

FINAL REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: TERBUT 500 SC

Product name(s): La Zina 500 SC; Tekno 500 SC

Chemical active substance(s):

Terbuthylazine, 500 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: PUH Chemirol Sp. o.o.

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Version history

When	What
December 2021	ZRMs evaluated dRR updated by Applicant.
June 2022	Final Version after Commenting period

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6 Mammalian Toxicology (KCP 7)

6.1 Summary

Table 6.1-1: Information on TERBU 500 SC/ TERBUT 500 SC *

Product name and code	TERBUT 500 SC/ TERBU 500 SC
Formulation type	suspension concentrate [Code: SC]
Active substance(s) (incl. content)	terbuthylazine; 500 g/L
Function	herbicide
Product already evaluated as the 'representative formulation' during the approval of the active substance(s)	No
Product previously evaluated in another MS according to Uniform Principles	No

* Information on the detailed composition of TERBU 500SC/ TERBUT 500 SC can be found in the confidential dRR Part C.

Justified proposals for classification and labelling

According to the criteria given in Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008, the following classification and labelling with regard to toxicological data is proposed for the preparation:

Table 6.1-2: Justified proposals for classification and labelling for TERBUT 500 SC according to Regulation (EC) No 1272/2008

Hazard class(es), categories	STOR RE 2
Hazard pictograms or Code(s) for hazard pictogram(s)	GHS08
Signal word	Warning
Hazard statement(s)	H373 – May cause damage to organs through prolonged or repeated exposure.
Precautionary statement(s)	<p>WARNING SECTION OF THE LABEL: P260 – Do not breathe dust/fume/gas/mist/vapours/spray. P280 – Wear protective gloves/protective clothing/eye protection/face protection. P314 – Get medical advice/attention if you feel unwell.</p> <p>Other section of the label: P270 - Do not eat, drink or smoke when using this product. P501 - Dispose of contents/container to...</p> <p>And P280 as follows: Operator: „Stosować rękawice ochronne oraz odzież roboczą (kombinezon) w trakcie przygotowywania cieczy roboczej oraz wykonywania zabiegu” “Wear protective gloves and work wear (coverall) during mixing/loading and application”. Worker: „Stosować rękawice ochronne oraz odzież roboczą (długie spodnie, koszula z długim rękawem) podczas inspekcji terenu poddanego opryskowi.” “Wear protective gloves and workwear (long trousers, long-sleeve shirt) during inspection of treated area”. Bystander/resident: „Podczas wykonywania zabiegu należy zachować 5 metrową strefę buforową oraz dysze ograniczające znos”. “Keep a 5 meter buffer zone and drift-reduction nozzles during application”.</p> <p>Section First aid: P314 – Get medical advice/attention if you feel unwell.</p>
Additional labelling phrases	<p>EUH401 – To avoid risks to human health and the environment, comply with the instructions for use. EUH208 – Contains 1,2-benzisothiazol-3(2H)-one. May produce an allergic reaction.</p>

Table 6.1-3: Summary of risk assessment for operators, workers, residents and bystanders for TERBUT 500 SC

	Result	PPE / Risk mitigation measures
Operators	Acceptable	Gloves during mixing/loading
Workers	Acceptable	Gloves when handling treated crops
Residents	Acceptable	Vehicle mounted drift reduction with 5 meters buffer zone
Bystanders	Acceptable	

No unacceptable risk for resident and bystanders was identified when the product is used as intended and provided that the PPE/ risk mitigation measures stated in Table 6.1-3 are applied.

A summary of the critical uses and the overall conclusion regarding exposure for operators, workers and residents/bystanders is presented in the following table.

Table 6.1-4 Critical uses and overall conclusion of exposure assessment

1	2	3	4	5	6	7	8	9	10			
Use- No.*	Crops and situation (e.g. growth stage of crop)	F, Fn, Fpn G, Gn, Gpn or I**	Application		Application rate		PHI (d)	Remarks: (e.g. safener/synergist (L/ha)) critical gap for operator, worker, resident or by- stander exposure based on [Expo- sure model]	Acceptability of exposure as- sessment			
			Method / Kind (incl. applica- tion technique ***)	Max. number (min. interval between applications) a) per use b) per crop/ season	Max. applica- tion rate kg as/ha a) a.s. 1 b) a.s. 2	Water L/ha min / max			Operator	Worker	Residents	Bystander
	Maize (BBCH 12-16)	F	Spray, medium sprayer	1 ; 1	a) 0.500	200-400	-					
	Maize (BBCH 00-05)	F	Spray, medium sprayer	1 ; 1	a) 0.500	200-400						

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1

** F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application

*** e.g. LC: low crops, HC: high crop, TM: tractor-mounted, HH: hand-held

Explanation for column 10 “Acceptability of exposure assessment”

A	Exposure acceptable without PPE / risk mitigation measures
R	Further refinement and/or risk mitigation measures required
N	Exposure not acceptable/ Evaluation not possible

Data gaps

Noticed data gaps are:

6.2 Toxicological Information on Active Substance(s)

Information regarding classification of the active substances and on EU endpoints and critical areas of concern identified during the EU review are given in Table 6.2-1.

Table 6.2-1: Information on active substance(s)

Terbuthylazine	
Common Name	Terbuthylazine
CAS-No.	5915-41-3
Classification and proposed labelling	
With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended)	<p>Hazard classes (s), categories: Acute Tox. 4 STOR RE 2 Aquatic Acute 1 Aquatic Chronic 1</p> <p>Code(s) for hazard pictogram(s): GHS07, GHS08</p>

Terbutylazine	
	<p>Signal word: Warning</p> <p>Hazard statement(s): H302 - Harmful if swallowed. H373 – May cause damage to organs through prolonged or repeated exposure. H400 – Very toxic to aquatic life. H410 – Very toxic to aquatic life with long lasting effects</p> <p>Precautionary statement(s): P280 - Wear protective gloves/protective clothing/eye protection/face protection. P301 + P312 – IF SWALLOWED: Call a POISON CENTER or doctor/physician if you feel unwell. P308 + P313 – IF exposed or concerned: Get medical advice/attention.</p>
Additional C&L proposal	NA
Agreed EU endpoints	
AOEL systemic	0.0032 mg/kg bw/d (corrected for 79% oral absorption)
Reference	EFSA Journal 2011; 9(1):1969/ DAR Addendum confirmatory data, update November 2015
Conditions to take into account/critical areas of concern with regard to toxicology	
According to EFSA Journal 2011; 9(1):1969	<p>Operator exposure without PPE and with PPE at mixing/loading in German Model are much above 100% of the AOEL, with PPE during m/l and application are below AOEL. In UK POEM are above 100% of AOEL in each case.</p> <p>Worker exposure in EUROPOEM II re-entry model: without PPE are above 100% AOEL, with PPE– below 100% AOEL.</p> <p>Bystanders exposure are below 100% AOEL.</p>

6.3 Toxicological Evaluation of Plant Protection Product

A summary of the toxicological evaluation for TERBUT 500 SC is given in the following tables. Full summaries of studies on the product that have not been previously considered within an EU peer review process are described in detail in Appendix 2.

Table 6.3-1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for TERBUT 500 SC

Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Reg. 1272/2008)	Reference
LD ₅₀ oral, rat (calculation method)	> 2000 mg/kg bw	Yes	None	M. Kolodziej, 2021
LD ₅₀ dermal, rat (calculation method)	> 2000 mg/kg bw	Yes	None	M. Kolodziej, 2021
LC ₅₀ inhalation, rat (calculation method)	> 20 mg/L air	Yes	None	M. Kolodziej, 2021
Skin irritation, (calculation method)	Non Irritant	Yes	None	M. Kolodziej, 2021

Eye corrosive, (calculation method)	Non corrosive	Yes	None	M. Kolodziej, 2021
Skin sensitisation, (calculation method)	Non Sensitising	Yes	None	M. Kolodziej, 2021
Specific target organ toxicity (calculation method)	≥10%		STOT RE2, H373	M. Kolodziej, 2021
Supplementary studies for combinations of plant protection products	No data – not required			

Table 6.3-2: Additional toxicological information relevant for classification/labelling of TERBUT 500 SC

	Substance (concentration in product, % w/w)	Classification of the substance (acc. to the criteria in Reg. 1272/2008)	Reference	Classification of product (acc. to the criteria in Reg. 1272/2008)
Toxicological properties of active substance(s) (relevant for classification of product)	Terbutylazine (46 % (w/w))	STOT RE. 2 H373 (≥ 10 %)	DAR Addendum confirmatory data, update November 2015	STOT RE. 2 H373
Toxicological properties of non-active substance(s) (relevant for classification of product)	-	-	-	-
Further toxicological information	-	-	-	-

* Please use concentration range or concentration limit (e.g. 1-10% or > 1%) as provided in MSDS.

** Material safety data sheet by the applicant

6.4 Toxicological Evaluation of Groundwater Metabolites

The following data on metabolites with the potential to reach the groundwater in concentrations above 0.1 µg/L and requiring relevance assessment were submitted. Note that the relevance assessment of the metabolites is reported in Part B.10; the submitted toxicological studies are summarized in this document.

