FINAL REGISTRATION REPORT

Part B

Section 10

Assessment of the relevance of metabolites in groundwater

Detailed summary of the risk assessment

Product code: SHA 0724 A

Product name: COREY

Chemical active substances:

Rimsulfuron, 150 g/kg

Nicosulfuron, 300 g/kg

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

Applicant: SHARDA Cropchem España S.L.

Submission date: February 2020

MS Finalisation date: 12/2020; 01/2022

Version history

When	What
12/2020	Assessment by expert
January 2022	Applicant update
January 2022	Final RMS Assessment after Commenting period

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10 Relevance of metabolites in groundwater

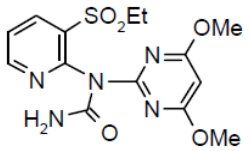
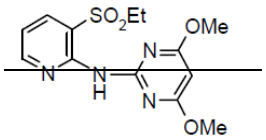
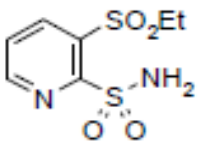
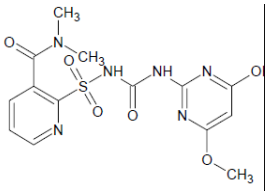
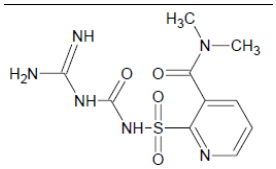
10.1 General information

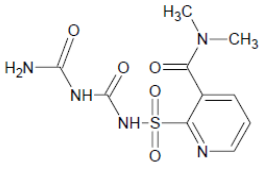
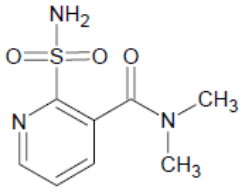
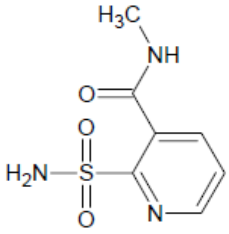
The IN-J290 and ADMP are predicted to occur in groundwater at concentrations below 0.1 µg/L (see dRR Part B, Chapter 8.8). Assessment of the relevance of these metabolites according to the stepwise procedure of the EC guidance document SANCO/221/2000 –rev.10 is therefore not required.

The metabolites IN-70941, IN-70942, IN-E9260, HMUD, AUSN, UCSN, ASDM and MU-466 are predicted to occur in groundwater at concentrations above 0.1 µg/L (see dRR Part B, Chapter 8.8). Assessment of the relevance of these metabolites according to the stepwise procedure of the EC guidance document SANCO/221/2000 –rev.10 is therefore required.

General information on the metabolites are 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	
Rimsulfuron	IN-70941		Max PEC_{gw} Based on:	0.924 µg/L Hamburg PEARL scenario
	~~IN-70942~~		~~Max PEC_{gw}~~ ~~Based on:~~	~~0.101 µg/L~~ ~~Thiva PEARL scenario~~
	IN-E9260		Max PEC_{gw} Based on:	0.817µg/L Thiva PEARL scenario
Nicosulfuron	HMUD		Max PEC_{gw} Based on: Max PEC_{gw} Based on	0.990 µg/L Hamburg PEARL scenario <0.1 µg/L 3 years monitoring study
	AUSN		Max PEC_{gw} Based on:	1.526 µg/L Hamburg PEARL scenario

Name of active substance	Metabolite name and code	Structural/molecular formula	Trigger for relevance assessment	
			Max PEC_{gw} Based on	0.657 µg/L 3 years monitoring study
	UCSN		Max PEC_{gw} Based on: Max PEC_{gw} Based on	1.298 µg/L Thiva PEARL scenario 0.657 µg/L 3 years monitoring study
	ASDM		Max PEC_{gw} Based on: Max PEC_{gw} Based on	0.986 µg/L Hamburg PEARL scenario 0.477 µg/L 3 years monitoring study
	MU-466		Max PEC_{gw} Based on:	0.130 µg/L Thiva PEARL scenario

10.2 Relevance assessment of IN-70941

Summary:

