

FINAL REGISTRATION REPORT

Part B

Section 10

Assessment of the relevance of metabolites in groundwater

Detailed summary of the risk assessment

Product code: H-01-2022

Product name(s): Terbutylazyna 500 SC

Chemical active substance:

terbuthylazine, 500 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: ProAgri International Sp. z o.o.

Submission date: April 2024

MS Finalisation date: August 2024; March 2025

Version history

When	What
08.2024	ZRMS assessment
03.2025	The final Registration Report

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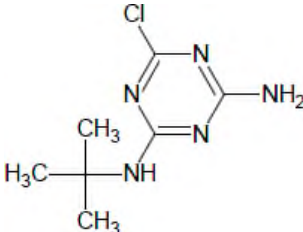
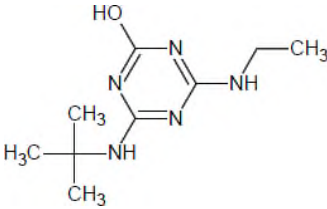
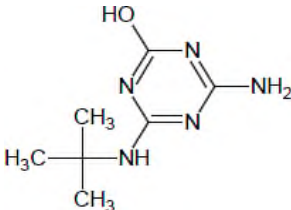
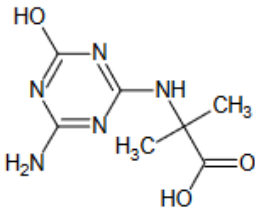
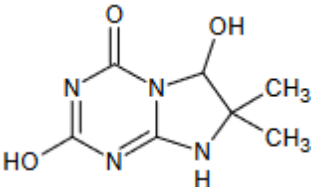
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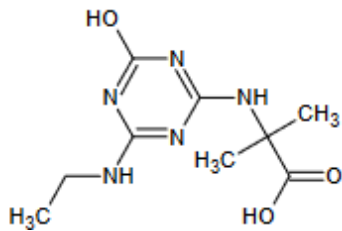
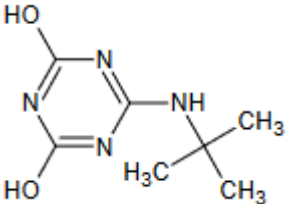
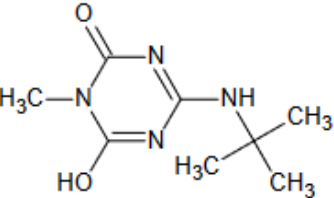
10 Relevance of metabolites in groundwater

10.1 General information

The metabolites: MT1, MT13, MT14, LM2, LM3, LM4, LM5 and LM6 are predicted to occur in groundwater at concentrations above 0.1 µg/L (see dRR Part B Section 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 is provided in Table 10.1-1.

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	
terbuthylazine	MT1 desethyl-terbuthylazine (N-tert-butyl-6-chloro-1,3,5-triazine-2,4-diamine)		Max PEC _{gw} Based on:	0.118059 µg/L Okehampton / PEARL 5.5.5 application every 3 rd year
terbuthylazine	MT13 hydroxy-terbuthylazine (4-(tert-butylamino)-6-(ethylamino)-1,3,5-triazin-2-ol)		Max PEC _{gw} Based on:	7.139466 µg/L Thiva / PEARL 5.5.5 application every 3 rd year
terbuthylazine	MT14 desethyl-hydroxy terbuthylazine (4-amino-6-(tert-butylamino)-1,3,5-triazin-2-ol)		Max PEC _{gw} Based on:	0.994989 µg/L Okehampton / PEARL 5.5.5 application every 3 rd year
terbuthylazine	LM2 N-(4-amino-6-hydroxy-1,3,5-triazin-2-yl)-2-methylalanine		Max PEC _{gw} Based on:	1.302434 µg/L Hamburg / PEARL 5.5.5 application every 3 rd year
terbuthylazine	LM3 2,6-dihydroxy-7,7-dimethyl-7,8-dihydroimidazo[1,2-a][1,3,5]triazin-4(6H)-one		Max PEC _{gw} Based on:	0.94583 µg/L Hamburg / PEARL 5.5.5 application every 3 rd year

