FINAL REGISTRATION REPORT

Part B

Section 10

Assessment of the relevance of metabolites in groundwater

Detailed summary of the risk assessment

Product code: SHA 4307 A

Product name: PRIMARY MX

Chemical active substances:

Rimsulfuron, 30 g/kg

Nicosulfuron 120 g/kg

Mesotrione 360 g/kg

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

Applicant: SHARDA Cropchem España S.L.

Submission date: February 2020

Update date: 08.2021

MS Finalisation date: 05.2022;12.2022;03.2023

Version history

When	What
August 2021	Applicant update
May 2022	zRMS first assessment
December 2022	Final zRMS assessment
March 2023	Applicant update after 2nd commenting period

Table of Contents

10 Relevance of metabolites in groundwater

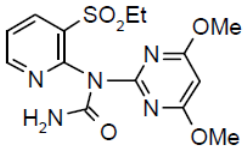
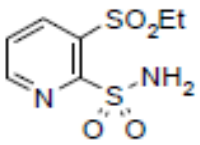
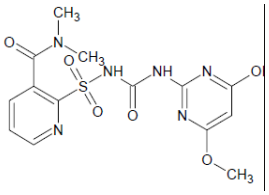
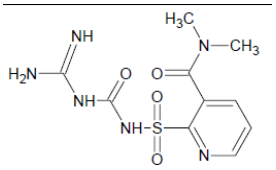
10.1 General information

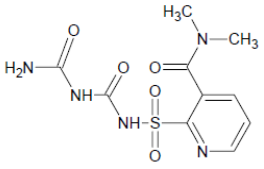
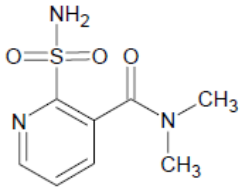
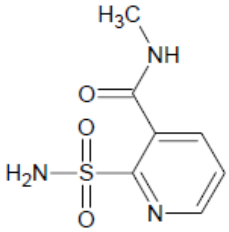
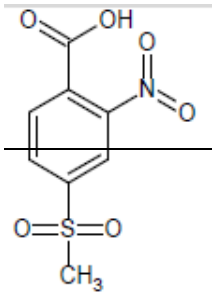
The metabolites IN-70942, IN-J0290, ADMP, ~~and~~ AMBA and MNBA are predicted to occur in groundwater at concentrations below 0.1 µg/L (see dRR Part B, Chapter 8.8). Assessment of the relevance of these metabolites according to the stepwise procedure of the EC guidance document SANCO/221/2000 – rev.10 is therefore not required and not include in table 10.1-1.

The metabolites IN-70941, IN-E9260, HMUD, AUSN, UCSN, ASDM~~,~~ and MU-466 ~~and MNBA~~ 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:	0.448~~0.600~~ µg/L Hamburg PEARL scenario
	IN-E9260		Max PEC_{gw} Based on:	0.408~~0.539~~ µg/L Thiva PEARL scenario
Nicosulfuron	HMUD		Max PEC_{gw} Based on: Max PEC_{gw} Based on:	0.990~~1.319~~ µg/L Hamburg PEARL scenario <0.1 µg/L 3 years monitoring study
	AUSN		Max PEC_{gw} Based on: Max PEC_{gw} Based on:	1.526~~2.015~~ µg/L Hamburg PEARL scenario 0.657 µg/L 3 years monitoring study

Name of active substance	Metabolite name and code	Structural/molecular formula	Trigger for relevance assessment	
	UCSN		Max PEC_{gw} Based on: Max PEC_{gw} Based on:	1.2981.717 µg/L Thiva PEARL scenario 0.657 µg/L 3 years monitoring study
	ASDM		Max PEC_{gw} Based on: Max PEC_{gw} Based on:	0.9861.311 µg/L Hamburg PEARL scenario 0.477 µg/L 3 years monitoring study
	MU-466		Max PEC_{gw} Based on:	0.1300.173 µg/L Thiva PEARL scenario
~~Mesotrione~~	~~MNBA~~		~~Max PEC_{gw}~~ ~~Based on:~~	~~0.1020.134 µg/L~~ ~~Hamburg PELMO scenario, specific pH endpoints~~