The relevance of the groundwater metabolite IN-70941 has already been assessed and the assessment agreed at EU level (see EFSA Journal 2018;16(5):5258), and the relevance assessment is applicable as well for the GAP and groundwater scenarios considered in this dRR (i.e., the conclusions reached at Step 4 and 5 of the relevance assessment made at the EU-level are valid also with regard to the PEC_{gw} calculated for the GAP and groundwater scenarios considered in this dRR). IN-70941 is 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 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-70941

	Assessment step	Result of assessment	
	STEP 1	Metabolite of no concern?	No
tication of ground water	STEP 2	Max PEC_{gw}	0.924 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	Non genotoxic
		Stage 3	Toxic properties of metabolite;	None
			Classification of parent	Aquatic Acute 1 Aquatic Chronic 1
			Classification of metabolite	Not available
Consumer health risk assessment	STEP 4		Estimated consumer exposure via drinking water and other sources; threshold of concern approach	No acceptable (> 0.75 µg/L)
	STEP 5		Refined risk assessment	Acceptable
			Predicted exposure (% of ADI)	0.14 %
			ADI based on	Parent (0.1 mg/kg bw/d)

10.2.1 STEP 1: Exclusion of degradation products of no concern

IN-70941 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-70941 were performed (see Part B, Section 8, chapter 8.8). The uses for which concentrations of IN-70941 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

Considered as non-relevant according to EFSA Journal 2005; 45, 1-61.

10.2.3.1 STEP 3, Stage 1: screening for biological activity

10.2.3.2 STEP 3, Stage 2: screening for genotoxicity

10.2.3.3 STEP 3, Stage 3: screening for toxicity

10.2.4 STEP 4: Exposure assessment – threshold of concern approach

The potential exposure to IN-70941 is > 0.75 µg/L but <10 µg/L. A further assessment in Step 5 is required.

10.2.5 STEP 5: Refined risk assessment

IN-70941 has a PEC_{gw} between 0.75 µg/L and 10 µg/L but for which the threshold of concern approach in Step 4 is not acceptable. 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-70941 are 0.14 % of ADI (infant), 0.09 % of ADI (child), 0.03 % of ADI (adult).

The ADI for IN-70941 is based on the parent ADI of 0.1 mg/kg bw/day.

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 PECgw (µg/L)	Weight (kg)	Exposure (L/day)	TMDI (µg/kg bw/day)	ADI (µg/kg bw/day)	% ADI
Bottle fed infant	0.924	5	0.75	0.14	100	0.14
Child		10	1	0.09	100	0.09
Adult		60	2	0.03	100	0.03

~~10.3 Relevance assessment of IN-70942~~

~~**Summary:**~~

~~The relevance of the groundwater metabolite IN-70942 has already been assessed and the assessment agreed at EU level (see DAR 2003 and EFSA Journal 2005; 45, 1-61), and the relevance assessment is applicable as well for the GAP and groundwater scenarios considered in this dRR (i.e., the conclusions reached at Step 4 and 5 of the relevance assessment made at the EU level are valid also with regard to the PEC_{gw} calculated for the GAP and groundwater scenarios considered in this dRR). IN-70942 given a maximum PECgw value of 0.101 µg/L in Thiva scenario from PEARL model, but according to the field dissipation studies this metabolite was considered as minor metabolite and no field DT_{50} could be derived. Furthermore, EFSA considered that the endpoints used to risk assessment calculations represent a worst case for the metabolites IN-70942 and IN-E9260. Whilst the use of laboratory values has uncertainty as DT_{50} were extrapolated beyond the study durations, the use of formation fractions and DT_{50} values from the laboratory studies for these 2 metabolites clearly results in more conservative PECs being calculated than would result if the data from the field studies had been used as the basis for the calculations. Besides, metabolite IN-70942 was screened for herbicidal activity in 17 species giving no activity. The Applicant has done QSAR's predictions for mutagenicity and carcinogenicity to support the non risk for ground water using Toxtree v 2.6.13 (submitted separately) being predicted as non mutagenic nor carcinogenic. Therefore as metabolite IN-70942 doesn't pose an unacceptable risk for ground water not relevance assessment has been done.~~

~~IN-70942 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 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-70942**~~