Comments of ZRMs:	<p>According to EFSA Journal 2019;17(9):5817, <i>Updated peer review of the pesticide risk assessment for the active substance terbutylazine in light of confirmatory submitted:</i></p> <ul style="list-style-type: none"> - for the metabolites LM5 and MT1, MT13, MT14, the reference values for terbutylazine are applicable in consumer risk assessment, - in the case of metabolites LM3 and LM6 the toxicological data were insufficient to determine reference values, what does not allow to finalise the consumer risk assessment. <p>The results of consumer risk calculations indicate that the use of TERBUT 500 SC (La Zina 500 SC; Tekno 500 SC) can cause unacceptable risk for toddlers' and infants' health imposed by the exposure to the metabolite MT13 (assuming normal allocation of total daily intake for chemicals acc. to WHO recommendation). The</p>
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	<p>exposure of infants and toddlers to metabolite MT13 contained in the food and drinking water will exceed the value of ADI in the presented scenario.</p> <p>The critical area of concern includes the results of total exposure estimation to groundwater metabolites of terbuthylazine (MT1, MT13, MT14, LM5) which account to 46.68 % and 69.91 % for toddler and infants, respectively.</p>
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6.4.1 MT1 - desethyl terbuthylazine- terbuthylazine metabolite

<p>Comments of ZRMs:</p>	<ul style="list-style-type: none"> - According to the available data, the metabolite MT1 is considered relevant because of its pesticidal activity but it has no genotoxic potential. - The maximum PEC_{gw} of MT1 (acc. to the application rate presented in the GAP table) amounts to 0.253191 µg/L. The predicted max. PEC_{gw} value is below the upper limit for metabolites (<0.75 µg/L). - Although the consumer risk calculation for this metabolite is not required, the results of risk calculations are presented below. This calculation was used in the total risk assessment concerning the exposure to terbuthylazine metabolites. <table border="1" style="width: 100%; border-collapse: collapse; text-align: center;"> <thead> <tr> <th style="width: 30%;"></th> <th style="width: 35%;">Exposure (µg/kg b.w./d) (using default body weight values)¹</th> <th style="width: 35%;">% ADI (reference value of the parent substance: 0.004 mg/kg b.w./d)</th> </tr> </thead> <tbody> <tr> <td>Adults (70¹/60² kg b.w.)</td> <td>0.0072/0.0084</td> <td>0.18/0.21</td> </tr> <tr> <td>Toddlers (12¹/10² kg b.w.)</td> <td>0.0211/0.025</td> <td>0.53/0.63</td> </tr> <tr> <td>Infants (5 kg b.w.)</td> <td>0.038</td> <td>0.95</td> </tr> </tbody> </table> <p>Conclusions:</p> <p>Taking into account the results of available toxicological studies, the metabolite MT1 has no genotoxic potential. The results of consumer risk calculations indicate that the use of TERBUT 500 SC (La Zina 500 SC; Tekno 500 SC) according to the list of intended uses presented in GAP Table, causes no unacceptable risk for health resulting from exposure to metabolite MT1.</p> <p>¹According to EFSA Journal 2012;10(3):2579, Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured data.</p> <p>²WHO Guidelines for drinking-water quality: fourth edition incorporating the first addendum, 2017</p>		Exposure (µg/kg b.w./d) (using default body weight values) ¹	% ADI (reference value of the parent substance: 0.004 mg/kg b.w./d)	Adults (70 ¹ /60 ² kg b.w.)	0.0072/0.0084	0.18/0.21	Toddlers (12 ¹ /10 ² kg b.w.)	0.0211/0.025	0.53/0.63	Infants (5 kg b.w.)	0.038	0.95
	Exposure (µg/kg b.w./d) (using default body weight values) ¹	% ADI (reference value of the parent substance: 0.004 mg/kg b.w./d)											
Adults (70 ¹ /60 ² kg b.w.)	0.0072/0.0084	0.18/0.21											
Toddlers (12 ¹ /10 ² kg b.w.)	0.0211/0.025	0.53/0.63											
Infants (5 kg b.w.)	0.038	0.95											

For metabolite MT1 (desethyl terbuthylazine) simulations gave PEC_{gw} values in the range from <0.001 to 0.25µg/l (peak concentration with FOCUS PEARL Okehampton, 500 g a.s./ha). The results represent conservative first tier exposure estimates. **According to the Monitoring Studies for Tebuthylazine in ground water and EFSA Journal 2011; 9(1):1969:**In the field leaching study in Northern Italy, annual average concentrations ranged from <0.01 up to 0.73µg/l in fields receiving basin irrigation. The maximum annual average concentration in fields receiving more conventional irrigation was 0.22µg/l. The conditions during the field leaching study in Northern Italy are likely to represent highly vulnerable conditions in terms of groundwater contamination in the EU due to the combination of soils, climate and extensive use of terbuthylazine on maize in the areas investigated. In addition, this metabolite was not detected in an extensive and targeted German groundwater monitoring program. In further groundwater monitoring studies in Italy, Spain and Portugal, the 90th percentile concentration was always <0.1µg/l. On

the basis of the additional information from field leaching and groundwater monitoring programs, it is clear that the first tier FOCUS groundwater exposure assessment represents a conservative assessment and such high concentrations are unlikely to be encountered under realistic use conditions.

Data on MT1 (desethyl-terbuthylazine) was also presented in the original DAR (Section B.9.9.1.2. See also Attachment 1) which showed some signs of herbicidal activity. In addition, screening data (Corbin J, 2009) was provided as part of the resubmission and is presented in this Additional Report (see Section B.9.9.2. See also Attachment 1). The conclusion was that the metabolite MT1 is herbicidally active. The biological activity of the metabolite is broadly similar to that of terbuthylazine when applied at a dose at which the parent demonstrates good herbicidal activity on key species (common amaranth, fat hen, common chickweed, and wild oats) at the field rate of 750 g a.s./ha. On this basis, this metabolite should be considered as being ‘relevant’ in terms of the guidance document.

MT1 was found to be of comparatively high acute oral toxicity in the rat (LD50 =236 mg/kg bw. Based on a comparison with the 90 day study with MT1 and the two 90 day studies with terbuthylazine in the original DAR it appears that MT1 produces some but not all the effects seen in the terbuthylazine studies at similar dose levels. It appears to have similar or slightly lower short term toxicity than parent. The 90 day study is not considered suitable for determining a reference value for MT1 (no NOAEL and lacking detail).

MT1 was identified as a rat metabolite of terbuthylazine by both Notifiers (11U: Syngenta, M1: Oxon). It was identified as a metabolite in urine, bile and faeces, although not at very high levels in the studies by Syngenta (≤6.2%; DAR Table B.6.18) and Oxon (8.44-8.85%, DAR Table B.6.19). This metabolite is, however, proposed to be the initial metabolite in the metabolic pathways proposed by both Notifiers (DAR Figures B.6.9 and B.6.10), therefore systemic exposure to the metabolite is therefore likely to be considerably greater than these levels. Consumer exposure to MT1 in drinking water is therefore considered to be adequately covered by the ADI proposed for terbuthylazine.

MT1 is not considered to be a ‘relevant metabolite’.

Table 6.4-1: Summary of the results of toxicity studies for MT1 Desethyl-terbuthylazine (GS26379)

Type of test, species	Result	Acceptability	Reference*
Acute oral - RAT	300-500 mg/kg bw		Teunissen M.S (2004)
Bacterial mutagenicity (TA1535, TA1537, TA98, TA100, WP2 _{uvrA})	Negative		Verspeek-Rip C.M. (2004)
Gene Mutation Assay- Mouse L5178Y TK+/- cells	Weakly positive		Jones E (2004)
in vivo micronucleus test (rat bone marrow)	Negative		Fox V. (2006)
in vivo unscheduled DNA synthesis (rat liver)	Negative		Fox V. (2006)
90 day study (rat)	Reduced bodyweight gain Total WBC reduced		Smith P et al, (1971)

No new studies are necessary.

6.4.2 MT13 (hydroxy terbuthylazine) – terbuthylazine metabolite

Comments of	- According to the available data, the metabolite MT13 has no pesticidal activ-
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ZRMs:	ity and it is not genotoxic.													
	- The maximum PEC _{gw} of MT13 (acc. to the application rate presented in the GAP table) amounts to 14.62 µg/L. The predicted max. PEC _{gw} value exceeds the upper limit for metabolites and the consumer risk calculation for this metabolite is required.													
		<table border="1"> <thead> <tr> <th></th> <th>Exposure (µg/kg b.w./d) (using default body weight values)¹</th> <th>% ADI (reference value of the parent substance: 0.004 mg/kg b.w./d)</th> </tr> </thead> <tbody> <tr> <td>Adults (70¹/60² kg b.w.)</td> <td>0.42/0.49</td> <td>10.44/12.18</td> </tr> <tr> <td>Toddlers (12¹/10² kg b.w.)</td> <td>1.22/1.46</td> <td>30.45/36.55</td> </tr> <tr> <td>Infants (5 kg b.w.)</td> <td>2.19</td> <td>54.75</td> </tr> </tbody> </table>		Exposure (µg/kg b.w./d) (using default body weight values) ¹	% ADI (reference value of the parent substance: 0.004 mg/kg b.w./d)	Adults (70 ¹ /60 ² kg b.w.)	0.42/0.49	10.44/12.18	Toddlers (12 ¹ /10 ² kg b.w.)	1.22/1.46	30.45/36.55	Infants (5 kg b.w.)	2.19	54.75
		Exposure (µg/kg b.w./d) (using default body weight values) ¹	% ADI (reference value of the parent substance: 0.004 mg/kg b.w./d)											
	Adults (70 ¹ /60 ² kg b.w.)	0.42/0.49	10.44/12.18											
Toddlers (12 ¹ /10 ² kg b.w.)	1.22/1.46	30.45/36.55												
Infants (5 kg b.w.)	2.19	54.75												
According to WHO recommendation ³ , normal allocation of the total daily intake for chemicals with drinking water is 20% of ADI.														
<p>Conclusions:</p> <p>Taking into account the results of all available toxicological studies, the metabolite MT13 has no genotoxic potential. The results of consumer risk calculations indicate that the use of TERBUT 500 SC (La Zina 500 SC; Tekno 500 SC) according to the list of intended uses presented in GAP Table, can cause unacceptable risk for toddlers' and infants' health resulting from the exposure to the metabolite MT13.</p> <p>¹According to EFSA Journal 2012;10(3):2579, Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured data.</p> <p>²WHO Guidelines for drinking-water quality: fourth edition incorporating the first addendum, 2017</p> <p>³Guidelines for drinking-water quality, fourth edition. WHO, Geneva (2011).</p>														

For metabolite MT13 (2-hydroxy terbuthylazine), simulations gave PEC_{gw} values in the range from 0.29 to 14.62 µg/l (peak concentration with FOCUS PEARL Thivia, 500 g a.s./ha). In the simulations, which used a more conservative formation fraction highest PEC was 14.62 µg/l. Although the prediction of concentration in excess of 10µg/l may cause specific concerns in some MS, the RMS considers that these results represent conservative first tier exposure estimates only. **According to the Monitoring Studies for Tebuthylazine in ground water and EFSA Journal 2011; 9(1):1969:**The 2-hydroxy terbuthylazine metabolite was not detected above 0.1µg/l in the field leaching study performed in Northern Italy, even when other metabolites such as the desethyl-hydroxy terbuthylazine and the lysimeters leachate metabolites LM5 and LM6 were detected above 0.1µg/l as an annual average at some locations. In addition, this metabolite was only detected in two wells (at < 0.05µg/l) in an extensive and targeted German groundwater monitoring program. In further recent groundwater monitoring studies in Italy in maize growing regions, the 90th percentile concentration was only 0.03µg/l. On the basis of the additional information from field leaching and groundwater monitoring programs, it is clear that the first tier FOCUS groundwater exposure assessments based on conservative approach represent a very conservative assessment and such high concentrations are unlikely to be encountered under realistic use conditions.