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 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-70941 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 10.2-1: Summary of the relevance assessment for IN-70941

	Assessment step		**Result of assessment**	
	STEP 1		Metabolite of no concern?	No
Quantification of groundwater contamination	STEP 2		Max PEC_{gw}	0.4480~~0.600~~ 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;	Not toxicologically relevant.
			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	Acceptable (< 0.75 µg/L)
	STEP 5		Refined risk assessment	-
			Predicted exposure (% of ADI)	-
			ADI based on	-

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

IN-70941 was screened for genotoxic activity by *in vitro* genotoxicity studies: in vitro gene mutation, gene mutation test with mammalian cells and a chromosome aberration test. IN-70941was non-genotoxic as shown by above tests.
Summary of all studies is presented below:

Table 10.2.3.2-1: Summary of the results of genotoxicity studies for IN-70941

Type of test, species (Guideline)	Result	Reference*
In vitro gene mutation (US EPA FIFRA Subdivision F, 84-2)	non-genotoxic	Reynolds, V.L. (1989) / EU reviewed
In vitro mammalian cell mutagenicity (CHO-K cells) – (OECD 476)	non-genotoxic	*DAR Volume 3, Annex B-B6, 2003 (San and Clark, 2003)
In vitro chromosomal aberration (Human lymphocytes) – (OECD 473)	non-genotoxic	*DAR Volume 3, Annex B-B6, 2003 (Gudi and Rao, 2004)

10.2.3.3 STEP 3, Stage 3: screening for toxicity

According to the EFSA Conclusions (EFSA Journal 2005; 45, 1-61) .this metabolite was not toxicologically relevant. Summary of all studies is presented below

Table 10.2.3.3-1: Summary of the results of toxicity studies for IN-70941

Type of test, species (Guideline)	Result	Reference*
IN-70941, Acute oral – male rate (not a guideline study)	ALD: ≥ 11000 mg/kg bw	*DAR Volume 3, Annex B-B6, 2003 (xxx, 1989)
IN-70941, Oral subacute (ten days) – male rat (not a guideline study)	NOAEL: <2200 mg/kg bw/d	*DAR Volume 3, Annex B-B6, 2003 (xxx, 1989)
Rimsulfuron, Acute oral – rat (U.S. EPA FIFRA, Subdivision F, 81-1; EEC Method B.1, Directive 92/69/EEC)	LD_{50}: ≥ 5000 mg/kg bw	*DAR Volume 3, Annex B-B6, 2003 xxx, 1988a
Rimsulfuron, Oral subacute (2 week; 10 doses, weekends excluded; gavage) – male rat (not a guideline study)	NOAEL: 2200 mg/kg bw/d	*DAR Volume 3, Annex B-B6, 2003 xxx, 1988c. Study is considered as supplementary.

* indicates that a study was reviewed at EU level

ALD Approximate Lethal Dose

10.2.4 STEP 4: Exposure assessment – threshold of concern approach

The potential exposure to IN-70941 is < 0.75 µg/L. Therefore, the assessment in Step 5 is not required.

10.2.5 STEP 5: Refined risk assessment

Not required.

10.3 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 10.3-1: 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}	0.4080~~0.539~~ 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	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	-
			Predicted exposure (% of ADI)	-
			ADI based on	-

10.3.1 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.

10.3.2 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.

10.3.3 STEP 3: Hazard assessment – identification of relevant metabolites

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

10.3.3.1 STEP 3, Stage 1: screening for biological activity

10.3.3.2 STEP 3, Stage 2: screening for genotoxicity

IN-E9260 was screened for genotoxic activity by *in vitro* genotoxicity studies: mammalian cytogenitcity test and gene mutation study, and also by *in vivo* genotoxicity study (in vivo comet assay in rats). IN-E9260 was non-genotoxic as shown by above tests.
Summary of all available studies is presented below:

Table 10.3.3.2-1: Summary of the results of genotoxicity studies for IN-E9260

Type of test, species (Guideline)	Result	Reference*
In vitro mammalian cytogenicity test (OECD 473)	non-genotoxic	Forichon, A. (1992) / EU reviewed
In vitro gene mutation (EEC Method B.14, Directive 92/69/EEC)	non-genotoxic	Reynolds, V. L. (1989) / EU reviewed
In vivo comet assay in rats (Rat, liver and duodenum cells) – (OECD 489)	non-genotoxic	*CA 5.8.1.10, (xxx, C., 2016) Report No. 8346539**