	~~Assessment step~~		~~Result of assessment~~	
	~~STEP 1~~		~~Metabolite of no concern?~~	~~No~~
~~cation of ground water contami~~	~~STEP 2~~		~~Max PEC_{gw}~~	~~0.101 µg/L~~
			~~Based on~~	~~FOCUS PEARL, Thiva, maize~~
~~d as se ss~~	~~STEP 3~~	~~Stage 1~~	~~Biological activity comparable to~~	~~No~~

			the parent?	
		Stage 2	Genotoxic properties of metabolite	No
		Stage 3	Toxic properties of metabolite;	None
			Classification of parent	Aquatic Acute 1 Aquatic Chronic 1
			Classification of metabolite	Non available
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

10.3.1 STEP 1: Exclusion of degradation products of no concern

IN 70942 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 70942 were performed (see Part B, Section 8, chapter 8.8). The uses for which concentrations of IN 70942 were considered to exceed 0.1 µg/L are listed in Table 10.2 1. IN 70942 given a maximum PECgw value of 0.101 µg/L in Thiva scenario from PEARL model, but according to the field dissipation studies this metabolite was considered as minor metabolite and no field DT_{50} could be derived. Furthermore, EFSA considered that the endpoints used to risk assessment calculations represent a worst case for the metabolites IN 70942 and IN E9260. Whilst the use of laboratory values has uncertainty as DT_{50} were extrapolated beyond the study durations, the use of formation fractions and DT_{50} values from the laboratory studies for these 2 metabolites clearly results in more conservative PECs being calculated than would result if the data from the field studies had been used as the basis for the calculations. Besides, metabolite IN 70942 was screened for herbicidal activity in 17 species giving no activity. The Applicant has done QSAR's predictions for mutagenicity and carcinogenicity to support the non risk for ground water using Toxtree v 2.6.13 (submitted separately) being predicted as non mutagenic nor carcinogenic. Therefore, as this metabolite doesn't pose an unacceptable risk for the ground water the assessment was not done. Details are given in Part B, Section 8, chapter 8.8.

10.3.3 STEP 3: Hazard assessment – identification of relevant metabolites

Not required.

10.3.3.1 STEP 3, Stage 1: screening for biological activity

The metabolite IN 70942 has lost the sulfonylurea group that is the characteristic toxophore group of this kind of herbicides. Furthermore, IN 70942 were screened for their biological effects (reported in the DAR under Point B.9.9.2 – no references given). It was tested for herbicidal activity in pre- and post-emergence studies at different application rates on 17 difference plant species. No herbicidal effects were noted in any of the species tested. It is therefore concluded IN 70942 is not biologically active. Further-

more, the aquatic toxicity is also lower than the parent.

10.3.3.2 STEP 3, Stage 2: screening for genotoxicity

As there is not available genotoxicity information for metabolite IN-70942 in DAR nor in the Rimsulfuron EFSA Journal 2005, QSAR predictions by ToxTree v2.6.13 have been done in order to support this assessment. The predictions shown, that, IN-70942 is nor mutagenic, nor genotoxic carcinogen, nor non-genotoxic carcinogen. A predictions report and the predictions as such are submitted separately.

10.3.3.3 STEP 3, Stage 3: screening for toxicity

Rimsulfuron is not classified as acutely or chronically toxic or very toxic / for reproductive toxicity / as a carcinogen or the corresponding classification in accordance to CLP 1272/2008. There are no reasons to expect that IN-70942 may be toxic or highly toxic than Rimsulfuron. According to the ToxTree prediction IN-70942 is not carcinogen, nor mutagen and therefore considered as non relevant.

10.3.4 STEP 4: Exposure assessment – threshold of concern approach

The PEC_{gw} for IN-70942 was < 0.75 µg/L. The potential exposure to IN-70492 via all sources is < 0.02 µg/kg body weight/day as shown by the calculation below. Therefore, a further assessment in Step 5 is not required.

-	MaxPECgw (µg/L)	Weight (kg)	Exposure (L/day)	TMDI (µg/kg bw/d)
bottle fed infant	0.101	5	0.75	0.015
child		10	1	0.010
adult		60	2	0.003

10.3.5 STEP 5: Refined risk assessment

Not required.

