

# FINAL REGISTRATION REPORT

## Part B

### Section 10

#### **Assessment of the relevance of metabolites in groundwater**

Detailed summary of the risk assessment

Product code: **TERBUT 500 SC**

Product names: **TERBUT 500 SC/  
TAZOPRYM 500 SC / CORNAO 500 SC**

Chemical active substance:

Terbuthylazine, 500 g/L

Central Zone

Zonal Rapporteur Member State: Poland

**CORE ASSESSMENT/**

(authorization)

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

Submission date: 04/2020

MS Finalisation date: 10.2021; 03.2022

## Version history

When	What
October 2021	Assessment by the expert
March 2022	Final Registration Report

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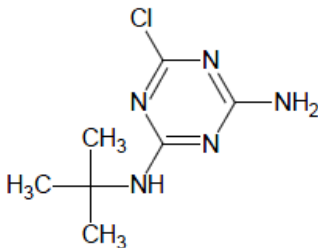
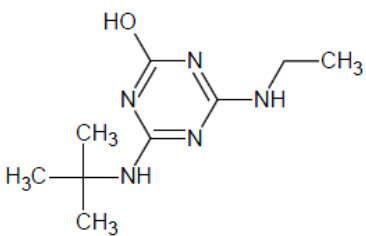
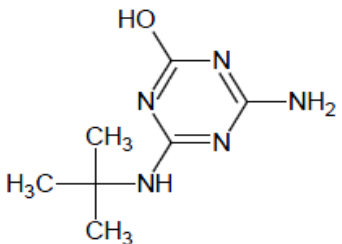
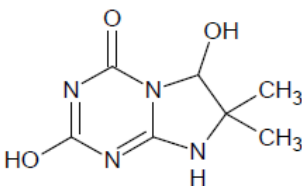
## 10 Relevance of metabolites in groundwater

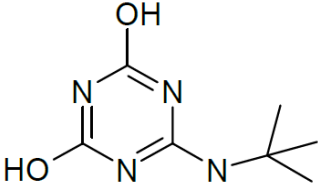
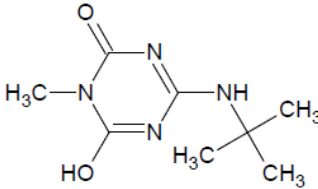
### 10.1 General information

The metabolites: MT1, MT13, MT14, LM3, LM5 and LM6 are predicted to occur in groundwater at concentrations above 0.1 µg/L (see dRR Section8). 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 metabolites**

Name of active substance	Metabolite name and code	Structural/molecular formula	Trigger for relevance assessment	
Terbuthylazine	Desethyl-terbuthylazine (MT1) N-tert-butyl-6-chloro-1,3,5-triazine-2,4-diamine		Max PEC <sub>gw</sub>  Based on:	1.437 µg/L  PEARL 4.4.4 Hamburg scenario, post-emergence use
	Hydroxy-terbuthylazine (MT13) 4-(tert-butylamino)-6-(ethylamino)-1,3,5-triazin-2-ol		Max PEC <sub>gw</sub>  Based on:	18.305 µg/L  PELMO 5.5.3 Thiva scenario, pre-emergence use
	Desethyl hydroxy-terbuthylazine (MT14) 4-amino-6-(tert-butylamino)-1,3,5-triazin-2-ol		Max PEC <sub>gw</sub>  Based on:	2.884 µg/L  PEARL 4.4.4 Hamburg scenario, post-emergence use
	LM3 2,6-dihydroxy-7,7-dimethyl-7,8-dihydroimidazo[1,2-a][1,3,5]triazin-4(6H)-one		Max PEC <sub>gw</sub>  Based on:	15.344 µg/L  PELMO 5.5.3 Thiva scenario, pre-emergence use

Name of active substance	Metabolite name and code	Structural/molecular formula	Trigger for relevance assessment	
	LM5 6-( <i>tert</i> -butylamino)-1,3,5-triazine-2,4-diol		Max PEC <sub>gw</sub>  Based on:	2.404 µg/L  PEARL 4.4.4 Thiva scenario, post-emergence use
	LM6 4-( <i>tert</i> -butylamino)-6-hydroxy-1-methyl-1,3,5-triazin-2(1H)-one		Max PEC <sub>gw</sub>  Based on:	6.377 µg/L  PELMO 5.5.3 Thiva scenario, pre-emergence use

