.					
² WHO Guidelines for drinking-water quality: fourth edition incorporating the first addendum, 2017					

Summary:

The relevance of the groundwater metabolite IN-L-9223 has already been assessed (see EFSA Journal 2015;13(7):4201 and confirmatory data (RAR 01 vol 1, appendix VI). The conclusion on the relevance of the metabolite IN-L-9223 is still pending the final decision on EU level.

A summary of the relevance assessment is given in Table 10.2-1 and the corresponding studies are listed in the corresponding sections.

Table 10.5-1: Summary of the relevance assessment for IN-L9223

	Assessment step		Result of assessment	
	STEP 1		Metabolite of no concern?	No
Quantification of groundwater contamination	STEP 2		Max PEC _{gw}	3.174 µg/L
			Based on	Jokionen PEARL scenario
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;	None
			Classification of parent	None
			Classification of metabolite	None
Consumer health risk assessment	STEP 4		Estimated consumer exposure via drinking water and other sources; threshold of concern approach	Not acceptable (> 0.75 µg/L)
	STEP 5		Refined risk assessment	No data
			Predicted exposure (% of ADI)	No data
				ADI based on

10.5.1 STEP 1: Exclusion of degradation products of no concern

IN-L9223 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 IN-L9223 were performed (see Part B, Section 8, chapter 8.8). The uses for which concentrations of IN-L9223 were considered to exceed 0.1 µg/L are listed in Table 10.2-1. Details are given in Part B, Section 8, chapter 8.8.

10.5.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.5.3.1 STEP 3, Stage 1: screening for biological activity

The metabolite IN-L9223 has been evaluated in the peer review in view of the Annex I inclusion of Thifensulfuron-methyl. The metabolites has no biological activity as compared to the parent compound (EFSA Journal 2015;13(7):4201).

10.5.3.2 STEP 3, Stage 2: screening for genotoxicity

IN-L9223 was screened for genotoxic activity by the following data package of *in vitro* genotoxicity studies: Ames test, gene mutation test with mammalian cells, and a chromosome aberration test. IN-L9223 was non-genotoxic as shown by a negative Ames test, negative gene mutation test with mammalian cells, negative chromosome aberration test. IN-L9223 is considered not relevant and is further evaluated in Stage 3.

The studies were reviewed at EU level and they are summarized in Part B, Section 6.

10.5.3.3 STEP 3, Stage 3: screening for toxicity

The parent, Thifensulfuron-methyl, to IN-L9223 is not classified as acutely or chronically toxic or very toxic, nor for reproductive toxicity, nor as a carcinogen. There are no reasons to expect that IN-L9223 may be toxic or highly toxic. IN-L9223 has not been subject to targeted testing. IN-L9223 is not considered relevant and is further evaluated in Step 4.

10.5.4 STEP 4: Exposure assessment – threshold of concern approach

The potential exposure to IN-L9223 is > 0.75 µg/L but <10 µg/L. A further assessment in Step 5 is required.

10.5.5 STEP 5: Refined risk assessment

The conclusion on the toxicological profile of metabolite IN-L9223, as well as risk assessment of this metabolite, is still pending on the EU level.

10.6 Relevance assessment of IN-A4098

Comments of ZRMs:	Acc. to EFSA Journal 2015;13(7):4201, the metabolite IN-A4098 has no pesticidal activity and has moderate acute toxicity: Acute Tox 4., oral LD₅₀ = 1000 mg/kg bw, rat (noteworthy, higher than parent substance). According to EFSA supporting publication 2020:EN-1627, 86 pp. doi:10.2903/sp.efsa.2020.EN-N1627, metabolite IN-A4098 is not toxicologically relevant. The maximum PEC_{gw} IN-A4098 amounts to 0.279 µg/L and is below the upper limit for metabolites (<0.75 µg/L). ~~The available data indicate that the genotoxic potential of IN-A4098 cannot be ruled out (data gap). It might be of concern for consumer exposure because the results exceed the limit for the relevant metabolites, i.e. 0.01 µg/L (the maximum PEC_{gw} amounts to 0.279 µg/L).~~ ~~Further genotoxicity studies and toxicological data is needed to complete consumer~~
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	~~risk assessment~~
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According to EFSA Supporting publication 2020:EN-1627 metabolite IN-A4098 is not toxicologically relevant

Summary:

The relevance of the groundwater metabolite IN-A4098 has already been assessed (see EFSA Journal 2015;13(7):4201 and confirmatory data (RAR 01 vol 1, appendix VI). The conclusion is that metabolite IN-A4098 is ‘not relevant’ groundwater metabolite, but still pending the resolution of its genotoxicity potential and final decision on EU level.