10.3.3.3 STEP 3, Stage 3: screening for toxicity

According to the EFSA Conclusions (EFSA Journal 2005; 45, 1-61) .this metabolite was not toxicologically relevant. Summary of all studies is presented below

Table 10.3.3.3-1: Summary of the results of toxicity studies for IN-E9260

Type of test, species (Guideline)	Result	Reference*
IN-9260, Acute oral (OECD 401)	LD_{50}: ≥ 2000 mg/kg bw	*DAR Volume 3, Annex B-B6, 2003 (xxx, 1991)
IN-9260, Oral subacute (4 weeks) (OECD 407)	≥50 mg/kg bw/d: liver weight ↑, 150 mg/kg bw/d: food consumption ↓, body weight gain ↓, food efficiency ↓, polyuria, forestomach lesions, liver weight ↑, kidney weight ↑, NOAEL: < 50 mg/kg bw/d	*DAR Volume 3, Annex B-B6, 2003 (xxx, 1992)
IN-9260, Acute dermal (OECD 402)	LD_{50} > 2000 mg/kg	*DAR Volume 3, Annex B-B6, 2003 (xxx, 1991a)
IN-9260, Skin irritation (OECD 404)	Not irritating	*DAR Volume 3, Annex B-B6, 2003 (xxx, 1992b)

Type of test, species (Guideline)	Result	Reference*
IN-9260, Eye irritation (OECD 405)	Mild eye irritant	*DAR Volume 3, Annex B-B6, 2003 (xxx, 1992a)
IN-9260, Skin sensitisation (OECD 406)	Not a skin senstitiser	*DAR Volume 3, Annex B-B6, 2003 (xxx, 1992c)
Rimsulfuron, Acute oral – rat (U.S. EPA FIFRA, Subdivision F, 81-1; EEC Method B.1, Directive 92/69/EEC)	LD_{50}: ≥ 5000 mg/kg bw	*DAR Volume 3, Annex B-B6, 2003 xxx, 1988a
Rimsulfuron, Oral subacute (2 week; 10 doses, weekends excluded; gavage) – male rat (not a guideline study)	NOAEL: 2200 mg/kg bw/d	*DAR Volume 3, Annex B-B6, 2003 xxx, 1988c. Study is considered as supplementary.
Oral 90-day study – rat (U.S. EPA FIFRA Subdivision F, 83-1)	≥ 1500 ppm: body weight ↓, phosphorus (females) ↓, ≥ 7500: body weight gain ↓, effects on parameters of haematology, clinical chemistry, liver morphology 20000 ppm: urinalysis NOAEL: 3.35 mg/kg bw/d	*DAR Volume 3, Annex B-B6, 2003 xxx, 1989a xxx, 1991a (supplement 1)

* indicates that a study was reviewed at EU level

10.3.4 STEP 4: Exposure assessment – threshold of concern approach

The potential exposure to IN-E9260 is < 0.75 µg/L. Therefore, the assessment in Step 5 is not required.

10.3.5 STEP 5: Refined risk assessment

Not required.

10.4 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 10.4-1: Summary of the relevance assessment for HMUD

	Assessment step		**Result of assessment**	
	STEP 1		Metabolite of no concern?	No
Quantification of groundwater contamination	STEP 2		Max PEC_{gw}	0.990~~1.319~~ 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~~0.01~~ %
			ADI based on	Parent (2 mg/kg bw/d) parent compound nicosulfuron according to EFSA Scientific

10.4.1 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.

10.4.2 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.

10.4.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.4.3.1 STEP 3, Stage 1: screening for biological activity

Not available.

10.4.3.2 STEP 3, Stage 2: screening for genotoxicity

According to the EFSA Scientific Report (2007) 120, 1-91, 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.

10.4.3.3 STEP 3, Stage 3: screening for toxicity

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

10.4.4 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.

10.4.5 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~~0.010~~ % of ADI (infant), 0.005~~0.007~~ % of ADI (child), 0.002 % of ADI (adult).

