FINAL REGISTRATION REPORT

Part B

Section 10

Assessment of the relevance of metabolites in groundwater

Detailed summary of the risk assessment

Product code: **MEZOFLOR 103 SC**

Product names: **MEZOFLOR 103 SC, FLOCORN 103 SC**

Chemical active substances:

Mesotrione, 100 g/L
Florasulam, 3 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

Applicant: **Synthos Agro Sp. z o. o.**

Submission date: 07/2023

MS Finalisation date: 12/2023, 12/2024

Version history

When	What
07/2023	Initial dRR
12/2023	zRMS assessment of dRR
12/2024	The final Registration Report

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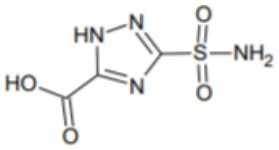
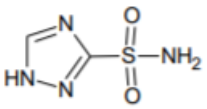
10 Relevance of metabolites in groundwater

10.1 General information

The metabolites ASTCA and TSA are predicted to occur in groundwater at concentrations above 0.1 µg/L (see dRR B8 chapter 8.8.3.2.). 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 assessmnent	
Florasulam	ASTCA		Max PEC_{gw} Based on:	0.201 µg/L Thiva (PELMO 6.6.4)
	TSA		Max PEC_{gw} Based on:	0.164 µg/L Thiva (PELMO 6.6.4)

10.2 Relevance assessment of ASTCA and TSA

Smmary:

The relevance of the groundwater metabolite ASTCA and TSA has already been assessed and the assessment agreed at EU level (see, EFSA Journal 2015; 13(1):3984) 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). ASTCA and TSA 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 ASTCA

Comments of zRMS:	Taking into account toxicological data, i.e.: - Ames test: negative - Gene mutation assay *in vitro* with mammalian cells: negative - Chromosomal aberration assay *in vitro*: negative, the metabolite ASTCA is considered toxicologically non-relevant (EFSA Journal 2015;13(1): 3984). The PECgw is below the upper limit for metabolites (<0.75 µg/l). Consequently, the consumer risk calculation for ASTCA is not required.

	Assessment step		Result of assessment	
Quantification of groundwater contamination	STEP 1		Metabolite of no concern?	No
	STEP 2		Max PEC_{gw}	0.201 µg/L
			Based on	Thiva (PELMO 6.6.4)
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 toxic or very toxic
			Classification of parent	Not toxic or very toxic
			Classification of metabolite	Not toxic or very toxic
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 reqired
			Predicted exposure (% of ADI)	Not reqired
			ADI based on	Not reqired

* N/A: not applicable

Table 10.2-2: Summary of the relevance assessment for TSA

Comments of zRMS:	Taking into account toxicological data, i.e.: - Ames test: negative - Gene mutation assay *in vitro* with mammalian cells: negative - Chromosomal aberration assay *in vitro*: negative, the metabolite TSA is considered toxicologically non-relevant (EFSA Journal 2015;13(1): 3984). The PECgw is below the upper limit for metabolites (<0.75 µg/l). Consequently, the consumer risk calculation for TSA is not required.

	Assessment step		Result of assessment	
	STEP 1		Metabolite of no concern?	No
Quantification of groundwater contamination	STEP 2		Max PEC_{gw}	0.164 µg/L
			Based on	Thiva (PELMO 6.6.4)
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 toxic or very toxic
			Classification of parent	Not toxic or very toxic
			Classification of metabolite	Not toxic or very toxic
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 reqired
			Predicted exposure (% of ADI)	Not reqired
			ADI based on	Not reqired

* N/A: not applicable

10.2.1 STEP 1: Exclusion of degradation products of no concern

ASTCA and TSA do not meet the criteria for products of no concern as defined in step 1 of the guidance and therefore need further assessment.

10.2.2 STEP 2: Quantification of potential groundwater contamination

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

10.2.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.2.3.1 STEP 3, Stage 1: screening for biological activity

The biological activity of ASTCA and TSA do not have comparable target activity as the florasulam as shown in biological tests. ASTCA and TSA is considered not relevant and is further evaluated in Stage 2.

