FINAL REGISTRATION REPORT

Part B

Section 10

Assessment of the relevance of metabolites in groundwater

Detailed summary of the risk assessment

Product code: SAE053H/01

Product name(s): KAGURA/GENKI

Chemical active substances:

Mesotrione, 80 g/L
Nicosulfuron, 30 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

Document number - SAEDoc-00021 CEU

(authorization)

Applicant: Sumi Agro Europe Limited

Submission date: November 2019

Updated July 2021

MS Finalisation date: 18/02/2022

Version history

When	What
November 2019	dRR submitted by applicant
August 2020	Dossier sent for evaluation to Merit Mark (PL)
April 2021	The B10 is being revised because submission by the applicant of a revised B8 document indicates that an additional metabolite requires a consumer risk assessment and PECs should be amended for two previously considered metabolites.
July 2021	Since slightly different PEC groundwater values were presented in the B8 as modified in May 2021, the ADI consumption numbers have been re-calculated.
October 2021	zRMS finalised evaluation
January 2022	Final version prepared by zRMS after Commenting period
February 2022	Final version prepared by zRMS after Commenting period

Table of Contents

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

10 Relevance of metabolites in groundwater

zRMS Comments:

The submitted PECgw values for metabolites of both active substances are in accordance with PELMO, PEARL and MACRO modeling results.

Mesotrione. The maximum PEC_{GW} values for its metabolites are below the trigger value of 0.1 µg/L. No further action is required.

Nicosulfuron. For the metabolies AUSN, UCSN, ASDM, HMUD the PECgw values are above the trigger value of 0.1 µg/L if applied every third year:
The following PECgw values will be considered.

Metabolite	Max PECgw
HMUD	0.385 µg/L FOCUS model PEARL; Hamburg, every third year
AUSN	1.70 µg/L FOCUS model PEARL; Thiva, every third year
UCSN	1.10 µg/L FOCUS model PEARL; Thiva, every third year
ASDM	0.991 µg/L FOCUS model PEARL; Thiva, every third year

Toxicological relevance of the metabolites of nicosulfuron:
HMUD:

- According to the available toxicological data (EFSA Scientific Report (2007) 120, 1-91), the metabolite HMUD has no pesticidal and is a minor rat metabolite that has a structure very similar to nicosulfuron, i.e. to the parent compound activity.
- The results of *in vitro* genotoxicity studies are negative (bacterial mutagenicity assay and chromosomal aberrations test in mammalian cells).
- The maximum PECgw of HMUD (acc. to the application rate presented in the GAP table) amounts to 0.385 µg/Lµg/L.
- Since the predicted max. PECgw value is below the upper limit for metabolites (<0.75 µg/L), the consumer risk calculation for this metabolite is not required.

AUSN:

- According to the available toxicological data (EFSA Scientific Report (2007) 120, 1-91), the metabolite AUSN has no pesticidal activity.

- The metabolite has low acute toxicity in rats (LD_{50} >2000 mg/kg bw) and negative results of genotoxicity tests (bacterial mutagenicity test and an *in vitro* clastogenicity and an *in vitro* cell mutation)
- The maximum PECgw of AUSN (acc. to the application rate presented in the GAP table) amounts to 1.70 µg/L.
- Since the predicted max. PECgw value is above the upper limit for metabolites (≥0.75 µg/L), the consumer risk calculation for this metabolite is required. Acc. to EFSA Scientific Report (2007) 120, 1-91, the reference value of the parent substance might apply to the metabolites. The results of exposure presented by the Applicant are accepted.

UCSN:

- According to the available toxicological data (EFSA Scientific Report (2007) 120, 1-91), the metabolite UCSN has no pesticidal activity.
- The metabolite has low acute toxicity in rats (LD_{50} >2000 mg/kg bw) and negative results of genotoxicity tests (bacterial mutagenicity test and an *in vitro* clastogenicity and an *in vitro* mammalian cell mutation)
- The maximum PECgw of AUSN (acc. to the application rate presented in the GAP table) amounts to 1.10 µg/L.
- Since the predicted max. PECgw value is above the upper limit for metabolites (≥0.75 µg/L), the consumer risk calculation for this metabolite is required. Acc. to EFSA Scientific Report (2007) 120, 1-91, the reference value of the parent substance might apply to the metabolites. The results of exposure presented by the Applicant are accepted.

ASDM:

- According to the available toxicological data (EFSA Scientific Report (2007) 120, 1-91), the metabolite ASDM has no pesticidal activity.
- The metabolite has low oral acute toxicity in rat (LD_{50} >2000 mg/kg bw) and mouse (LD_{50} >5000 mg/kg bw), low dermal acute toxicity in rat (LD_{50} >2000 mg/kg bw). and negative results of genotoxicity tests (bacterial mutagenicity test and an *in vitro* clastogenicity, an *in vitro* mammalian cell mutation and anin vivo mouse micronucleus test).
- The ASDM was found to be a skin sensitiser (maximization test).
- The maximum PECgw of ASDM (acc. to the application rate presented in the GAP table) amounts to 0.991 µg/L.
- Since the predicted max. PECgw value is above the upper limit for metabolites (≥0.75 µg/L), the consumer risk calculation for this metabolite is required. Acc. to EFSA Scientific Report (2007) 120, 1-91, the reference value of the parent substance might apply to the metabolites. The results of exposure presented by the Applicant are accepted.