The ADI for HMUD is based on the parent ADI of 2 mg/kg bw/day. (parent compound nicosulfuron, according to EFSA Scientific Report (2007) 120, 1-91).

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

	~~**Max PECgw (µg/L)**~~	~~**Weight (kg)**~~	~~**Exposure (L/day)**~~	~~**TMDI (µg/kg bw/day)**~~	~~**ADI (µg/kg bw/day)**~~	~~**% ADI**~~
~~**Bottle fed infant**~~	~~1.319~~	~~5~~	~~0.75~~	~~0.20~~	~~2000~~	~~0.010~~

~~**Child**~~		~~10~~	~~1~~	~~0.13~~	~~2000~~	~~0.007~~
~~**Adult**~~		~~60~~	~~2~~	~~0.04~~	~~2000~~	~~0.002~~

10.5 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 10.5-1: 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}	1.5262~~.015~~ µg/L 0.657 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)	0.012~~0.015~~ %
			ADI based on	Parent (2 mg/kg bw/d) parent compound nicosulfuron, according to EFSA Scientific Report (2007) 120, 1-91

10.5.1 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.

10.5.2 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.

10.5.3 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

According to the EFSA Scientific Report (2007) 120, 1-91AUSN 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.

10.5.3.3 STEP 3, Stage 3: screening for toxicity

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

10.5.4 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.

10.5.5 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~~0.015~~ % of ADI (infant), 0.008~~0.010~~ % of ADI (child), 0.003~~0.004~~ % of ADI (adult).

The ADI for AUSN is based on the parent ADI of 2 mg/kg bw/day. day (parent compound nicosulfuron, according to EFSA Scientific Report (2007) 120, 1-91).

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	1.562	5	0.75	0.23	2000	0.012
Child		10	1	0.16	2000	0.008
Adult		60	2	0.05	2000	0.003

	~~**Max PECgw (µg/L)**~~	~~**Weight (kg)**~~	~~**Exposure (L/day)**~~	~~**TMDI (µg/kg bw/day)**~~	~~**ADI (µg/kg bw/day)**~~	~~**% ADI**~~
~~**Bottle fed infant**~~	~~2.015~~	~~5~~	~~0.75~~	~~0.30~~	~~2000~~	~~0.015~~
~~**Child**~~		~~10~~	~~1~~	~~0.20~~	~~2000~~	~~0.010~~

~~**Adult**~~		~~60~~	~~2~~	~~0.07~~	~~2000~~	~~0.004~~

10.6 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 10.6-1: 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}	1.2981.717 µg/L 0.111 µg/L
			Based on	Thiva 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)	0.013 %
			ADI based on	Parent (2 mg/kg bw/d) parent compound nicosulfuron, according to EFSA Scientific Report (2007) 120, 1-91

10.6.1 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.

10.6.2 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.

10.6.3 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

U According to the EFSA Scientific Report (2007) 120, 1CSN 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.

10.6.3.3 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 UCSN 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

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~~0.013~~ % of ADI (infant), 0.007~~0.009~~ % of ADI (child), 0.002~~0.003~~ % of ADI (adult).

The ADI for UCSN is based on the parent ADI of 2 mg/kg bw/day. day (parent compound nicosulfuron, according to EFSA Scientific Report (2007) 120, 1-91).

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

	~~**Max PECgw (µg/L)**~~	~~**Weight (kg)**~~	~~**Exposure (L/day)**~~	~~**TMDI (µg/kg bw/day)**~~	~~**ADI (µg/kg bw/day)**~~	~~**% ADI**~~
~~**Bottle fed infant**~~	~~1.717~~	~~5~~	~~0.75~~	~~0.26~~	~~2000~~	~~0.013~~
~~**Child**~~		~~10~~	~~1~~	~~0.17~~	~~2000~~	~~0.009~~

~~**Adult**~~		~~60~~	~~2~~	~~0.06~~	~~2000~~	~~0.003~~

10.7 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 (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). 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 10.7-1: 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}	0.9861.311 µg/L 0.477 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)	0.0080.010 %
			ADI based on	Parent (2 mg/kg bw/d) parent compound nicosulfuron, according to EFSA Scientific Report (2007) 120, 1-91

10.7.1 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.

10.7.2 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.