Data on biological activity for MT13 (GS23158) have previously been assessed in the original DAR 2008 (Section B.9.9.1.2) and are copied at Attachment 1 of this document for convenience. It was concluded that these metabolites are not herbicidally active.

No new studies have been provided for MT13 in the resubmission(2010). MT13 was found to be of low acute oral toxicity in the rat. A NOAEL of 3.4 mg/kg bw/d was determined for a 90-day toxicity study in

the rat. An ADI for MT13 of 0.0034 mg/kg bw/d (3.4 µg/kg bw/d) can therefore be derived for MT13, based on the NOAEL from the 90-day study and applying a safety factor of 1000.

Table 6.4-2: Summary of the results of toxicity studies for MT13 hydroxy-terbuthylazine (GS 23158)

Type of test, species	Result	Acceptability	Reference*
Acute oral - RAT	LD50 > 2000 mg/kg bw.		xxxxxxxxxxxxx2001
90-day dietary rats	M: NOAEL and LOAEL of 16.7 and 34.1 mg/kg bw/day, based on decreased bodyweight, changes in clinical chemistry and urinalysis parameters and organ weight effects F: NOAEL and LOAEL of 0.7 and 7.6 mg/kg bw/day, based on altered oestrus cycle length and prolonged oestrus and/or dioestrus		xxxxxxxxxxxxx, 2002
Mutagenicity in bacterial cells (TA1535, TA1537, TA98, TA100, TA102, WP2uvrA)	negative		Deperate, 2001
Mouse micronucleus assay (L5178Y cells (TK))	Negative		xxxxxxxxxxxxx 2001
Calstogenicity (Human lymphocytes)	Negative		Fox, 2002

No studies are necessary.

No new studies have been provided for MT13. Data on biological activity for MT13 have previously been provided and it was concluded that it was not herbicidally active. MT13 was found to be of low acute oral toxicity in the rat; no evidence of genotoxicity was seen in a battery of studies *in vitro*. A NOAEL of 3.4 mg/kg bw/d was determined for a 90-day toxicity study in the rat. An ADI for MT13 of 0.0034 mg/kg bw/d (3.4 µg/kg bw/d) can therefore be derived for MT13, based on the NOAEL from the 90-day study and applying a safety factor of 1000.

MT13 was identified as a minor rat metabolite (<1%) in the Oxon metabolism study (DAR Table B.6.19; M13), but was not identified as a metabolite in the Syngenta study. As this metabolite is potentially an intermediate in the formation of MT14 (desethylhydroxy-terbuthylazine, GS 28620), systemic exposure may be higher but is not possible to quantify. MT13 is not considered to be a relevant metabolite according to current EC guidance.

6.4.3 MT14 desethyl-hydroxy terbuthylazine-terbuthylazine metabolite

Comments of ZRMs:	<ul style="list-style-type: none"> - According to the available data, the metabolite MT14 has no pesticidal activity and it is not genotoxic. - The maximum PEC_{gw} of MT14 (acc. to the application rate presented in the GAP table) amounts to 2.098676 µg/L. The predicted max. PEC_{gw} value exceeds the upper limit for the metabolites. Thus, the consumer risk calculation for this metabolite is required.
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	Exposure (µg/kg b.w./d) (using default body weight values) ¹	% ADI (reference value of the parent substance: 0.004 mg/kg b.w./d)
Adults (70 ¹ /60 ² kg b.w.)	0.06/0.07	1.5/1.75
Toddlers (12 ¹ /10 ² kg b.w.)	0.17/0.21	4.24/5.25
Infants (5 kg b.w.)	0.31	7.87

Conclusions:
 Taking into account the results of all available toxicological studies, the metabolite MT14 has no genotoxic potential. The results of consumer risk calculations indicate that the use of TERBUT 500 SC (La Zina 500 SC; Tekno 500 SC) according to the list of intended uses presented in GAP Table, **causes no unacceptable risk for health resulting from the exposure to the metabolite MT14.**

¹According to EFSA Journal 2012;10(3):2579, Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured data.
²WHO Guidelines for drinking-water quality: fourth edition incorporating the first addendum, 2017

For metabolite MT14 (desethyl-hydroxy terbuthylazine), simulations gave PEC_{gw} values up to 2.10 µg/l (peak concentration with FOCUS PEARL Hamburg, 500 g a.s./ha) Results represent conservative first tier exposure estimates. In the field leaching study in Northern Italy, annual average concentrations were found up to 0.38µg/l. In addition, this metabolite was only detected in two wells at concentrations between 0.05 to 0.06µg/l in an extensive and targeted German groundwater program. **According to the Monitoring Studies for Tebuthylazine in ground EFSA Journal 2011; 9(1):1969:**On the basis of the additional information from field leaching and German groundwater monitoring program, it is clear that the first tier FOCUS groundwater exposure assessment represents a very conservative assessment and such high concentrations are unlikely to be encountered under realistic use conditions.

An overview of the results of the accepted toxicological studies for groundwater metabolite MT14 is given in the following table. Full summaries of studies on the metabolite that have not previously been considered within an EU peer review process are described in detail in Appendix 2 (A 1.10 Other/Special Studies).

Table 6.4-3: Summary of the results of toxicity studies for MT14 desethyl-hydroxy terbuthylazine

Type of test, species	Result	Acceptability	Reference*
Acute oral LD50 (rats)	LD50> 2000 mg/kg bw.		XXXXXXXXXXXXXX
90-day dietary rats	NOAEL and LOAEL of 10.3 and 45.7 mg/kg bw/day, based on increased mortality and water consumption, changes in haematology,		XXXXXXXXXXXXXX

Type of test, species	Result	Acceptability	Reference*
	clinical chemistry and urinalysis parameters and increased kidney weight, renal (histo)pathology secondary to chronic renal failure.		
Mutagenicity in bacterial cells	negative		Deperade 2000
Clastogenicity in CHO (Chinese Hamster Ovary) cells	negative.		XXXXXXXXXXXXXXXX
Mouse Lymphoma assay	negative		XXXXXXXXXXXXXXXX

* indicates that a study was reviewed at EU level

MT14 was identified as a rat metabolite in studies submitted by both Notifiers. It was identified as a metabolite in urine and faeces, although not at very high levels in the studies by Syngenta ($\leq 7.8\%$; DAR Table B.6.18) and Oxon (4.41-11.6%, DAR Table B.6.19). MT14 is not considered to be a relevant metabolite according to current EC guidance.

6.4.4 LM1-terbuthylazine metabolite

Comments of ZRMs:	- According to EFSA Journal 2019;17(9):5817, the metabolite LM1 has no pesticidal activity (the compound is the breakdown product of LM5) and is not toxicologically relevant .
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The Notifiers have studies ongoing with this metabolite. The metabolite does not possess any structural alerts for genotoxicity according to DEREK and does not contain any additional functional groups that are not present in terbuthylazine or its metabolites (including metabolites MT1, MT13, MT14 and M20 which have been tested for genotoxicity). A mammalian gene mutation test is also available but was concluded too late to be included in the resubmission so has not been evaluated.

LM1 also known as ammelide is a mammalian metabolite of melamine. Melamine has a long history of use in a range of products i.e. in combination with formaldehyde to produce melamine resin as durable thermosetting plastics, and melamine foam, a polymeric cleaning product. Other end products include countertops, fabrics, glues and flame retardants. It is also a major component of pigment yellow 150 (colorant for inks and plastics), fertilizers, and derivatives of arsenical drugs for the treatment of African sleeping sickness (trypanosomiasis).

Melamine is a metabolite of cyromazine (an Annex I listed active substance see EFSA Scientific Report (2008) 168, 1-94 Conclusion on the peer review of cyromazine). The RMS produced an extensive review of the published literature on melamine and concluded melamine was found to have no toxicological relevance for groundwater according to the guidance document on groundwater metabolites. The RMS proposed to set an ADI of 0.063 mg/kg bw/day for melamine based on the review, however the meeting considered that the ADI of the parent (cyromazine) should be considered relevant for melamine risk assessment. The ADI for cyromazine was set at 0.06 mg/kg bw/day. Based on this it is likely toxicity of metabolite LM1 is less than that of terbuthylazine and the tested metabolites

6.4.5 LM2-terbuthylazine metabolite

The Notifiers have studies ongoing with this metabolite. The metabolite does not possess any structural alerts for genotoxicity according to DEREK and does not contain any additional functional

groups that are not present in terbuthylazine or its metabolites (including metabolites MT1, MT13, MT14 and M20 which have been tested for genotoxicity). An Ames test is also available but was concluded too late to be included in the resubmission so has not been considered.

LM2 contains an additional carboxylic acid functional group when compared to terbuthylazine and is a hydroxyl metabolite. Also it does not contain any additional functional groups that are not pre-sent in terbuthylazine or its metabolites (including metabolites MT1, MT13, MT14 and M20 which have been tested for genotoxicity). It can be reasonably predicted that the toxicity of metabolite LM2 is less than that of terbuthylazine and the tested metabolites.

6.4.6 LM3-terbuthylazine metabolite

Comments of ZRMs:	- Acc. to available data, the metabolite LM3 has no pesticidal activity and it is not genotoxic. The consumer risk for this metabolite cannot be concluded (no specific reference values could be derived on the basis of the available toxicological data).
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The Notifiers have provided an Ames assay with this metabolite and it is negative. The metabolite does not possess any structural alerts for genotoxicity according to DEREK and does not contain any additional functional groups that are not present in terbuthylazine or its metabolites (including metabolites MT1, MT13, MT14 and M20 which have been tested for genotoxicity). A mammalian gene mutation test is also available but was concluded too late to be included in the resubmission so has not been considered.