10.4 Relevance assessment of IN-E9260

Summary:

The relevance of the groundwater metabolite IN-E9260 has already been assessed and the assessment agreed at EU level (see DAR and EFSA Journal 2005; 45, 1-61), and the relevance assessment is applicable as well for the GAP and groundwater scenarios considered in this dRR (i.e., the conclusions reached at Step 4 and 5 of the relevance assessment made at the EU-level are valid also with regard to the PEC_{gw} calculated for the GAP and groundwater scenarios considered in this dRR). IN-E9260 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 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 IN-E9260

	Assessment step	Result of assessment

	STEP 1		Metabolite of no concern?	No
Quantification of groundwater contamination	STEP 2		Max PEC_{gw}	0.817 µg/L
			Based on	Thiva 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	Aquatic Acute 1 Aquatic Chronic 1
Consumer health risk assessment	STEP 4		Estimated consumer exposure via drinking water and other sources; threshold of concern approach	No acceptable (> 0.75 µg/L)
	STEP 5		Refined risk assessment	Acceptable
			Predicted exposure (% of ADI)	0.12 %
			ADI based on	Parent (0.1 mg/kg bw/d)

10.4.1 STEP 1: Exclusion of degradation products of no concern

IN-E9260 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 IN-E9260 were performed (see Part B, Section 8, chapter 8.8). The uses for which concentrations of IN-E9260 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

Considered as non-relevant according to EFSA Journal 2005; 45, 1-61.

10.4.3.1 STEP 3, Stage 1: screening for biological activity

10.4.3.2 STEP 3, Stage 2: screening for genotoxicity

10.4.3.3 STEP 3, Stage 3: screening for toxicity

10.4.4 STEP 4: Exposure assessment – threshold of concern approach

The potential exposure to IN-E9260 is > 0.75 µg/L but <10 µg/L. A further assessment in Step 5 is required.

10.4.5 STEP 5: Refined risk assessment

IN-E9260 has a PEC_{gw} between 0.75 µg/L and 10 µg/L but for which the threshold of concern approach in Step 4 is not acceptable. 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-E9260 are 0.12 % of ADI (infant), 0.08% of ADI (child), 0.03 % of ADI (adult).

The ADI for IN-E9260 is based on the parent ADI of 0.1 mg/kg bw/day.

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 PECgw (µg/L)	**Weight (kg)**	**Exposure (L/day)**	**TMDI (µg/kg bw/day)**	**ADI (µg/kg bw/day)**	**% ADI**
Bottle fed infant	0.817	5	0.75	0.12	100	0.12
Child		10	1	0.08	100	0.08
Adult		60	2	0.03	100	0.03

10.5 Relevance assessment of HMUD

Summary:

The relevance of the groundwater metabolite HMUD has already been assessed and the assessment agreed at EU level (see EFSA Scientific Report (2007) 120, 1-91), and the relevance assessment is applicable as well for the GAP and groundwater scenarios considered in this dRR (i.e., the conclusions reached at Step 4 and 5 of the relevance assessment made at the EU-level are valid also with regard to the PEC_{gw} calculated for the GAP and groundwater scenarios considered in this dRR). HMUD 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 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 HMUD

	Assessment step	**Result of assessment**	
	STEP 1	Metabolite of no concern?	No
ication of ground water	STEP 2	Max PEC_{gw}	0.990 µg/L <0.1 µg/L

			Based on	Hamburg PEARL scenario 3 years monitoring study
Hazard assessment	STEP 3	Stage 1	Biological activity comparable to the parent?	Not available
		Stage 2	Genotoxic properties of metabolite	Not genotoxic *in vitro*
		Stage 3	Toxic properties of metabolite;	Not toxicologically relevant.
			Classification of parent	None
			Classification of metabolite	Not available
Consumer health risk assessment	STEP 4		Estimated consumer exposure via drinking water and other sources; threshold of concern approach	No acceptable (> 0.75 µg/L)
	STEP 5		Refined risk assessment	Acceptable
			Predicted exposure (% of ADI)	0.008 %
			ADI based on	Parent (2 mg/kg bw/d)

10.5.1 STEP 1: Exclusion of degradation products of no concern

HMUD 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 HMUD were performed (see Part B, Section 8, chapter 8.8). The uses for which concentrations of HMUD 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

Not available.

10.5.3.2 STEP 3, Stage 2: screening for genotoxicity

HMUD 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. HMUD was non-genotoxic as shown by a negative Ames test, negative gene mutation test with mammalian cells, negative chromosome aberration test.