terbuthylazine	LM4 N-[4-(ethylamino)-6-hydroxy-1,3,5-triazin-2-yl]-2-methylalanine		Max PEC _{gw} Based on:	2.963227 µg/L Hamburg / PEARL 5.5.5 application every 3 rd year
terbuthylazine	LM5 6-(tert-butylamino)-1,3,5-triazine-2,4-diol		Max PEC _{gw} Based on:	1.212409 µg/L Hamburg / PEARL 5.5.5 application every 3 rd year
terbuthylazine	LM6 4-(tert-butylamino)-6-hydroxy-1-methyl-1,3,5-triazin-2(1H)-one		Max PEC _{gw} Based on:	3.911373 µg/L Thiva / PEARL 5.5.5 application every 3 rd year

10.2 Relevance assessment

Summary:

The relevance of the groundwater metabolites MT1, MT13, MT14, LM1, LM2, LM3, LM4, LM5 and LM6 have already been assessed and the assessment agreed at EU level. Nonetheless the relevance assessment has been performed in this document since PEC_{gw} values obtained for H-01-2022 differ from PEC_{gw} values evaluated at EU level.

Summary of the relevance assessment for MT1, MT13, MT14, LM1, LM2, LM3, LM4, LM5 and LM6

[illegible]

		assessment								
		Predicted exposure (% of ADI)	not relevant	max. 26.78% of ADI	max. 3.73% of ADI	max. 4.88% of ADI	max. 3.55% of ADI	max. 11.10% of ADI	max. 4.55% of ADI	max. 14.68% of ADI
		ADI based on	not relevant	0.004 mg/kg bw/day (ADI for therbutylazine)	0.004 mg/kg bw/day (ADI for therbutylazine)	0.004 mg/kg bw/day (ADI for therbutylazine)	0.004 mg/kg bw/day (ADI for therbutylazine)	0.004 mg/kg bw/day (ADI for therbutylazine)	0.004 mg/kg bw/day (ADI for therbutylazine)	0.004 mg/kg bw/day (ADI for therbutylazine)

* N/A: not applicable

10.2.1 STEP 1: Exclusion of degradation products of no concern

Metabolites MT1, MT13, MT14, LM1, LM2, LM3, LM4, LM5 and LM6 do not meet the criteria for products of no concern as defined in Step 1 of the guidance. Three soil metabolites and six lysimeters leachate metabolites need further assessment.

10.2.2 STEP 2: Quantification of potential groundwater contamination

PEC_{gw} calculations after leaching from soil for MT1, MT13, MT14, LM1, LM2, LM3, LM4, LM5 and LM6 were performed (see Part B, Section 8). The max. PEC_{gw} values are in Table 10.2-1. Details are given in Part B, Section 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 MT1 is comparable target activity as the parent active compound. MT1 is considered relevant and is further evaluated in Stage 2 (EFSA Journal 2011; 9(1):1969). The metabolites MT13, MT14, LM1, LM2, LM3, LM4, LM5 and LM6 does not have comparable target activity as the parent active compound and are considered not relevant (EFSA Journal 2011; 9(1):1969).

Full summaries of biological screening studies on the metabolite that have not been previously considered within an EU peer review process.

10.2.3.2 STEP 3, Stage 2: screening for genotoxicity

MT1, MT13, MT14, LM1, LM2, LM3, LM4, LM5 and LM6 were screened for genotoxic activity and summary of assessment is included EFSA Journal 2019;17(9):5817 (confirmatory data). None of the metabolites has genotoxic activity.