A summary of the relevance assessment is given in Table 10.2-1 and the corresponding studies are listed in the corresponding sections.

Table 10.6-1: Summary of the relevance assessment for IN-A4098

	Assessment step		Result of assessment	
	STEP 1		Metabolite of no concern?	no
Quantification of groundwater contaminant	STEP 2		Max PEC _{gw}	0.279 µg/L
			Based on	Hamburg PEARL scenario
Hazard assessment	STEP 3	Stage 1	Biological activity comparable to the parent?	No
		Stage 2	Genotoxic properties of metabolite	Final decision pending
		Stage 3	Toxic properties of metabolite;	None
			Classification of parent	None
			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

10.6.1 STEP 1: Exclusion of degradation products of no concern

IN-A4098 does not meet the criteria for products of no concern as defined in step 1 of the guidance and therefore needs further assessment.

10.6.2 STEP 2: Quantification of potential groundwater contamination

PEC_{gw} calculations after leaching from soil for IN-A4098 were performed (see Part B, Section 8, chapter 8.8). The uses for which concentrations of IN-A4098 were considered to exceed 0.1 µg/L are listed in

Table 10.2-1. Details are given in Part B, Section 8, chapter 8.8.

10.6.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.6.3.1 STEP 3, Stage 1: screening for biological activity

The metabolite IN-A4098 has been evaluated in the peer review in view of the Annex I inclusion of Thifensulfuron-methyl. The metabolites has no biological activity as compared to the parent compound (EFSA Journal 2015;13(7):4201).

10.6.3.2 STEP 3, Stage 2: screening for genotoxicity

IN-A4098 was screened for genotoxic activity by the following data package of *in vitro* genotoxicity studies: Ames test, gene mutation test with mammalian cells, and a chromosome aberration test. IN-A4098 was non-genotoxic as shown by a negative Ames test, negative gene mutation test with mammalian cells, negative chromosome aberration test.

These studies were presented in confirmatory data post commenting (RAR 01 vol 1, appendix VI) and were reviewed at EU level. They are summarized in Part B, Section 6.

It can be concluded that IN-A4098 is not genotoxic, however, the same dataset was considered and discussed by MS on the context of the confirmatory data for other sulfonylureas. An opinion is already available (EFSA Journal 2020;18(3):6053)¹ however, issue is still not definitely solved. Therefore, the final conclusion is still pending on the EU level.

10.6.3.3 STEP 3, Stage 3: screening for toxicity

The parent, Thifensulfuron-methyl, to IN-A4098 is not classified as acutely or chronically toxic or very toxic, nor for reproductive toxicity, nor as a carcinogen. There are reasons to expect that IN-A4098 may be toxic or highly toxic and IN-A4098 has been subject to targeted testing.

These studies were presented in confirmatory data post commenting and were reviewed at EU level. They are summarized in Part B, Section 6.

IN-A4098 is considered not relevant (however pending the resolution of its genotoxicity potential) and is further evaluated in Step 4.

10.6.4 STEP 4: Exposure assessment – threshold of concern approach

The PEC_{gw} for IN-A4098 was $< 0.75 \mu\text{g/L}$. IN-A4098 is not considered to exceed the toxicological threshold of concern as defined in EC guidance document SANCO/221/2000 –rev.11.

10.6.5 STEP 5: Refined risk assessment

PEC_{gw} calculations for IN-A4098 are $< 0.75 \mu\text{g/L}$ and a refined risk assessment at Step 5 is therefore not required.