10.5.3.3 STEP 3, Stage 3: screening for toxicity

According to the EFSA Scientific Report (2007) 120, 1-91, this metabolite was not toxicologically relevant.

10.5.4 STEP 4: Exposure assessment – threshold of concern approach

The potential exposure to HMUD 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

HMUD has a PEC_{gw} between 0.75 µg/L and 10 µg/L but for which the threshold of concern approach in Step 4 is not acceptable. 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 HMUD are 0.008 % of ADI (infant), 0.005 % of ADI (child), 0.002 % of ADI (adult).

The ADI for HMUD is based on the parent ADI of 2 mg/kg bw/day.

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 PECgw (µg/L)	**Weight (kg)**	**Exposure (L/day)**	**TMDI (µg/kg bw/day)**	**ADI (µg/kg bw/day)**	**% ADI**
Bottle fed infant	0.990	5	0.75	0.15	2000	0.008
Child		10	1	0.10	2000	0.005
Adult		60	2	0.03	2000	0.002

10.6 Relevance assessment of AUSN

Summary:

The relevance of the groundwater metabolite AUSN has already been assessed and the assessment agreed at EU level (see EFSA Scientific Report (2007) 120, 1-91), and the relevance assessment is applicable as well for the GAP and groundwater scenarios considered in this dRR (i.e., the conclusions reached at Step 4 and 5 of the relevance assessment made at the EU-level are valid also with regard to the PEC_{gw} calculated for the GAP and groundwater scenarios considered in this dRR). AUSN 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 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 AUSN

	Assessment step		**Result of assessment**	
	STEP 1		Metabolite of no concern?	No
Quantification of groundwater contamination	STEP 2		Max PEC_{gw}	1.526 µg/L 0.657 µg/L
			Based on	Hamburg PEARL scenario 3 years monitoring study
Hazard assess	STEP 3	Stage 1	Biological activity comparable to the parent?	Not available

		Stage 2	Genotoxic properties of metabolite	Not genotoxic *in vitro*
		Stage 3	Toxic properties of metabolite;	Not toxicologically relevant.
			Classification of parent	None
			Classification of metabolite	Not available
Consumer health risk assessment	STEP 4		Estimated consumer exposure via drinking water and other sources; threshold of concern approach	No acceptable (> 0.75 µg/L)
	STEP 5		Refined risk assessment	Acceptable
			Predicted exposure (% of ADI)	0.012 %
			ADI based on	Parent (2 mg/kg bw/d)

10.6.1 STEP 1: Exclusion of degradation products of no concern

AUSN 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 AUSN were performed (see Part B, Section 8, chapter 8.8). The uses for which concentrations of AUSN 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

Not available.

10.6.3.2 STEP 3, Stage 2: screening for genotoxicity

AUSN 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. AUSN was non-genotoxic as shown by a negative Ames test, negative gene mutation test with mammalian cells, negative chromosome aberration test.

10.6.3.3 STEP 3, Stage 3: screening for toxicity

According to the EFSA Scientific Report (2007) 120, 1-91, this metabolite was not toxicologically relevant, the oral LD_{50} in rat is higher than 2000 mg/kg bw.

10.6.4 STEP 4: Exposure assessment – threshold of concern approach

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

10.6.5 STEP 5: Refined risk assessment

AUSN has a PEC_{gw} between 0.75 µg/L and 10 µg/L but for which the threshold of concern approach in Step 4 is not acceptable. 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 AUSN are 0.012 % of ADI (infant), 0.008 % of ADI (child), 0.003 % of ADI (adult).

The ADI for AUSN is based on the parent ADI of 2 mg/kg bw/day.

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 PECgw (µg/L)	**Weight (kg)**	**Exposure (L/day)**	**TMDI (µg/kg bw/day)**	**ADI (µg/kg bw/day)**	**% ADI**
Bottle fed infant	1.526	5	0.75	0.23	2000	0.012
Child		10	1	0.15	2000	0.008
Adult		60	2	0.05	2000	0.003

10.7 Relevance assessment of UCSN

Summary:

The relevance of the groundwater metabolite UCSN has already been assessed and the assessment agreed at EU level (see EFSA Scientific Report (2007) 120, 1-91), and the relevance assessment is applicable as well for the GAP and groundwater scenarios considered in this dRR (i.e., the conclusions reached at Step 4 and 5 of the relevance assessment made at the EU-level are valid also with regard to the PEC_{gw} calculated for the GAP and groundwater scenarios considered in this dRR). UCSN 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 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 UCSN