## 10.2 Relevance assessment of MT1, MT13, MT14, LM3, LM5 and LM6

### Summary:

The groundwater metabolites MT1, MT13, MT14, LM3, LM5 and LM6 are considered as relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10. A summary of the relevance assessment for metabolites is given in Table 10.2-1. Studies supporting PEC<sub>gw</sub> data are based on result summarised in peer review (EFSA Journal 2011; 9(1):1969) and updated peer review of the pesticide (EFSA Journal 2019;17(9):5817) terbuthylazine.

**Table 10.2-1: Summary of the relevance assessment for metabolites.**

	Assessment step		Result of assessment	MT1	MT13	MT14	LM3	LM5	LM6
	STEP 1		Metabolite of no concern?	NO	NO	NO	NO	NO	NO
Quantification of groundwater contamination	STEP 2		Max PEC <sub>gw</sub>	1.437 µg/L	18.305 µg/L	2.884 µg/L	15.344 µg/L	2.404 µg/L	6.377 µg/L
			Based on	PEARL 4.4.4 Hamburg	PELMO 5.5.3 Thiva	PEARL 4.4.4 Hamburg	PELMO 5.5.3 Thiva	PEARL 4.4.4 Thiva	PELMO 5.5.3 Thiva
Hazard assessment	STEP 3	Stage 1	Biological activity comparable to the parent?	YES	NO	NO	NO	NO	NO

		Stage 2	Genotoxic properties of metabolite	Non-genotoxic	Non-genotoxic	Non-genotoxic	Non-genotoxic	Non-genotoxic	Non-genotoxic	
		Stage 3	Toxic properties of metabolite;	Parental pesticidal activity	No activity	No activity	No activity	No activity	No activity	
			Classification of parent	Acute Tox. 4 H302, STOT RE 2 H373						
			Classification of metabolite	Acute Tox. 4	Acute Tox. 4	Acute Tox. 4	Not considered as toxic	Acute Tox. 4	Not considered as toxic	
Consumer health risk assessment	STEP 4		Estimated consumer exposure via drinking water and other sources; threshold of concern approach	Not acceptable (>0.75 µg/L)	Not acceptable (>0.75 µg/L)	Not acceptable (>0.75 µg/L)	Not acceptable (>0.75 µg/L)	Not acceptable (>0.75 µg/L)	Not acceptable (>0.75 µg/L)	
	STEP 5	Refined risk assessment	Acceptable	Acceptable	Acceptable	Acceptable	Acceptable	Acceptable		
		Predicted exposure (% of ADI) - infant	5.39	68.64	10.82	57.54	9.02	23.91		
		Predicted exposure (% of ADI) - child	3.59	45.76	7.21	38.36	6.01	15.94		
		Predicted exposure (% of ADI) - adult	1.20	15.25	2.40	12.79	2.00	5.31		
		ADI based on	0.004 mg/kg bw (parent dose), based on the no observed adverse effect level (NOAEL) of the 1-year dog and 2-year rat studies, and applying an uncertainty factor of 100							

\* N/A: not applicable

### 10.2.1 STEP 1: Exclusion of degradation products of no concern

Each metabolite 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

According to calculations performed using PELMO 5.3.3 and PEARL 4.4.4, each metabolite of terbutylazine occurs in groundwater in concentration over 0.1 µg/L in at least one scenario.

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**

As shown in peer review for terbuthylazine (EFSA Journal 2011; 9(1):1969), only metabolite MT1 has pesticidal activity comparable to parental activity. None of the other metabolites is considered relevant and has at least 50% of parental activity.

#### **10.2.3.2 STEP 3, Stage 2: screening for genotoxicity**

According to Updated peer review of the pesticide risk assessment for the active substance terbuthylazine in light of confirmatory data submitted (EFSA Journal 2019;17(9):5817), none of the mentioned metabolites has genotoxic activity.