Metabolite LM3 contains an additional carboxylic acid functional group (when compared to terbuthylazine and the tested metabolites), but in this respect is structurally similar to the carboxylic acid metabolites MT5, MT8 (GS 33022) and MT10 (GS 31398). It can be reasonably predicted that the toxicity of metabolite LM3 is less than that of terbuthylazine and the tested metabolites.

6.4.7 LM4-terbuthylazine metabolite

The metabolite does not possess any structural alerts for genotoxicity according to DEREK and does not contain any additional functional groups that are not present in terbuthylazine or its metabolites (including metabolites MT1, MT13, MT14 and M20 which have been tested for genotoxicity) and is structurally very similar to MT13 and MT14. An Ames assay is also available but was concluded too late to be included in the resubmission so have not been considered.

The metabolite does not contain any additional functional groups that are not present in terbuthylazine or its metabolites (including metabolites MT1, MT13, MT14 and M20 which have been tested for genotoxicity) and is structurally very similar to MT13 and MT14 which have been tested for toxicity. Deleted comment assessment relies on consumer assessment below.

6.4.8 LM5-terbuthylazine metabolite

Comments of ZRMs:	- Acc. to the available data, the metabolite LM5 has no pesticidal activity and is not genotoxic. The maximum PEC_{gw} of LM5 (acc. to the application rate presented in the GAP table) amounts to 1.691832 $\mu\text{g/L}$. The predicted max. PEC_{gw} value exceeds the limit for metabolites ($>0.75 \mu\text{g/L}$) and the consumer risk calculation is required. The results of consumer risk calculations indicate that the use of TERBUT 500 SC (La Zina 500 SC; Tekno 500 SC) according to the list of intended uses presented in GAP Table, causes no unacceptable risk for health resulting from the exposure to the metabolite LM5.
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	Exposure ($\mu\text{g}/\text{kg b.w./d}$) (using default body weight values) ¹	% ADI (reference value of the parent substance: 0.004 mg/kg b.w./d)
Adults (70 ¹ /60 ² kg b.w.)	0.048/0.056	1.21/1.4
Toddlers (12 ¹ /10 ² kg b.w.)	0.14/0.17	3.5/4.25
Infants (5 kg b.w.)	0.25	6.34

¹According to EFSA Journal 2012;10(3):2579, Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured data.

The Notifiers have provided an Ames assay with this compound and it is negative. The metabolite does not possess any structural alerts for genotoxicity according to DEREK and does not contain any additional functional groups that are not present in terbuthylazine or its metabolites (including metabolites MT1, MT13, MT14 and M20 which have been tested for genotoxicity). An in-vitro chromosome aberration test and a mammalian gene mutation test are also available but were concluded too late to be included in the resubmission so have not been considered.

The metabolite does not contain any additional functional groups that are not present in ter-buthylazine or its metabolites (including metabolites MT1, MT13, MT14 and M20 which have been tested for genotoxicity). It can be reasonably predicted that the toxicity of metabolite LM5 is less than that of terbuthylazine.

6.4.9 LM6-terbuthylazine metabolite

Comments of ZRMs:	- Acc. to the available data, the metabolite LM6 has no pesticidal activity and is not genotoxic. The consumer risk for this metabolite cannot be concluded (no specific reference values could be derived on the basis of the available toxicological data).
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In the resubmission package the Notifiers have provided a reverse mutation assay, a mouse lymphoma assay, in vitro chromosome aberration study in Human Lymphocytes, and an in vivo rat bone marrow micronucleus test. Although positive at cytotoxic levels in the gene mutation assay overall it is considered non-genotoxic. The metabolite does not possess any structural alerts for genotoxicity according to DEREK and is structurally similar to MT13 and MT14.

The metabolite is structurally similar to MT13 and MT14. It can be reasonably predicted that the toxicity of metabolite LM6 is less than that of terbuthylazine.

6.5 Dermal Absorption (KCP 7.3)

Comments of ZRMs:	The information on the detailed composition of the representative formulation (Terbuthylazine 500 SC) provided during the evaluation is sufficient to conclude that TERBUT 500 SC and Terbuthylazine 500 SC are not similar formulations, however the differences in the composition of these product do not influence the dermal absorption. Additionally, the Applicant introduced a non-significant change in the composition of the product TERBUT 500 SC, which results in declassification regarding skin sensitization. The use of the absorption rates derived from a study performed on Terbuthylazine 500 SC (contained in the DAR for terbuthylazine) is acceptable and amounts to 0.1 and 2.5 % for concentrate and dilution, respectively.
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A summary of the dermal absorption rates for the active substances in TERBUT 500 SC are presented in the following table.

Table 6.5-1: Dermal absorption rates for active substances in TERBUT 500 SC

	Terbuthylazine	
	Value	Reference
Concentrate	0.10%	EFSA Journal 2011; 9(1):1969
Dilution (dilution factor)	2.50%	EFSA Journal 2011; 9(1):1969

6.5.1 Justification for proposed values - terbuthylazine

Dermal absorption studies for TERBUT 500 SC ~~500 SC~~ have not been performed but based on Guidance on Dermal Absorption (EFSA Journal 2017;15(6):4873) it could be assumed that TERBUT 500 SC is closely related to formulation which was evaluated as representative product in the EU review of terbuthylazine. According to composition of TERBUT 500 SC and Terbuthylazine 500 SC provide in DAR, the properties of the composition are compatible . Namely, the amount of active substance in Terbuthylazine 500 SC is higher by 1% than TERBUT 500 SC and this products represents of the same type of formulation. Additionally, the both of formulation have the same amount of water (44%) and additives (9%). Based on this information, it is consider that the use of dermal absorption data stated in EFSA Journal 2011; 9(1):1969 (that is 0.1% for concentrate and 2.5% for dilution) is justified.

Table 6.5-2: Default dermal absorption rates for terbuthylazine

	Value	Justification for value	Acceptability of justification
Concentrate	0.10%	EFSA Journal 2011; 9(1):1969	yes (see the explanation above)
Dilution	2.50%	EFSA Journal 2011; 9(1):1969	yes (see the explanation above)

6.6 Exposure Assessment of Plant Protection Product (KCP 7.2)

Table 6.6-1: Product information and toxicological reference values used for exposure assessment

Product name and code	TERBUT 500 SC
Formulation type	SC
Category	Herbicide
Active substance(s) (incl. content)	Terbuthylazine 500 g/L
AOEL systemic	0.0032 mg/kg bw/d
Inhalation absorption	100%
Oral absorption	100%
Dermal absorption	Concentrate: 0.10%

	Dilution: 2.50% (EFSA Journal 2011; 9(1):1969)*
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* The following values of dermal absorption of coming from representative dermal absorption study done on CLICK 500 SC presented during inclusion process of terbuthylazine on Annex I . The recipes of Click 500 SC and Terbut 500 SC are comparable which was confirmed during the evaluation process of following Terbut 500 SC dossier by polish Evaluators.

6.6.1 Selection of critical use(s) and justification

The critical GAP used for the exposure assessment of the plant protection product is shown in Table 6.1-4. A list of all intended uses within the zone is given in Part B, Section 0.

6.6.2 Operator exposure (KCP 7.2.1)

Comments of zRMS:	<p>The calculations of operator exposure to terbuthylazine contained on the formulation Terbut 500 SC (La Zina 500 SC; Tekno 500 SC) presented by the Applicant are accepted.</p> <p><u>Conclusions:</u></p> <p>According to the estimations based on AOEM, the use of Terbut 500 SC causes acceptable health risk for operator equipped with PPE. The operator exposure to the active substance amounts to a lower value than the AOEL when operator is equipped with protective gloves and work wear during mixing and loading.</p> <p>Thus, the following sentence regarding the use of PPE is recommended by the evaluator to be placed in the label:</p> <p><i>„Stosować rękawice ochronne oraz odzież roboczą (kombinezon) w trakcie przygotowywania cieczy roboczej oraz wykonywania zabiegu”</i> “Wear protective gloves and work wear (coverall) during mixing/loading and application”.</p>
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6.6.2.1 Estimation of operator exposure

A summary of the exposure models used for estimation of operator exposure to the active substances during application of TERBUT 500 SC according to the critical use(s) is presented in Table 6.6-2. The outcome of the estimation is presented in Table 6.6-3 (acute exposure) and **Błąd! Nie można odnaleźć źródła odwołania.** (longer term exposure). Detailed calculations are in Appendix 3.

Table 6.6-2: Exposure models for intended uses

Critical use(s)	TERBUT 500 SC (max. 1 L product/ha)
Model(s)	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015

Table 6.6-3: Estimated operator exposure (acute exposure)

Model data	Level of PPE	Terbutylazine	
		Total absorbed dose (mg/kg/day)	% of systemic AAOEL
Tractor mounted boom spray application outdoors to low crops Application rate: 0.5 kg a.s./ha			
“EFSA Model” version 30.03.2015	no PPE*	0.0042547	132.96
	+ type of PPE (e.g. Gloves mixing/loading)	0.0027303	85.32
	+ type of PPE	0.0012866	40.21

6.6.2.2 Measurement of operator exposure

Since the operator exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and consideration of the above mentioned personal protective equipment (PPE), a study to provide measurements of operator exposure was not necessary and was therefore not performed.