10.2.3.3 STEP 3, Stage 3: screening for toxicity

In accordance with ATP10 (Harmonised C&L classification) terbuthylazine is toxicologically classified as Acute Tox. 4, H302 STOT RE 2, H373. In accordance with EFSA Journal 2019;17(9):5817 (confirmatory data) metabolites LM3 and LM6 can not be considered as non-relevant. Metabolites MT1, MT13, MT14, LM1, LM2, LM4 and LM5 are relevant because of its culminative concentration above ADI.

10.2.4 STEP 4: Exposure assessment – threshold of concern approach

The PEC_{gw} for metabolite MT1 was < 0.75 µg/L. There is no consumer exposure via other routes. The metabolite MT1 is not considered to exceed the toxicological threshold of concern as defined in EC guidance document SANCO/221/2000 –rev.10.

The potential exposure to MT13, MT14, LM1, LM2, LM3, LM4, LM5 and LM6 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

PEC_{gw} values for MT13, MT14, LM1, LM2, LM3, LM4, LM5 and LM6 are between 0.75 µg/L and 10 µg/L. A refined assessment of the potential toxicological significance including ADI for terbuthylazine is presented below. For all metabolites the ADI of 0.004 mg/kg bw/day was used for calculations.

Calculation of risk (% ADI) for 5-kg bottle-fed infant (consuming 0.75 L/day, body weight 5 kg):

Table 10.2-2: Risk assessment for infant

Metabolite	Max. PEC _{gw} (µg/L)	Exposure via drinking water (mg/kg bw/day)	ADI (mg/kg bw/day)	% of ADI	acceptable Yes/No
MT13	7.139466	0.001071	0.004	26.78	Yes
MT14	0.994989	0.000149	0.004	3.73	Yes
LM2	1.302434	0.000195	0.004	4.88	Yes
LM3	0.945830	0.000142	0.004	3.55	Yes
LM4	2.963227	0.000444	0.004	11.10	Yes
LM5	1.212409	0.000182	0.004	4.55	Yes
LM6	3.911373	0.000587	0.004	14.68	Yes

Calculation of risk (% ADI) for 10-kg child (consuming 1.0 L/day, body weight 10 kg):

Table 10.2-3: Risk assessment for child

Metabolite	Max. PEC _{gw} (µg/L)	Exposure via drinking water (mg/kg bw/day)	ADI (mg/kg bw/day)	% of ADI	acceptable Yes/No
MT13	7.139466	0.000714	0.004	17.85	Yes
MT14	0.994989	0.000099	0.004	2.48	Yes
LM2	1.302434	0.000130	0.004	3.25	Yes
LM3	0.94583	0.000095	0.004	2.38	Yes
LM4	2.963227	0.000296	0.004	7.40	Yes
LM5	1.212409	0.000121	0.004	3.03	Yes
LM6	3.911373	0.000391	0.004	9.78	Yes

Calculation of risk (% ADI) for 60-kg adult (consuming 2.0 L/day, body weight 60 kg):

Table 10.2-4: Risk assessment for adult

Metabolite	Max. PEC _{gw} (µg/L)	Exposure via drinking water (mg/kg bw/day)	ADI (mg/kg bw/day)	% of ADI	acceptable Yes/No
MT13	7.139466	0.000238	0.004	5.95	Yes
MT14	0.994989	0.000033	0.004	0.83	Yes
LM2	1.302434	0.000043	0.004	1.08	Yes
LM3	0.94583	0.000032	0.004	0.80	Yes
LM4	2.963227	0.000099	0.004	2.48	Yes
LM5	1.212409	0.000040	0.004	1.00	Yes
LM6	3.911373	0.000130	0.004	3.25	Yes

In accordance with the performed risk assessment, it was concluded that MT13, MT14, LM1, LM2, LM3, LM4, LM5 and LM6 are not considered relevant according to the criteria laid down in the EC guidance document SAN-CO/221/2000 – rev.11. No further action is required.

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

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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.
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Not relevant.