10.2.3.2 STEP 3, Stage 2: screening for genotoxicity

ASTCA and TSA were 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. ASTCA and TSA were non-genotoxic as shown by a negative Ames test, negative gene mutation test with mammalian cells, negative chromosome aberration test. ASTCA and TSA are considered not relevant and is further evaluated in Stage 3. The genotoxicity studies are evaluated in Part B, Section 6.

10.2.3.3 STEP 3, Stage 3: screening for toxicity

The parent, florasulam, to ASCTA and TSA is not classified as acutely or chronically toxic or very toxic / for reproductive toxicity / as a carcinogen (or corresponding classification in accordance to CLP

1272/2008). There are no reasons to expect that ASTCA and TSA may be toxic or highly toxic. ASTCA and TSA have not been subject to targeted testing. ASTCA and TSA are not considered relevant and is further evaluated in Step 4.

10.2.4 STEP 4: Exposure assessment – threshold of concern approach

ASTCA and TSA were not considered relevant in the hazard assessment of Step 3.

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

10.2.5 STEP 5: Refined risk assessment

Not reqired

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

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

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

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
IIA 6.12.1 (Annex IIA 5.8.1)	Michael, S. M.	2008	Salmonella Escherichia coli/Mammalian-Microsome Reverse Mutation Assay Preincubation Method with a Confirmatory Assay with ASTCA Metabolite of Florasulam Covance Laboratories Inc DAS Report No.: 071120 (Accession Number) 257169 GLP/GEP (Y/N):Y Published (Y/N): N	Y	Dow AgroScience
IIA 6.12.2 (Annex IIA 5.8.2)	Schisler,M.R. and Geter, D.R.	2008	Evaluation of Florasulam ASTCA Metabolite in the Chinese Hamster ovary Ell/hypoxanthine-guanine-phosphoribosyl Transferase (cho/hgprt) Forward Mutation Assay Toxicology & Environmental Research and Consulting DAS Report No.: 071133 (Accession Number) 257174 GLP/GEP (Y/N): Y Published (Y/N): N	Y	Dow AgroScience
IIA 6.12.3 (Annex IIA 5.8.3)	Schisler, M.R , Kleinert, K.M. and D. R. Geter, D.R	2008	Evaluation of Florasulam ASTCA Metabolite in an in vitro Chromosomal Aberration Assay Utilizing Rat Lymphocytes Toxicology & Environmental Research and Consulting DAS Report No.: 071132 (Accession Number) 257142 GLP/GEP (Y/N): Y Published (Y/N): N	Y	Dow AgroScience
IIA 6.12.4 (Annex IIA 5.8.4)	Nagane, R.M.	2011a	Bacterial Reverse Mutation Test of TSA Metabolite of Florasulam using Salmonella typhimurium Jai Research Foundation DAS Report No.: 110432 (Accession Number) 2010127 GLP/GEP (Y/N): Y Published (Y/N): N	Y	Dow AgroScience
IIA 6.12.5 (Annex IIA 5.8.5)	Nagane, R.M.	2011b	In vitro Mammalian Cell Gene Forward Mutation Test at the hgprt Locus of the Chinese Hamster Ovary (CHO)-K1 Cell Line using TSA metabolite of florasulam Jai Research Foundation DAS Report No.: 110430 (Accession Number) 2010107 GLP/GEP (Y/N): Y Published (Y/N): N	Y	Dow AgroScience
IIA 6.12.6	Nagane, R.M.	2011c	In vitro Mammalian Chromosome Aberration Test of TSA Metabolite of Florasulam in Human Peripheral Blood	Y	Dow

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
(Annex IIA 5.8.6)			Lymphocytes Jai Research Foundation DAS Report No.: 110431 (Accession Number) 2010112 GLP/GEP (Y/N): Y Published (Y/N): N		AgroScience

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:	