6.6.3 Worker exposure (KCP 7.2.3)

Comments of zRMS:	<p>The estimations of worker exposure to the active substance contained in Terbut 500 SC (based on EUROPOEM II) performed by the Applicant are accepted.</p> <p><u>Conclusions:</u> According to the estimation results, the use of Terbut 500 SC (La Zina 500 SC; Tekno 500 SC) containing terbuthylazine (500 g/L) does not cause unacceptable health risk for a worker wearing work wear and protective gloves during field inspection, even in case of 8h exposure. Nevertheless, it is forbidden to re-enter area treated with Terbut 500 SC (La Zina 500 SC; Tekno 500 SC) until spray deposit on plant surfaces has dried. Following sentence regarding the use of PPE is recommended by the evaluator to be placed in the section of precautions for the workers: <i>„Stosować rękawice ochronne oraz odzież roboczą (długie spodnie, koszula z długim rękawem) podczas inspekcji terenu poddanego opryskowi.”</i> “Wear protective gloves and workwear (long trousers, long-sleeve shirt) during inspection of treated area”.</p>
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6.6.3.1 Estimation of worker exposure

Table 6.6-4 shows the exposure model(s) used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with TERBUT 500 SC according to the critical use(s). Outcome of the estimation is presented in Table 6.6-5 (acute exposure) and **Błąd! Nie można odnaleźć źródła odwołania.** (longer term exposure). Detailed calculations are in Appendix 3.

Table 6.6-4: Exposure models for intended uses

Critical use(s)	TERBUT 500 SC (max. 1 L product/ha)
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015 EUROPOEM II

Table 6.6-5: Estimated worker exposure (acute exposure)

		Terbutylazine	
Model data	Level of PPE	Total absorbed dose (mg/kg bw/day)	% of systemic AAOEL
Application rate		0.500 kg a.s./ha	
8 hours/day(1), TC: 0.25 cm ² /person/h (2) Body weight: 60 kg	no PPE ⁽³⁾	0.0125	391
	with PPE ⁽⁴⁾	0.0025	78

According to ~~Guidance on Pesticides Exposure Assessment of Operators, Workers, Residents and Bystanders, (EFSA Journal 2014;12(10):3874)~~ EUROPOEM II to the calculation used the value of 2500 transfer coefficient (TC (cm²/h) arms, body and legs covered - workwear; bare hands) and 8 hours work/day (only crop inspection and irrigation-type). Having regard to the above values, the predicted exposure values for TERBUT 500 SC with PPP are significantly below 100% of systemic AOEL and therefore exposure of the worker with using PPP is acceptable

6.6.3.2 Refinement of generic DFR value (KCP 7.2)

Not required.

6.6.3.3 Measurement of worker exposure

Since the worker exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and considering above mention PPE, a study to provide measurements of worker exposure was not necessary and was therefore not performed.

6.6.4 Resident and bystander exposure (KCP 7.2.2)

Comments of zRMS:	<p>The reference value acutely toxic active substance (RVAAS) for the terbutylazine is not allocated. Consequently, it is assumed that the estimation of bystander exposure is covered by the calculation of resident exposure towards the active substance and its metabolite.</p> <p>The estimations of resident exposure provided by the Applicant are accepted.</p> <p><u>Conclusions:</u></p> <p>The exposure of bystander and resident (children and adult) to Terbut 500 SC (La Zina 500 SC; Tekno 500 SC) causes acceptable risk to human health if:</p> <ul style="list-style-type: none"> • min. 5-meter buffer zone is kept during spraying,
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	<ul style="list-style-type: none"> • drift-reduction nozzles are used. <p>Following sentence regarding the use of risk mitigation measures is recommended by the evaluator to be placed in the section of precautions for bystander/resident:</p> <p>„Podczas wykonywania zabiegu należy zachować 5 metrową strefę buforową oraz dysze ograniczające znos”.</p> <p>“Keep a 5 meter buffer zone and drift-reduction nozzles during application”.</p>
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6.6.4.1 Estimation of resident and bystander exposure

The acute exposure assessment for bystanders covers the exposure that a resident could reasonably be expected to incur in a single day. Therefore, there is no need for a separate acute risk assessment for residents.

No bystander risk assessment is required for PPPs that do not have significant acute toxicity or the potential to exert toxic effects after a single exposure. Exposure in this case will be determined by average exposure over a longer duration, and higher exposures on one day will tend to be offset by lower exposures on other days. Therefore, exposure assessment for residents also covers bystander exposure.

Table 6.6-6 shows the exposure model(s) used for estimation of resident and bystander exposure to terbuthylazine. The outcome of the estimation is presented in **Błąd! Nie można odnaleźć źródła odwołania.** (longer term resident exposure) and

Critical use(s)	TERBUT 500 SC (max.1L product/ha)
Model	“EFSA Model” version 30.03.2015

Table 6.6-7 (acute bystander exposure). Detailed calculations are in Appendix 3.

Table 6.6-6: Exposure models for intended uses

Critical use(s)	TERBUT 500 SC (max.1L product/ha)
Model	“EFSA Model” version 30.03.2015

Table 6.6-7: Estimated resident exposure (longer term exposure)

	Terbuthylazine	
Model data	Total absorbed dose (mg/kg/day)	% of systemic AOEL
Tractor mounted boom spray application outdoors to low crops Application rate: 0.5 kg a.s./ha		
Bystanders (adult) Drift rate: 0.47 (1 m) Body weight: 60 kg	0.0014211	44.41
Bystanders (children) Drift rate: 0.327 (1 m) Body weight: 10 kg	0.0041474	129.61
Residents (adult) Drift rate: 0.47 (1 m) Body weight: 60 kg	0.0014211	44.41
Residents (children)	0.0041474	129.61

Drift rate: 0.327 (1 m) Body weight: 10 kg		
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Exposure for children exceed a trigger value of 100% for systemic AOEL. Therefore, vehicle mounted drift reduction with 5 meters buffer zone have to be concerned to risk refinement.

Table 6.6-8: Estimated resident exposure (longer term exposure) – risk refinement

	Terbutylazine	
Model data	Total absorbed dose (mg/kg/day)	% of systemic AOEL
Tractor mounted with drift reduction boom spray application outdoors to low crops Application rate: 0.5 kg a.s./ha		
Bystanders (adult) Drift rate: 0.24 (5 meters) Body weight: 60 kg	0.0012322	38.51
Bystanders (children) Drift rate: 0.22 (5 meters) Body weight: 10 kg	0.0031714	99.11
Residents (adult) Drift rate: 0.24 (5 meters) Body weight: 60 kg	0.0012322	38.51
Residents (children) Drift rate: 0.22 (5 meters) Body weight: 10 kg	0.0031714	99.11

6.6.4.2 Measurement of resident and/or bystander exposure

Since the resident and/or bystander exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) for terbutylazine will not be exceeded under conditions of intended uses and considering above mentioned risk mitigation measures, a study to provide measurements of resident/bystander exposure was not necessary and was therefore not performed.

6.6.5 Combined exposure

Not relevant. The product contains only one active substance.

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
KCP 7	M. Kolodziej	2021	Toxicological classification of product TERBUT 500 SC 500 SC based on calculation method taking into consideration health hazards of constituent substances. Chemiroł Sp. z o.o non GLP Unpublished	N	Chemiroł Sp. z o.o.

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
KCP 7.0/01	Verspeek-Rip. C.M.	2002	EVALUATION OF THE MUTAGENIC ACTIVITY OF 2-HYDROXY-TERBUTHYLAZINE IN THE SALMONELLA TYPHIMURIUM REVERSE MUTATION ASSAY AND THE ESCHERICHIA COLI REVERSE MUTATION ASSAY (WITH INDEPENDENT REPEAT) Notox B.V s'Hertogenbosch, The Netherlands Report N. 335543 Oxon Italia S.p.A, Pero, Italy GLP: yes published: no	N	OXN
KCP 7.0/02	Verspeek-Rip. C.M.	2002	EVALUATION OF THE MUTAGENIC ACTIVITY OF 2-HYDROXY-TERBUTHYLAZINE IN AN <i>IN VITRO</i> MAMMALIAN CELL GENE MUTATION TEST WITH L5178Y MOUSE LYMPHOMA CELLS (WITH INDEPENDENT REPEAT) Notox B.V s'Hertogenbosch, The Netherlands Report N. 335554 Oxon Italia S.p.A, Pero, Italy GLP: yes published: no	N	OXN
KCP 7.0/03	xxxxxxxxxxxx	2002	ASSESSMENT OF ACUTE ORAL TOXICITY WITH 2-HYDROXY-TERBUTHYLAZINE IN THE RAT (ACUTE CLASS METHOD) [REDACTED] Report N. 335532 Oxon Italia S.P.A, Pero, Italy GLP: yes published: no	Y	OXN

KCP 7.0/04	Meerts I.	2002	EVALUATION OF THE ABILITY OF 2-HYDROXY-TERBUTHYLAZINE TO INDUCE CHROMOSOME ABERRATIONS IN CULTURED PERIPHERAL HUMAN LYMPHOCYTES Notox B.V s'Hertogenbosch, The Netherlands Report N. 335565 Oxon Italia S.p.A, Pero, Italy GLP: yes published: no	N	OXN
KCP 7.0/05	xxxxxxxxxxx	2003	2-HYDROXY-TERBUTHYLAZINE: REPEATED DOSE 90 DAY ORAL TOXICITY STUDY IN WISTAR RATS [REDACTED] Report N. 3345-01 Oxon Italia S.p.A, Pero, Italy GLP: yes published: no	Y	OXN
KCP 7.0/06	xxxxxxxxxxx	2001	GS 28620 TECH. (METABOLITE OF GS 13529) - 90-DAY ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD), [REDACTED] [REDACTED] 20001005, 14.12.2001	Y	OXN (SYN access)
KCP 7.0/07	xxxxxxx	2001	GS 23158 (METABOLITE OF GS 13529): L5178Y TK+/- MOUSE LYMPHOMA MUTATION ASSAY, [REDACTED] [REDACTED] CTL/VV0268/REG/REPT / 20011055, 12.12.2001	Y	OXN (SYN access)
KCP 7.0/08	Deperate E.	2000	GS 28620 (METABOLITE OF GS 13529) - SALMONELLA AND ESCHERICHIA/MAMMALIAN-MICROSOME MUTAGENICITY TEST, Novartis Crop Protection AG, Stein, Switzerland, 20001001, 21.08.2000	N	OXN (SYN access)