10.7.3 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

ASDM was screened for genotoxic activity by the following data package of *in vitro* genotoxicity studies: Ames test, Mouse micronucleus, 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.
Summary of all available studies is presented below:

Table 10.7.3.2-1: Summary of the results of genotoxicity studies for ASDM

Type of test, species (Guideline)	Result	Reference*
Ames test (OECD 471)	non-genotoxic	xxx (1993) / EU reviewed
Mouse micronucleus (OECD 474)	non-genotoxic	xxxx (1995) / EU reviewed
In vitro clastogenicity (OECD 473)	non-genotoxic	Dance, C.A. (1993) / EU reviewed
Cell mutation assay (OECD 476)	non-genotoxic	xxx (2003) / EU reviewed

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, 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.

Summary of all available studies is presented below:

Table 10.7.3.3-1: Summary of the results of toxicity studies for ASDM

Type of test, species (Guideline)	Result	Reference*
Acute oral toxicity rat	LD_{50}: > 2000 mg/kg bw	xxx (1993a) / EU reviewed
Acute oral toxicity mouse	LD_{50}: > 5000 mg/kg bw	xxx (1992a) / EU reviewed
Acute dermal toxicity rat	LD_{50}: > 2000 mg/kg bw	xxx (1993b) / EU reviewed
28 day oral toxicity study in the rat (gavage)	NOAEL: > 1000 mg/kg bw/d	xxx (1993) / EU reviewed
90 day oral toxicity study in the rat	NOAEL: > 1000 mg/kg bw/d	xxx (1998) / EU reviewed

Type of test, species (Guideline)	Result	Reference*
One generation reproduction study	NOAEL: > 1000mg/kg bw/d	xxx. (1998a) / EU reviewed
Developmental toxicity study in the rat	NOAEL maternal: > 1000 mg/kg bw/d NOAEL developmental: = 200 mg/kg bw/d	xxx (1998b) / EU reviewed

* indicates that a study was reviewed at EU level

10.7.4 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.

10.7.5 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~~0.010~~ % of ADI (infant), 0.005~~0.007~~ % of ADI (child), 0.002 % of ADI (adult).

The ADI for ASDM is based on the parent ADI of 2 mg/kg bw/day. (parent compound nicosulfuron, according to EFSA Scientific Report (2007) 120, 1-91).

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

	~~Max PECgw (µg/L)~~	~~Weight (kg)~~	~~Exposure (L/day)~~	~~TMDI (µg/kg bw/day)~~	~~ADI (µg/kg bw/day)~~	~~% ADI~~
~~**Bottle fed infant**~~	~~1.311~~	~~5~~	~~0.75~~	~~0.20~~	~~2000~~	~~0.010~~
~~**Child**~~		~~10~~	~~1~~	~~0.13~~	~~2000~~	~~0.007~~
~~**Adult**~~		~~60~~	~~2~~	~~0.04~~	~~2000~~	~~0.002~~

10.8 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 10.8-1: Summary of the relevance assessment for MU-466

	Assessment step		**Result of assessment**	
	STEP 1		Metabolite of no concern?	No
Quantification of groundwater contamination	STEP 2		Max PEC_{gw}	0.1300~~0.173~~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

10.8.1 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.

10.8.2 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.

10.8.3 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

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

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.

10.8.4 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.

10.8.5 STEP 5: Refined risk assessment

Not relevant.

~~10.9 Relevance assessment of MNBA~~

~~**Summary:**~~

~~The relevance of the groundwater metabolite MNBA has already been assessed and the assessment agreed at EU level (see EFSA Journal 2016;14(3):4419), 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). MNBA 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 MNBA

	Assessment step		Result of assessment	
	STEP 1		Metabolite of no concern?	No
Quantification of groundwater contamination	STEP 2		Max PEC_{gw}	0.1020.134 µg/L <0.1 µg/L
			Based on	Hamburg PELMO scenario, specific pH endpoints worst case endpoints
Hazard assessment	STEP 3	Stage 1	Biological activity comparable to the parent?	No
		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 MNBAwere performed (see Part B, Section 8, chapter 8.8). The uses for which concentrations of MNBA 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~~