Conlusions:

Taking into account all the toxicological data, the grounwater metabolites of nicosulfuron are considered toxicologically non-relevant. The results of consumer risk calculations indicate that the use of SAE053H/01 (Kagura/Genki) according to the list of intended uses presented in GAP Table, causes **no risk for health for the adults, toddlers and infants.**

	It should be noted that EFSA recommends Member States to request an *in vitro* micronucleus test instead of an *in vitro* chromosome aberration test to properly cover aneugenicity in the case of assessment of groundwater metabolites (EFSA Supporting publication 2020:EN-1837). This data will need to be assessed in the EU approval procedure at the latest. Otherwise a data gap will be set in the EFSA conclusion.

Please note: The intended maximal application rate to be registered is 1.2 L product/ha, which is equivalent to 96 g mesotrione/ha and 36 g nicosulfuron/ha.

Predicted environmental concentrations in groundwater evaluated according to the FOCUS methodology were clearly below 0.1 µg/L for **mesotrione** and its soil metabolites MNBA and AMBA in all simulations (see dRR Part B Section 8 Point 8.8). Therefore, there is no need to further address the relevance of the metabolites of mesotrione.

The **nicosulfuron** metabolites *ASDM, AUSN, HMUD, MU-466 and UCSN* are predicted to occur in groundwater at concentrations above 0.1 µg/L (see dRR Part B Section 8 Point 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.

The relevance of these groundwater metabolites has already been assessed and the assessment agreed at EU level (see EFSA Conclusion for nicosulfuron (EFSA Scientific Report (2007) 120, 1-91)).

Referring to the EFSA Conclusion for nicosulfuron (EFSA Scientific Report (2007) 120, 1-91) all metabolites identified as having the potential to occur in groundwater at levels above 0.1 µg/L are “non-relevant”.

Referring to the EFSA Conclusion for nicosulfuron (EFSA Scientific Report (2007) 120, 1-91) all metabolites identified as having the potential to occur in groundwater at levels above 0.1 µg/L are not biologically active.

Referring to the EFSA Conclusion for nicosulfuron (EFSA Scientific Report (2007) 120, 1-91) all metabolites identified as having the potential to occur in groundwater at levels above 0.1 µg/L are “non-relevant” regarding genotoxicity.

The active substance nicosulfuron has not been classified as being toxic or very toxic, reproductive toxic or carcinogenic. There is no indication that metabolites identified > 0.1 µg/l might be toxic or highly toxic. No further assessment is therefore triggered for these metabolites.

These relevance assessment is applicable as well for the GAP and groundwater scenarios considered in this dRR also with regard to the PEC_{gw} calculated for the GAP and groundwater scenarios considered in this dRR.
These groundwater metabolites are not considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10.

Metabolites which have not been identified as being relevant according to the hazard screening should be further tested in an exposure assessment to make sure that any contamination of groundwater will not lead to unacceptable exposure of consumers via their drinking water.

This concept proposes that for compounds for which a full set of toxicological data is not available and a quantitative risk assessment cannot be provided; a pragmatic approach following a "threshold of concern"

can be applied. A toxicological threshold of concern of 1.5 µg/person/day, or 0.02 µg/kg body weight/day, has been proposed, which is in line with the threshold developed by the US-FDA. Assuming a consumption of 2 liters of water per day, such an acceptable exposure level relates to an acceptable estimated upper limit for the concentration of a metabolite of 0.75 µg/L.

PEC groundwater values for the all metabolites were below 2 µg/L. For HMUD and MU-466 they were below 0.75 µg/L. For ADMP, they stayed below at or below 0.001 µg/L (for further information see dRR Part B8).

A refined risk assessment for consumers with regard to the nicosulfuron metabolites ASDM, AUSN and UCSN is therefore necessary since the level of 0.75 µg L^{-1} is expected to be exceeded in groundwater (for further information see dRR Part B8).

According to EFSA Conclusion for nicosulfuron (EFSA Scientific Report (2007) 120, 1-91) the ADI of nicosulfuron (2 mg/kg bw/d) can be applied also for the metabolites.

Following the WHO guideline for drinking water quality, and the approach for the metabolites (EFSA Scientific Report (2007) 120, 1-91) for an adult of 60 kg bw consuming 2 L/day, a 10-kg child consuming 1L/day and a 5-kg bottle-fed infant consuming 0.75L/day, the following daily intakes were estimated, based on the highest predicted concentration in groundwater for ASDM and AUSN:

Metabolite	Max. PECgw (µg/L) (FOCUS groundwater location)	Intake in µg/day			Intake in mg/kg bw/day			%ADI of nicosulfuron		
		Adult	Toddler	Infant	Adult	Toddler	Infant	Adult	Toddler	Infant
UCSN	~~0.974~~ 1.10	2.20	1.10	0.825	0.00004	0.00011	0.00017	0.002	0.006	0.008
AUSN	~~1.54~~ 1.70	3.40	1.70	1.275	0.00006	0.00017	0.00026	0.003	0.009	0.013
ASDM	~~0.954~~ 0.991	1.982	0.991	0.743	0.00003	0.00010	0.00015	0.002	0.005	0.007

In comparison to the ADI of nicosulfuron, the sum of the metabolites leads to a maximum additional contribution which corresponds to 0.06% ADI Nicosulfuron.

Based on the calculations, no risk for the consumer could be identified.

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

None

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

None