	Assessment step		**Result of assessment**	
	STEP 1		Metabolite of no concern?	No
Quantification of groundwater contamination	STEP 2		Max PEC_{gw}	1.298 µg/L 0.111 µg/L
			Based on	Thiva PEARL scenario 3 years monitoring study
Hazard assess	STEP 3	Stage 1	Biological activity comparable to the parent?	Not available

		Stage 2	Genotoxic properties of metabolite	Not genotoxic *in vitro*
		Stage 3	Toxic properties of metabolite;	Not toxicologically relevant.
			Classification of parent	None
			Classification of metabolite	Not available
Consumer health risk assessment	STEP 4		Estimated consumer exposure via drinking water and other sources; threshold of concern approach	No acceptable (> 0.75 µg/L)
	STEP 5		Refined risk assessment	Acceptable
			Predicted exposure (% of ADI)	0.010 %
			ADI based on	Parent (2 mg/kg bw/d)

10.7.1 STEP 1: Exclusion of degradation products of no concern

UCSN 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 UCSN were performed (see Part B, Section 8, chapter 8.8). The uses for which concentrations of UCSN 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

Not available.

10.7.3.2 STEP 3, Stage 2: screening for genotoxicity

UCSN 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. UCSN was non-genotoxic as shown by a negative Ames test, negative gene mutation test with mammalian cells, negative chromosome aberration test.

10.7.3.3 STEP 3, Stage 3: screening for toxicity

According to the EFSA Scientific Report (2007) 120, 1-91, this metabolite was not toxicologically relevant, the oral LD_{50} in rat is higher than 2000 mg/kg bw.

10.7.4 STEP 4: Exposure assessment – threshold of concern approach

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

10.7.5 STEP 5: Refined risk assessment

UCSN has a PEC_{gw} between 0.75 µg/L and 10 µg/L but for which the threshold of concern approach in Step 4 is not acceptable. 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 UCSN are 0.010 % of ADI (infant), 0.007 % of ADI (child), 0.002 % of ADI (adult).

The ADI for UCSN is based on the parent ADI of 2 mg/kg bw/day.

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 PECgw (µg/L)	**Weight (kg)**	**Exposure (L/day)**	**TMDI (µg/kg bw/day)**	**ADI (µg/kg bw/day)**	**% ADI**
Bottle fed infant	1.298	5	0.75	0.19	2000	0.010
Child		10	1	0.13	2000	0.007
Adult		60	2	0.04	2000	0.002

10.8 Relevance assessment of ASDM

Summary:

The relevance of the groundwater metabolite ASDM has already been assessed and the assessment agreed at EU level (see EFSA Scientific Report (20007) 120, 1-91), and the relevance assessment is applicable as well for the GAP and groundwater scenarios considered in this dRR (i.e., the conclusions reached at Step 4 and 5 of the relevance assessment made at the EU-level are valid also with regard to the PEC_{gw} calculated for the GAP and groundwater scenarios considered in this dRR). ASDM 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 given in Table 10.2-1 and the corresponding studies are listed in the corresponding sections.

Table 10.8-1: Summary of the relevance assessment for ASDM

	Assessment step		**Result of assessment**	
	STEP 1		Metabolite of no concern?	No
Quantification of groundwater contamination	STEP 2		Max PEC_{gw}	0.986 µg/L 0.477 µg/L
			Based on	Hamburg PEARL scenario 3 years monitoring study
Hazard assess	STEP 3	Stage 1	Biological activity comparable to the parent?	Not available

		Stage 2	Genotoxic properties of metabolite	Not genotoxic *in vitro*
		Stage 3	Toxic properties of metabolite;	Not toxicologically relevant.
			Classification of parent	None
			Classification of metabolite	Not available
Consumer health risk assessment	STEP 4		Estimated consumer exposure via drinking water and other sources; threshold of concern approach	No acceptable (> 0.75 µg/L)
	STEP 5		Refined risk assessment	Acceptable
			Predicted exposure (% of ADI)	0.008 %
			ADI based on	Parent (2 mg/kg bw/d)

10.8.1 STEP 1: Exclusion of degradation products of no concern

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

10.8.2 STEP 2: Quantification of potential groundwater contamination

PEC_{gw} calculations after leaching from soil for ASDM were performed (see Part B, Section 8, chapter 8.8). The uses for which concentrations of ASDM 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.