KCP 7.0/09	Deperade E.	2001	GS 23158 TECH. (METABOLITE OF GS 13529) - SALMONELLA AND ESCHERICHIA/MAMMALIAN-MICROSOME MUTAGENICITY TEST, Syngenta Crop Protection Ag. Stein, Switzerland, 20011054, 12.12.2001	N	OXN (SYN access)
KCP 7.0/10	Fox V.	2002	GS 23158: IN VITRO CYTOGENETIC ASSAY IN HUMAN LYMPHOCYTES, Central Toxicology Laboratory (CTL), Cheshire, United Kingdom, CTL/SV1087/REG/REPT, 18.01.2002	N	OXN (SYN access)
KCP 7.0/11	Lloyd M.	2000	GS 28620 (METABOLITE OF GS 13529): MUTATION AT THE THYMIDINE KINASE (TK) LOCUS OF MOUSE LYMPHOMA L5178Y CELLS (MLA) USING THE MICROTITRE FLUCTUATION TECHNIQUE. [REDACTED] 252/268-D5140 / 20001002, 16.05.2000	N	OXN (SYN access)
KCP 7.0/12	Marshall R.	2001	GS 28620 (METABOLITE OF GS 13529): INDUCTION OF CHROMOSOME ABERRATIONS IN CULTURED CHINESE HAMSTER OVARY (CHO) CELLS, Covance Laboratories, North Yorkshire, United Kingdom, 252/269-D6172 / 20001003, 07.03.2001	N	OXN (SYN access)
KCP 7.0/13	xxxxxxx.	2000	GS 28620 TECH. (METABOLITE OF GS 13529) - ACUTE ORAL TOXICITY IN THE RAT (LIMIT TEST), [REDACTED] 20001004, 03.02.2000	Y	OXN (SYN access)
KCP 7.0/14	xxxxxxx	2001	GS 23158 TECH. (METABOLITE OF GS 13529) - ACUTE ORAL TOXICITY IN THE RAT (LIMIT TEST), [REDACTED] 20011053, 25.04.2001	Y	OXN (SYN access)

KCP 7.0/15	xxxxxxxxx.	2002	GS 23158 TECH. (METABOLITE OF GS 13529) - 90-DAY ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD), [REDACTED] 20011058, 18.12.2002	Y	OXN (SYN access)
KCP 7.0/16	xxxxxxxxxxxxxxxx	2000	GS 28620 tech. (Metabolite of GS 13529) – Acute oral toxicity in the rat (Limit test) Novartis Crop Protection AG, Basel, Switzerland [REDACTED] [REDACTED] Report No 20001004 GLP Not Published Syngenta File N° GS28620/0005	Y	SYN
KCP 7.0/17	xxxxxxxxxxxxxxxx	2001	GS 28620 tech. (Metabolite of GS 13529) – 90-Day oral toxicity study in rats (Administration in food) Syngenta Crop Protection AG, Basel, Switzerland [REDACTED] [REDACTED] Report No 20001005 GLP Not Published Syngenta File N° GS28620/0012	Y	SYN
KCP 7.0/18	Deperate E.	2000	GS 28620 (Metabolite of GS 13529) – Salmonella and Escherichia/mammalian-microsome mutagenicity test Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection AG, Stein, Switzerland, Report No 20001001 GLP Not Published Syngenta File N° GS28620/0010	N	SYN

KCP 7.0/19	Lloyd. M	2000	GS 28620 (Metabolite of GS 13529); Mutation at the thymidine kinase (tk) locus of mouse lymphoma L5178Y cells (MLA) using the microtitre fluctuation technique Novartis Crop Protection AG, Basel, Switzerland [REDACTED] [REDACTED] Report No 252/268-D51409 20001002 GLP Not Published Syngenta File N° GS28620/0007	N	SYN
KCP 7.0/20	Marshall R.	2001	GS 28620 (Metabolite of GS 13529); Induction of chromosome aberrations in cultured Chinese hamster ovary (CHO) cells Syngenta Crop Protection AG, Basel, Switzerland Covance Laboratories, North Yorkshire, United Kingdom, Report No 252/269-D6172 / 20001003 GLP Not Published Syngenta File N° GS28620/0011	N	SYN
KCP 7.0/21	xxxxxxxxxxxx	2001	GS 23158 tech. (Metabolite of GS 13529) – Acute oral toxicity in the rat (Limit test) Syngenta Crop Protection AG, Basel, Switzerland [REDACTED] [REDACTED] Report No 20011053 GLP Not Published Syngenta File N° GS23158/0010	Y	SYN

KCP 7.0/22	xxxxxxx.	2002	GS 23158 tech. (Metabolite of GS 13529) – 90-day oral toxicity study in rats (Administration in food) Syngenta Crop Protection AG, Basel, Switzerland [REDACTED] Report No 20011058 GLP Not Published Syngenta File N° GS23158/0020	Y	SYN
KCP 7.0/23	Deperate E.	2001	GS 23158 tech. (Metabolite of GS 13529) – Salmonella and Escherichia/mammalian- microsome mutagenicity test Syngenta Crop Protection AG, Basel, Switzerland Syngenta Crop Protection AG, Stein, Switzerland, Report No 20011054 GLP Not Published Syngenta File N° GS23158/0012	N	SYN
KCP 7.0/24	Fox V.	2002	GS 23158: In vitro cytogenetic assay in human lymphocytes Syngenta Crop Protection AG, Basel, Switzerland Central Toxicology Laboratory (CTL), Cheshire, United Kingdom, Report No CTL/SV1087/REG/REPT GLP Not Published Syngenta File N° GS23158/0013	N	SYN

KCP 7.0/25	Clay P.	2001	GS 23158 (Metabolite of GS 13529): L5178Y TK+/- mouse lymphoma mutation assay Syngenta Crop Protection AG, Basel, Switzerland [REDACTED] [REDACTED] Report No CTL/VV0268/REG/REPT / 20011055 GLP Not Published Syngenta File N° GS23158/0011	N	SYN
KCP 7.0/26	xxxxxxxxxxxx	1991	G28273 – Acute oral toxicity study in rats. Novartis Crop Protection AG, Basel, Switzerland [REDACTED] Report No 7801-91 GLP Not Published Syngenta File N° G28273/0034	Y	SYN
KCP 7.0/27	xxxxxxxxxxxx	1991	G28273 Diaminochlorotriazine – 90-day oral toxicity study in rats Novartis Crop Protection AG, Basel, Switzerland [REDACTED] [REDACTED] Report No F-00006 GLP Not Published Syngenta File N° G28273/0017	Y	SYN
KCP 7.0/28	Deperate E.	1987	G 28273 tech. – Salmonella/mammalian- microsome mutagenicity test Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No 871372 GLP Not Published Syngenta File N° G28273/0007	N	SYN

KCP 7.0/29	Strasser F.	1988	G28273 technical – Micronucleus test mouse Novartis Crop Protection AG, Basel, Switzerland [REDACTED] Report No 871369 GLP Not Published Syngenta File N° G28273/0006	N	SYN
KCP 7.0/30	xxxxxxxxxxxxx	2003	GS26379: Acute Oral Toxicity Study in the Rat – Up and Down Procedure Syngenta Crop Protection AG, Basel, Switzerland [REDACTED] [REDACTED] Report No AR7315 GLP Not Published Syngenta File N° GS26379/0020	Y	SYN
KCP 7.0/31	Callander R.	2003	GS26379: Bacterial Mutation Assay in S.Typhimurium and E.Coli Syngenta Crop Protection AG, Basel, Switzerland Central Toxicology Laboratory (CTL), Cheshire, United Kingdom, Report No YV6393 GLP Not Published Syngenta File N° GS26379/0021	N	SYN
KCP 7.0/32	Fox V.	2003	GS 26379: In Vitro Cytogenetic Assay in Human Lymphocytes Syngenta Crop Protection AG, Basel, Switzerland Central Toxicology Laboratory (CTL), Cheshire, United Kingdom, Report No SV1196 GLP Not Published Syngenta File N° GS26379/0022	N	SYN

KCP 7.0/33	xxxxxxx	1995	<p>2-year dietary chronic toxicity /oncogenicity study with G34048 technical in rats.</p> <p>Report No. F-00125 GLP: Yes Published: No Syngenta file No. G34048/0046</p>	Y	SYN
KCP 7.0/34	xxxxxxxxxxxx	2004	<p>Assessment of acute oral toxicity with terbuthylazine-desethyl in the rat (acute class method)</p> <p>Oxon Italia S.p.A. GLP, not published File No GS13529_10043</p>	Y	OXON
KCP 7.0/35	Verspeek-Rip C.M.	2004	<p>Evaluation of the mutagenic activity of terbuthylazine-desethyl in the Salmonella Typhimurium reverse mutation assay and the Escherichia Coli reverse mutation assay (with independent repeat)</p> <p>Oxon Italia S.p.A. NOTOX B.V., Hertogenbosch, Netherlands 400826 GLP, not published File No GS13529_10044</p>	N	OXON
KCP 7.0/36	Jones E.	2004	<p>GS 26379: L5178Y TK+/- Mouse Lymphoma Mutation Assay</p> <p>Syngenta Crop Protection AG, Basel, Switzerland Central Toxicology Laboratory (CTL), Cheshire, United Kingdom, VV0297-REG GLP, not published File No GS26379/0024</p>	N	SYN: oxon has data access

KCP 7.0/37	xxxxxxxxxx	2006	GS26379: Rat Bone Marrow Micronucleus Test Syngenta Crop Protection AG, Basel, Switzerland [REDACTED] GLP, not published File No GS26379/0026	Y	SYN: oxon has data access
KCP 7.0/38	xxxxxxxxxx	2006a	GS26379: In Vivo Rat Liver Unscheduled DNA Synthesis Assay Syngenta Crop Protection AG, Basel, Switzerland [REDACTED] GLP, not published File No GS26379/0025	Y	SYN: oxon has data access
KCP 7.0/39	xxxxxxxxxx	1971	90-Day subacute oral toxicity study with GS 26379 technical in albino rats. Novartis Crop Protection AG, Basel, Switzerland [REDACTED] Not GLP, not published File No GS26379/0001	Y	SYN: oxon has data access
KCP 7.0/40	Verspeek-Rip C.M.	2002a	Evaluation of the mutagenic activity of 2- hydroxy-terbutylazione in the <i>Salmonella</i> <i>typhimurium</i> reverse mutation assay and the <i>Escherichia coli</i> reverse mutation assay (with independent repeat) Notox B.V s'Hertogenbosch, The Netherlands Report N. 335543 Oxon Italia S.p.A, Pero, Italy GLP: Yes published: No	N	OXON (SYN access)