¹ Scientific Opinion of the Scientific Panel on Plant Protection Products and their Residues (PPR Panel) on the genotoxic potential of triazine amine (metabolite common to several sulfonylurea active substances); adopted 12 February 2020

10.7 Relevance assessment of IN-W8268

Comments of ZRMs:	Acc. to EFSA Journal 2015;13(7):4201, the metabolite IN-W8268 has no pesticidal activity. The available data indicate that the genotoxic potential of metabolite IN-W8268 cannot be ruled out (data gap). It might be of concern for consumer exposure because the results exceed the limit for the relevant metabolites, i.e. <u>0.01 µg/L (the maximum PEG_{gw} amounts to 0.343 µg/L).</u>
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Summary:

The relevance of the groundwater metabolite IN-W8268 has already been assessed (see EFSA Journal 2015;13(7):4201 and confirmatory data (RAR-01 vol 1, appendix VI) and the conclusion is that metabolite IN-W8268 is 'not relevant' groundwater metabolite.

A summary of the relevance assessment is given in Table 10.2-1 and the corresponding studies are listed in the corresponding sections.

Table 10.7-1: Summary of the relevance assessment for IN-W8268

	Assessment step		Result of assessment	
	STEP 1		Metabolite of no concern?	No
Quantification of groundwater contamination	STEP 2		Max PEC_{gw}	0.343 µg/L
			Based on	Jokionen PEARL-scenario
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;	None
			Classification of parent	None
			Classification of metabolite	None
Consumer health risk assessment	STEP 4		Estimated consumer exposure via drinking water and other sources; threshold of concern approach	Not acceptable (> 0.75 µg/L)
	STEP 5		Refined risk assessment	acceptable
			Predicted exposure (% of ADI)	1.76% of ADI
				ADI based on

10.7.1 STEP 1: Exclusion of degradation products of no concern

IN-W8268 does not meet the criteria for products of no concern as defined in step 1 of the guidance and therefore needs further assessment.

10.7.2 — STEP 2: Quantification of potential groundwater contamination

PEC_{gw} calculations after leaching from soil for IN-W8268 were performed (see Part B, Section 8, chapter 8.8). The uses for which concentrations of IN-W8268 were considered to exceed 0.1 µg/L are listed in Table 10.2-1. Details are given in Part B, Section 8, chapter 8.8.

10.7.3 — STEP 3: Hazard assessment — identification of relevant metabolites

10.7.3.1 — STEP 3, Stage 1: screening for biological activity

The metabolite IN-W8268 has been evaluated in the peer review in view of the Annex I inclusion of Thifensulfuron-methyl. The metabolite has no biological activity as compared to the parent compound (EFSA Journal 2015;13(7):4201).

10.7.3.2 — STEP 3, Stage 2: screening for genotoxicity

IN-W8268 was screened for genotoxic activity by the following data package of *in vitro* genotoxicity studies: micronucleus assay, gene mutation test with mammalian cells, and a chromosome aberration test. IN-W8268 was non-genotoxic as shown by a negative micronucleus assay, negative gene mutation test with mammalian cells.

These studies were presented in confirmatory data post commenting (RAR-01 vol 1, appendix VI) and were reviewed at EU level. They are summarized in Part B, Section 6.

IN-W8268 is considered not relevant and is further evaluated in Stage 3.

10.7.3.3 — STEP 3, Stage 3: screening for toxicity

The parent, Thifensulfuron-methyl, to IN-W8268 is not classified as acutely or chronically toxic or very toxic, nor for reproductive toxicity, nor as a carcinogen. There are reasons to expect that IN-W8268 may be toxic or highly toxic and IN-W8268 has been subject to targeted testing. The toxicity studies are evaluated in Part B, Section 6. IN-W8268 is considered not relevant and is further evaluated in Step 4.

10.7.4 — STEP 4: Exposure assessment — threshold of concern approach

The PEC_{gw} for IN-W8268 was < 0.75 µg/L. IN-W8268 is not considered to exceed the toxicological threshold of concern as defined in EC guidance document SANCO/221/2000 rev.11.

10.7.5 — STEP 5: Refined risk assessment

PEC_{gw} calculations for IN-W8268 are < 0.75 µg/L and a refined risk assessment at Step 5 is therefore not required.

Appendix 1 Lists of data considered in support of the evaluation

Appendix 2 Additional information