10.8.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.8.3.1 STEP 3, Stage 1: screening for biological activity

Not available.

10.8.3.2 STEP 3, Stage 2: screening for genotoxicity

ASDM 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. ASDM was non-genotoxic as shown by a negative Ames test, negative gene mutation test with mammalian cells, negative chromosome aberration test.

10.8.3.3 STEP 3, Stage 3: screening for toxicity

According to the EFSA Scientific Report (2007) 120, 1-91, this metabolite was not toxicologically relevant, the oral LD_{50} in rat is higher than 2000 mg/kg bw, the oral LD_{50} in mouse is higher than 5000 mg/kg bw, the dermal LD_{50} in rat is higher than 2000 mg/kg bw/day. This metabolite is non-irritating to skin, slight eye irritant and skin sensitizer.

No treatment-related adverse effects were seen in a 28- day and a 90-day study in the rat at dose levels of up to 1000 mg/kg bw/day. No genotoxic effects were observed in in vitro bacterial- and mammalian cell mutation and mammalian clastogenicity tests and in an in vivo

mouse micronucleus test. No effects on reproduction were seen in a one-generation study in the rat at dose levels up to 1000 mg/kg bw/day. No evidence of maternal toxicity was seen in a rat developmental study at dose levels of up to 1000 mg/kg bw/day while at the top dose in pups an increased incidence of dilated ureters were observed.

10.8.4 STEP 4: Exposure assessment – threshold of concern approach

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

10.8.5 STEP 5: Refined risk assessment

ASDM has a PEC_{gw} between 0.75 µg/L and 10 µg/L but for which the threshold of concern approach in Step 4 is not acceptable. 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 ASDM are 0.008 % of ADI (infant), 0.005 % of ADI (child), 0.002 % of ADI (adult).

The ADI for ASDM is based on the parent ADI of 2 mg/kg bw/day.

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 PECgw (µg/L)	Weight (kg)	Exposure (L/day)	TMDI (µg/kg bw/day)	ADI (µg/kg bw/day)	% ADI
Bottle fed infant	0.986	5	0.75	0.15	2000	0.008
Child		10	1	0.10	2000	0.005
Adult		60	2	0.03	2000	0.002

10.9 Relevance assessment of MU-466

Summary:

The relevance of the groundwater metabolite MU-466 has already been assessed and the assessment agreed at EU level (see EFSA Scientific Report (2007) 120, 1-91), and the relevance assessment is applicable as well for the GAP and groundwater scenarios considered in this dRR (i.e., the conclusions reached at Step 4 and 5 of the relevance assessment made at the EU-level are valid also with regard to the PEC_{gw} calculated for the GAP and groundwater scenarios considered in this dRR). MU-466 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 given in Table 10.2-1 and the corresponding studies are listed in the corresponding sections.

Table 10.9-1: Summary of the relevance assessment for MU-466

	Assessment step	Result of assessment	
	STEP 1	Metabolite of no concern?	No
tication of ground water	STEP 2	Max PEC_{gw}	0.130 µg/L

			Based on	Thiva PEARL scenario
Hazard assessment	STEP 3	Stage 1	Biological activity comparable to the parent?	Not available
		Stage 2	Genotoxic properties of metabolite	Not genotoxic *in vitro*
		Stage 3	Toxic properties of metabolite;	Not toxicologically relevant.
			Classification of parent	None
			Classification of metabolite	Not available
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	Not required
			Predicted exposure (% of ADI)	Not required
			ADI based on	Not required

10.9.1 STEP 1: Exclusion of degradation products of no concern

MU-466 does not meet the criteria for products of no concern as defined in step 1 of the guidance and therefore needs further assessment.

10.9.2 STEP 2: Quantification of potential groundwater contamination

PEC_{gw} calculations after leaching from soil for MU-466 were performed (see Part B, Section 8, chapter 8.8). The uses for which concentrations of MU-466 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.

10.9.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.9.3.1 STEP 3, Stage 1: screening for biological activity

Not available.