~~MNBA was not considered relevant in the hazard assessment of Step 3~~

~~The PEC_{gw} for MNBA was < 0.75 µg/L. There is no consumer exposure via other routes. MNBA 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.~~

Expert comment:
Mesotrione
According to the criteria regarding ecotoxicological effects laid out in Guidance Document on Relevant Metabolites (SANCO/221/200-Rev.2 of October 1999) MNBA and AMBA are not relevant metabolites (DAR, UK Addendum, Revision 2, September 2001).
In brief, MNBA and AMBA are classified as non-relevant metabolites in view of their lack in pesticidal activity, genotoxicity, and other toxicological properties. Consequently, the metabolites MNBA and AMBA are considered to be non-relevant metabolites in groundwater.
A study in male rats showed that MNBA was metabolised in the gut to AMBA
The metabolites MNBA and AMBA were considered to be not genotoxic. (Ames test, in vivo UDS test, chromosomal aberration, Micronucleus test) and have low acute and subchronic toxicity however this metabolite MNBA was identified as a potential skin sensitiser
Based on the classification of the parent active substance mesotrione and based on the available toxicological data on MNBA and AMBA, both metabolites MNBA and AMBA are considered to be non-relevant metabolites in ground water.

Nicosulfurone
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 nicosulfu-

ron as well as DAR nicosulfuron, June 2006, RMS: UK), ASDM was found to be of low acute oral toxicity in the rat ad mouse, was not a skin or eye irritant but was found to be skin sesitiser in a maximisation study. No clearly treatment-related effects were seen in 28-d and 90d studies in rat at dose levels of up to 1000mg/kg bw/d. Minimal effects on red blood cell parameters in males in the 90d study are not considered to be adverse. No evidence of genotoxicity was seen in an appriopriate battery test in vitro and in vivo. No evidence of an effect on reproduction was seen in one-generation study in rat at dose levels of up to 1000mg/kg bw/d. No evidence of maternal toxicity was seen in rat developmental study at dose levels of up to 1000mg/kg bw/d, some evidence of delayed foeatal developmental was seen at this does levels.
ADMP was found to be of moderate acute oral toxicity in the rat and was not mutagenic in the Ames test. AUSN, UCSN, and MU-466 were found to be of low acute oral toxicity in the rat; no evidence of genoxoticity was seen in vitro. Lysimeter product was found to be of low acute oral toxicity in the rat and was not mutagenic in an Ames test.
Nicosulfuron has been found to be of low toxicity and was not classified as toxic, and has no classification for the reproductive toxicity or carcinogenicity
AUSN and UCSN were found to be of low acute oral toxicity; ASDM was found to be of low acute sub-acute and sub-chronic toxicity and was not found to be a reproductive or developmental toxin.

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 rimsulfuron, suplementary studies were conducted with two major matebolites: IN-70941 and IN-E9260. Both were found in plants, soil, and sediments. The acute oral toxicity of IN-E9260 and IN-70941in rats was greater than 5000mg/kg. In a ten dose oral study in male rats a reversible hepatocellural hypertrophy was observed in the only dose group of 2200mg/kg bw/d. The NOAEL of a 4-week oral study in male and female rats with IN-E9260 was <50mg/kg bw/d. Increased liver weight was observed I male rats at 50mg/kg bw/d and reduced food consumption, body weight gain, food efficiency, increased incidences of polyuria and forestomach lesions and increased liver and kidney weights were observed at 150mg/kg bw/d. compared with the results of the subchronic (90d study with rimsulfuron the toxicity of the metabolite IN-E9260 in the short term study is not lower than the toxicity of the parent substance rimsulfuron. The effect on the liver is even stronger in the study with IN-E-9260.
No skin irritating was observed in a study with IN-E9260 after application of 0.5g to the shaved skin. The dermal LD50 was greater than 2000mg/kg bot both male and female rates. In a study on eye irritation very slights irititis, conjunctival redness and chemosis was observed in rabbit

Appendix 1 Lists of data considered in support of the evaluation

Tables considered not relevant can be deleted as appropriate.

MS to blacken authors of vertebrate studies in the version made available to third parties/public.

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
-	-	-	-	-	-

The following tables are to be completed by MS

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

Comments of zRMS:	Comment on statement; acceptable or not.

No additional information available.