KCP 7.0/41	Verspeek-Rip C.M.	2002b	Evaluation of the mutagenic activity of 2-hydroxy-terbuthylazine in an <i>in vitro</i> mammalian cell gene mutation test with 15178y mouse lymphoma cells (with independent repeat) Notox B.V s'Hertogenbosch, The Netherlands Report N. 335554 Oxon Italia S.p.A, Pero, Italy GLP: Yes published: No	N	OXON (SYN access)
KCP 7.0/42	xxxxxxxxxxxxxx	2002	Assessment of acute oral toxicity with 2-hydroxy-terbuthylazine in the rat (acute class method) [REDACTED] Report N. 335532 Oxon Italia S.P.A, Pero, Italy GLP: Yes Published: No	Y	OXON (SYN access)
KCP 7.0/43	Meerts I.	2002	Evaluation of the ability of 2-hydroxy-terbuthylazine to induce chromosome aberrations in cultured peripheral human lymphocytes. Notox B.V s'Hertogenbosch, The Netherlands Report N. 335565 Oxon Italia S.p.A, Pero, Italy GLP: Yes published: No	N	OXON (SYN access)
KCP 7.0/44	xxxxxxx	2003	2-Hydroxy-terbuthylazine: repeated dose 90 day oral toxicity study in Wistar rats. [REDACTED] Report N. 3345-01 GLP: Yes Published: No	Y	OXON (SYN access)

KCP 7.0/45	Moxon M.	2003	GS 13529: Subchronic Neurotoxicity Study in Rats Syngenta Crop Protection AG, Basel, Switzerland [Redacted] [Redacted] Report No PR1228 GLP Not Published Syngenta File N° GSI3529/1839		N	SYN
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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 Detailed evaluation of the studies relied upon

A 2.1 Statement on bridging possibilities

Comments of zRMS:	Based on the results of the calculation (for details check dRR part C) and in accordance with the provisions of the Regulation EC 1272/2008, the formulation TERBUT 50 SC does not require classification in regards to acute oral toxicity.
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A 1.1 Acute oral toxicity (KCP 7.1.1)

Reference:	7
Report	Toxicological classification of product TERBUT 500 SC based on calculation method taking into consideration health hazards of constituent substances.; M. Kolodziej, 2021
Guideline(s):	Yes (methods used comparable to Regulation (EC) 1272/2008)
Deviations:	No
GLP:	No
Acceptability:	Yes
Duplication (if vertebrate study)	No

According to point 7.1.1 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:

” A test for acute oral toxicity shall be carried out, unless the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, acute oral toxicity of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the toxic potential of the total mixture.”

The complete composition of the formulation with the classification of individual ingredients is available in part C.

Due to the fact, that all components of the formulation TERBUT 500 SC are known, the acute oral toxicity test is not necessary.

Materials and methods

We use the summation method using the formula:

$$ATE_{mix} = \frac{100}{\sum_{i=1}^n \frac{C_i}{ATE_i}}$$

Where:

- C_i - concentration of ingredient i (% w/w or % v/v)
- i – the individual ingredient from 1 to n

- n – the number of ingredients
- ATE_i - Acute Toxicity Estimate of ingredient i.

We use the table:

Table 3.1.2

Conversion from experimentally obtained acute toxicity range values (or acute toxicity hazard categories) to acute toxicity point estimates for classification for the respective routes of exposure.

Exposure routes	Classification Category or experimentally obtained acute toxicity range estimate	Converted acute toxicity point estimate (see Note 1)
Oral (mg/kg body-weight)	0 < Category 1 ≤ 5	0,5
	5 < Category 2 ≤ 50	5
	50 < Category 3 ≤ 300	100
	300 < Category 4 ≤ 2 000	500
Dermal (mg/kg bodyweight)	0 < Category 1 ≤ 50	5
	50 < Category 2 ≤ 200	50
	200 < Category 3 ≤ 1 000	300
	1 000 < Category 4 ≤ 2 000	1 100
Gases (ppmV)	0 < Category 1 ≤ 100	10
	100 < Category 2 ≤ 500	100
	500 < Category 3 ≤ 2 500	700
	2 500 < Category 4 ≤ 20 000	4 500
Vapours (mg/l)	0 < Category 1 ≤ 0,5	0,05
	0,5 < Category 2 ≤ 2,0	0,5
	2,0 < Category 3 ≤ 10,0	3
	10,0 < Category 4 ≤ 20,0	11
Dust/mist (mg/l)	0 < Category 1 ≤ 0,05	0,005
	0,05 < Category 2 ≤ 0,5	0,05
	0,5 < Category 3 ≤ 1,0	0,5
	1,0 < Category 4 ≤ 5,0	1,5

Note 1

These values are designed to be used in the calculation of the ATE for classification of a mixture based on its components and do not represent test results.

Results and discussions

Ingredients A and F₁ are classified in this class of hazard.

- A – 45.86% (Acute Tox. 4, H302; LD₅₀ = 1000 mg/kg bw)
- F₁ – 0.0225% (Acute Tox. 4, H302)

LD₅₀ for an ingredient A was used to the calculations (according to manufacturer MSDS). For the rest of ingredients the estimated values were taken.

$$ATE_{mix} = \frac{100}{\sum_{i=1}^n \frac{C_i}{ATE_{mix}}} = \frac{100}{\frac{45.86}{1000} + \frac{0.0225}{500}} = 2178$$

Conclusion

According to the table 3.1.2, a result (2 178 mg/kg bw > 2 000 mg/kg bw) does not classify the whole formulation as Acute Tox. 4, H302.

A 1.2 Acute percutaneous (dermal) toxicity (KCP 7.1.2)

Comments of zRMS:	Based on the results of the calculation (for details check dRR part C) and in accordance with the provisions of the Regulation EC 1272/2008, the formulation TERBUT 500 SC does not require classification in regards to acute dermal toxicity.
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A 1.2.1 Acute dermal toxicity

Reference:	7
Report	Toxicological classification of product TERBUT 500 SC based on calculation method taking into consideration health hazards of constituent substances.; M. Kolodziej, 2021
Guideline(s):	Yes (methods used comparable to Regulation (EC) 1272/2008)
Deviations:	No
GLP:	No
Acceptability:	Yes
Duplication (if vertebrate study)	No

According to point 7.1.2 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:

”A test for dermal toxicity shall be carried out on a case by case basis, unless the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, acute dermal toxicity of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the toxic potential of the total mixture.

Findings of severe skin irritation or corrosion in the dermal study may be used instead of performing a specific irritation study.”

The complete composition of the formulation with the classification of individual ingredients is available in part C.

Due to the fact, that all components of the formulation TERBUT 500 SC are known, the acute dermal toxicity test is not necessary.

Materials and methods

The active substances and the other co-formulants are not classified as acute, dermal toxic, it can be assumed that entire formulation is not classified in this class.

Conclusion

According to point 7.1.2 of part A of Annex Regulation No 284/2014, it is possible to waive from performing acute dermal toxicity tests.

A 1.3 Acute inhalation toxicity (KCP 7.1.3)

Comments of zRMS:	Based on the results of the calculation (for details check dRR part C) and in accordance with the provisions of the Regulation EC 1272/2008, the formulation TERBUT 500 SC does not require classification in regards to acute inhalation toxicity.
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A 1.3.1 Acute inhalation toxicity

Reference:	7
Report	Toxicological classification of product TERBUT 500 SC based on calculation method taking into consideration health hazards of constituent substances.; M. Kolodziej, 2021
Guideline(s):	Yes (methods used comparable to Regulation (EC) 1272/2008)
Deviations:	No
GLP:	No
Acceptability:	Yes
Duplication (if vertebrate study)	No

According to point 7.1.3 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:

” A study shall not be required if the applicant can justify an alternative approach under Regulation (EC) No 1272/2008, where applicable. For this purpose, acute inhalation toxicity of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the toxic potential of the total mixture.”

The complete composition of the formulation with the classification of individual ingredients is available in part C.

Due to the fact, that all components of the formulation TERBUT 500 SC are known, the acute inhalation toxicity test is not necessary.

Materials and methods

The active substance and the other co-formulants are not classified as acute, inhalation toxic, it can be assumed that entire formulation is not classified in this class.

Conclusion

According to point 7.1.3 of part A of Annex Regulation No 284/2014, it is possible to waive from performing acute inhalation toxicity tests.

A 1.4 Skin irritation (KCP 7.1.4)

Comments of	Based on the results of the calculation (for details check dRR part C) and in accordance
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zRMS:	with the provisions of the Regulation EC 1272/2008, the formulation TERBUT 500 SC does not require classification in regards to corrosive/irritant effect to the skin.
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A 1.4.1 Skin Corrosion

Reference:	7
Report	Toxicological classification of product TERBUT 500 SC based on calculation method taking into consideration health hazards of constituent substances.; M. Kolodziej, 2021
Guideline(s):	Yes (methods used comparable to Regulation (EC) 1272/2008)
Deviations:	No
GLP:	No
Acceptability:	Yes
Duplication (if vertebrate study)	No

According to point 7.1.4 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:

”The skin irritancy of the plant protection product shall be reported based on the tiered approach, unless the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, skin irritation properties of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the irritant potential of the total mixture.”

The complete composition of the formulation with the classification of individual ingredients is available in part C.

Due to the fact, that all components of the formulation TERBUT 500 SC are known, skin corrosive test is not necessary.

Materials and methods

For consideration of corrosive and irritant properties the following table applies:

Table 3.2.3

Generic concentration limits of ingredients classified for skin corrosive/irritant hazard (Category 1 or 2) that trigger classification of the mixture as corrosive/irritant to skin.