10.9.3.2 STEP 3, Stage 2: screening for genotoxicity

According to the EFSA Scientific Report (2007) 120, 1-91, this metabolite was not genotoxic *in vitro*.

10.9.3.3 STEP 3, Stage 3: screening for toxicity

According to the EFSA Scientific Report (2007) 120, 1-91, this metabolite was not toxicologically relevant.

10.9.4 STEP 4: Exposure assessment – threshold of concern approach

MU-466 was not considered relevant in the hazard assessment of Step 3

The PEC_{gw} for MU-466 was < 0.75 µg/L. There is no consumer exposure via other routes. MU-466 is not considered to exceed the toxicological threshold of concern as defined in EC guidance document SANCO/221/2000 – rev. 10.

10.9.5 STEP 5: Refined risk assessment

Not relevant.

nicosulfuron

According to the SANCO report for nicosulfuron (SANCO/3780/07-rev.1 22 January 2008) and EFSA Scientific Report (2007) 120, 1-91, entitled: Conclusion on the peer review of nicosulfuron as well as DAR nicosulfuron, June 2006, RMS: UK)

ASDM:

was found to be of low acute rat oral LD50 >2000 mg/kg bw mouse oral LD50 >5000 mg/kg bw rat dermal LD50 >2000 mg/kg bw non-irritating to skin, slight eye irritant, skin sensitiser, and low sub-acute and sub-chronic toxicity and was not found to be a reproductive or developmental toxin. No treatment-related adverse effects were seen in a 28- day and a 90-day study in the rat at dose levels of up to 1000 mg/kg bw/day. No genotoxic effects were observed in in vitro bacterial- and mammalian cell mutation and mammalian clastogenicity tests and in an in vivo mouse micronucleus test. No effects on reproduction were seen in a one-generation study in the rat at dose levels up to 1000 mg/kg bw/day. No evidence of maternal toxicity was seen in a rat developmental study at dose levels of up to 1000 mg/kg bw/day while at the top dose in pups an increased incidence of dilated ureters were observed.

ADMP:

was found to be of moderate acute oral toxicity in the rat oral LD50 737-1073 mg/kg bw and was not mutagenic in the Ames test.

AUSN:

was found to be of low acute oral toxicity in the rat LD50 >2000 mg/kg bw and was not mutagenic in an Ames test

UCSN:

was found to be of low acute oral toxicity in the rat LD50 >2000 mg/kg bw and was not mutagenic in an Ames test

MU-466:

was found to be of low acute oral toxicity in the rat LD50 >2000 mg/kg bw and was not mutagenic in an Ames test

HMUD:

Not genotoxic in vitro

The all metabolites of nicosulfuron are not considered toxicologically relevant

rimsulfuron

According to the SANCO report for rimsulfuron (SANCO/10528/05-rev.2 final 27 January 2006) and EFSA Scientific Report (2005) 45, 1-61, Conclusion on the peer review of rimsul-

furon, suplementary studies were conducted with two major matebolites: IN-70941 and IN-E9260.
IN-70941:
Approximate Lethal Dose, male rat, oral: ≥ 11000 mg/kg bw/d 10-day oral test, rats; NOEL < 2200 mg/kg bw/d (the only tested dose) Genotoxicity: In vitro gene mutation: (S. typh.): negative; In vitro gene mutation: (mammalian cells): negative In-vitro chromosome aberration: negative
IN-E9260:
LD50, rat, oral: ≥ 2000 mg/kg bw/d LD50, rat, dermal: ≥ 2000 mg/kg bw/d Skin and eye irritation: non irritant Skin sensitisation (M&K): not sensitising NOAEL 4-week rat, oral: < 50 mg/kg bw/d Genotoxicity: In vitro gene mutation (S. typh.): negative In vitro chromosome aberration: negative
The metabolites IN-E9260 and IN70941 are not considered toxicologically relevant

Appendix 1 Lists of data considered in support of the evaluation

List of 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
KCP 10.1	J.J. Izquierdo	2018	Title: Toxtree v2.6.13 evaluation on the human health hazard of the Rimsulfuron (CAS nº: 122931-48-0) and its metabolite IN-70942. Company Report No: JJI/01/2018 Source: Sharda Cropchen Ltd. non GLP Unpublished	N	Sharda Cropchem Ltd.

Appendix 2 Additional information