#### **10.2.3.3 STEP 3, Stage 3: screening for toxicity**

The parent, terbuthylazine, is classified as acutely toxic in category 4. Since cumulative concentration of metabolites MT1, MT13, MT14 and LM5 is over 100% of ADI, they are considered relevant.

According to Updated peer review of the pesticide risk assessment for the active substance terbuthylazine in light of confirmatory data submitted (EFSA Journal 2019;17(9):5817), metabolites LM3 and LM6 could not be considered as irrelevant, and metabolites MT1, MT13, MT14 and LM5 are relevant because of their cumulative influence.

### **10.2.4 STEP 4: Exposure assessment – threshold of concern approach**

The potential exposure to metabolites MT1, MT14, LM5 and LM6 is  $> 0.75 \mu\text{g/L}$  but  $< 10 \mu\text{g/L}$ . A further assessment in Step 5 is required.

The potential exposure to metabolites MT13 and LM3 is  $> 10 \mu\text{g/L}$ . However, according to field studies annual leachate concentration for MT13 does not exceed  $0.1 \mu\text{g/L}$  and for LM3 does not exceed  $0.75 \mu\text{g/L}$ . A further assessment in Step 5 is required.

### **10.2.5 STEP 5: Refined risk assessment**

The consumer risk assessment demonstrates an acceptable risk. The estimated safety margin including potential exposure via other routes besides drinking water for MT13 are 31% of ADI (infant), 54% of ADI (child), 85% of ADI (adult).

Justification for the selected ADI:

$0.004 \text{ mg/kg bw}$  (parent dose) is based on the no observed adverse effect level (NOAEL) of the 1-year dog and 2-year rat studies, and with applying an uncertainty factor of 100

For all metabolites the ADI of terbuthylazine ( $0.004 \text{ mg/kg bw/d}$ ) was used for calculations.

**Table 10.2-2: Calculation of risk (% ADI) for 5-kg bottle-fed infant (consuming 0.75 l/day):**

Result of assessment	MT1	MT13	MT14	LM3	LM5	LM6
Max PEC <sub>gw</sub> µg/L	1.437	18.305	2.884	15.344	2.404	6.377
Daily intake µg/kg	0.22	2.75	0.43	2.30	0.36	0.96
% of ADI	5.39	68.64	10.82	57.54	9.02	23.91

**Table 10.2-3: Calculation of risk (% ADI) for 10-kg child (consuming 1.0 l/day):**

Result of assessment	MT1	MT13	MT14	LM3	LM5	LM6
Max PEC <sub>gw</sub> µg/L	1.437	18.305	2.884	15.344	2.404	6.377
Daily intake µg/kg	0.14	1.83	0.29	1.53	0.24	0.64
% of ADI	3.59	45.76	7.21	38.36	6.01	15.94

**Table 10.2-4: Calculation of risk (% ADI) for 60-kg adult (consuming 2.0 l/day):**

Result of assessment	MT1	MT13	MT14	LM3	LM5	LM6
Max PEC <sub>gw</sub> µg/L	1.437	18.305	2.884	15.344	2.404	6.377
Daily intake µg/kg	0.048	0.61	0.10	0.51	0.080	0.21
% of ADI	1.20	15.25	2.40	12.79	2.00	5.31

**Based on the available data and the considerations given above, the ter-butylazine metabolites MT1, MT13, MT14, LM3, LM4, LM5 and LM6 will not pose a risk to the consumer.**

**Consequently these metabolites are of no concern and can be considered non-relevant in the context of the criteria outlined in the guidance document.**

**Metabolites LM1-LM6 can be considered non relevant according to the criteria given in SANCO/221/2000-rev 10.**

**It was not expected that metabolites MT1, MT13, MT14, LM3, LM4, LM5 and LM6 would represent a health hazard to the infants, toddlers and adult consumers.**



## 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**

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

**Appendix 2 Additional information**

<b>Comments of zRMS:</b>	<b>Comment on statement; acceptable or not.</b>
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