Sum of ingredients classified as:	Concentration triggering classification of a mixture as:	
	Skin Corrosive	Skin Irritant
	Category 1 (see note below)	Category 2
Skin Corrosive Categories 1A, 1B, 1C	≥ 5 %	≥ 1 % but < 5 %
Skin irritant Category 2		≥ 10 %
10 × Skin Corrosive Category 1A, 1B, 1C) + Skin irritant Category 2		≥ 10 %

Note

The sum of all ingredients of a mixture classified as Skin Corrosive Category 1A, 1B or 1C respectively, shall each be ≥ 5 % respectively in order to classify the mixture as either Skin Corrosive Category 1A, 1B or 1C. If the sum of the Skin Corrosive Category 1A ingredients is < 5 % but the sum of Category 1A+1B ingredients is ≥ 5 %, the mixture shall be classified as Skin Corrosive Category 1B. Similarly, if the sum of Skin Corrosive Category 1A+1B ingredients is < 5 % but the sum of Category 1A+1B+1C ingredients is ≥ 5 % the mixture shall be classified as Skin Corrosive Category 1C.

Results and discussions

Only ingredient F₂ is relevant.

- F₂ –0.009% (Skin Corr. 1A, H314)

The concentration of an ingredient F₂ is significantly lower than concentration triggering classification (0.5 %). Therefore the formulation is not classified as Skin Corr. 1A, H314.

Conclusion

The concentration of an ingredient F₂ is significantly lower than concentration triggering classification (0.5 %). Therefore the formulation is not classified as Skin Corr. 1A, H314.

A 1.4.2 Skin Irritation

Reference:	7
Report	Toxicological classification of product TERBUT 500 SC based on calculation method taking into consideration health hazards of constituent substances.; M. Kolodziej, 2021
Guideline(s):	Yes (methods used comparable to Regulation (EC) 1272/2008)
Deviations:	No
GLP:	No
Acceptability:	Yes
Duplication (if vertebrate study)	No

According to point 7.1.4 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:

”The skin irritancy of the plant protection product shall be reported based on the tiered approach, unless the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, skin irritation properties of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the irritant potential of the total mixture.”

The complete composition of the formulation with the classification of individual ingredients is available in part C.

Due to the fact, that all components of the formulation TERBUT 500 SC are known, skin corrosive test is not necessary.

Materials and methods

For consideration of corrosive and irritant properties the following table applies:

Table 3.2.3

Generic concentration limits of ingredients classified for skin corrosive/irritant hazard (Category 1 or 2) that trigger classification of the mixture as corrosive/irritant to skin.

Sum of ingredients classified as:	Concentration triggering classification of a mixture as:	
	Skin Corrosive	Skin Irritant
	Category 1 (see note below)	Category 2

Skin Corrosive Categories 1A, 1B, 1C	$\geq 5 \%$	$\geq 1 \%$ but $< 5 \%$
Skin irritant Category 2		$\geq 10 \%$
10 × Skin Corrosive Category 1A, 1B, 1C) + Skin irritant Category 2		$\geq 10 \%$

Note

The sum of all ingredients of a mixture classified as Skin Corrosive Category 1A, 1B or 1C respectively, shall each be $\geq 5 \%$ respectively in order to classify the mixture as either Skin Corrosive Category 1A, 1B or 1C. If the sum of the Skin Corrosive Category 1A ingredients is $< 5 \%$ but the sum of Category 1A+1B ingredients is $\geq 5 \%$, the mixture shall be classified as Skin Corrosive Category 1B. Similarly, if the sum of Skin Corrosive Category 1A+1B ingredients is $< 5 \%$ but the sum of Category 1A+1B+1C ingredients is $\geq 5 \%$ the mixture shall be classified as Skin Corrosive Category 1C.

Results and discussions

Ingredients E₁, F₁ and F₂ are relevant.

- E₁ – 0.18% (Skin Irrit. 2 H315)
- F₁ – 0.0225% (Skin Irrit. 2, H315)
- F₂ – 0.009% (Skin Corr. 1A, H314)

We use the summation method, consisting in adding up the percentages of all ingredients classified in the each class related to its concentration limits.

$$\frac{\sum C_{SkinCorr.}}{concentration\ limit} + \frac{\sum C_{SkinIrrit}}{concentration\ limit} = \frac{0.009\%}{0.5\%} + \frac{0.18\% + 0.0225\%}{10\%} = 0.04$$

Conclusion

The sum of concentrations related to concentration triggering classification is below 1 and therefore the formulation is not classified as Skin Irrit. 2, H315.

A 1.5 Eye irritation (KCP 7.1.5)

Comments of zRMS:	Based on the results of the calculation (for details check dRR part C) and in accordance with the provisions of the Regulation EC 1272/2008, the formulation TERBUT 500 SC does not require classification in regards to eye irritation/corrosion.
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A 1.5.1 Eye corrosion

Reference:	7
Report	Toxicological classification of product TERBUT 500 SC based on calculation method taking into consideration health hazards of constituent substances.; M. Kolodziej. 2021
Guideline(s):	Yes (methods used comparable to Regulation (EC) 1272/2008)
Deviations:	No
GLP:	No
Acceptability:	Yes
Duplication (if vertebrate study)	No

According to point 7.1.5 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:

” Eye irritation tests shall be provided, unless it is likely that severe effects on the eyes may be produced or the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, eye irritation properties of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the irritant potential of the total mixture.”

The complete composition of the formulation with the classification of individual ingredients is available in part C.

Due to the fact, that all components of the formulation TERBUT 500 SC are known, eye corrosion test is not necessary.

Materials and methods

For consideration of corrosive and irritant properties the following table applies:

Table 3.3.3

Generic concentration limits of ingredients of a mixture classified as Skin corrosive Category 1 and/ or eye Category 1 or 2 for effects on the eye that trigger classification of the mixture for effects on the eye (Category 1 or 2).

Sum of ingredients classified as:	Concentration triggering classification of a mixture as:	
	Irreversible Eye Effects	Reversible Eye Effects
	Category 1	Category 2
Eye Effects Category 1 or Skin Corrosive Category 1A, 1B, 1C	≥ 3 %	≥ 1 % but < 3 %
Eye Effects Category 2		≥ 10 %
(10 × Eye Effects Category 1) + Eye effects Category 2		≥ 10 %
Skin Corrosive Category 1A, 1B, 1C + Eye effects Category 1	≥ 3 %	≥ 1 % but < 3 %
10 × (Skin Corrosive Category 1A, 1B, 1C + Eye Effects Category 1) + Eye Effects Category 2		≥ 10 %

Results and discussions

Ingredients F₁ and F₂ are relevant.

- F₁ –0.0225% (Eye Dam. 1, H318)
- F₂ –0.009% (Skin Corr. 1A, H314)

We use the summation method, consisting in adding up the percentages of all ingredients classified in the each class related to its concentration limits.

$$\frac{\sum C_{SkinCorr.}}{\text{concentration limit}} + \frac{\sum C_{EyeDam}}{\text{concentration limit}} = \frac{0.0225\%}{3\%} + \frac{0.009\%}{2\%} = 0.012$$

Conclusion

The result (relative sum of concentrations) is below 1 and therefore the whole formulation is not classified as corrosive to eyes.

According to point 7.1.5 of part A of Annex Regulation No 284/2014, it is possible to waive from skin corrosion test.

A 1.5.1 Eye corrosive

Reference:	7
Report	Toxicological classification of product TERBUT 500 SC based on calculation method taking into consideration health hazards of constituent substances.; M. Kolodziej, 2021
Guideline(s):	Yes (methods used comparable to Regulation (EC) 1272/2008)
Deviations:	No
GLP:	No
Acceptability:	Yes
Duplication (if vertebrate study)	No

According to point 7.1.5 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:

” Eye irritation tests shall be provided, unless it is likely that severe effects on the eyes may be produced or the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, eye irritation properties of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the irritant potential of the total mixture.”

The complete composition of the formulation with the classification of individual ingredients is available in part C.

Due to the fact, that all components of the formulation TERBUT 500 SC are known, eye irritation test is not necessary.

Materials and methods

For consideration of corrosive and irritant properties the following table applies:

Table 3.3.3

Generic concentration limits of ingredients of a mixture classified as Skin corrosive Category 1 and/ or eye Category 1 or 2 for effects on the eye that trigger classification of the mixture for effects on the eye (Category 1 or 2).

Sum of ingredients classified as:	Concentration triggering classification of a mixture as:	
	Irreversible Eye Effects	Reversible Eye Effects
	Category 1	Category 2
Eye Effects Category 1 or Skin Corrosive Category 1A, 1B, 1C	≥ 3 %	≥ 1 % but < 3 %
Eye Effects Category 2		≥ 10 %
(10 × Eye Effects Category 1) + Eye effects Category 2		≥ 10 %
Skin Corrosive Category 1A, 1B, 1C + Eye effects Category 1	≥ 3 %	≥ 1 % but < 3 %
10 × (Skin Corrosive Category 1A, 1B, 1C + Eye Effects Category 1) + Eye Effects Category 2		≥ 10 %

Results and discussions

Ingredients E₁, F₁ and F₂ are relevant:

- E₁ – 0.18% (Eye Irrit. 2, H319)
- F₁ – 0.0225% (Eye Dam. 1, H318)
- F₂ – 0.009 % (Skin Corr. 1A, H314)

The summation method consisting of adding up the percentages of all ingredients classified in each class related to its concentration limits.

$$\frac{\sum C_{SkinCorr.}}{\text{concentration limit}} + \frac{\sum C_{EyeDam}}{\text{concentration limit}} + \frac{\sum C_{EyeIrrit}}{\text{concentration limit}}$$

$$= \frac{0.009\%}{0.5\%} + \frac{0.0225\%}{1\%} + \frac{0.18\%}{10\%} = 0.059$$

Conclusion

The relative result (0.06) is lower than 1 and therefore the whole formulation is not classified as irritant to eyes.

A 1.6 Skin sensitisation (KCP 7.1.6)

Comments of zRMS:	Based on the results of the calculation (for details check dRR part C) and in accordance with the provisions of the Regulation EC 1272/2008, the formulation TERBUT 500 SC does not require classification in regards to skin sensitisation.
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A 1.6.1 Skin Sensitisation

Reference:	7
Report	Toxicological classification of product TERBUT 500 SC based on calculation method taking into consideration health hazards of constituent substances.; M. Kolodziej, 2021
Guideline(s):	Yes (methods used comparable to Regulation (EC) 1272/2008)
Deviations:	No
GLP:	No
Acceptability:	Yes
Duplication (if vertebrate study)	No

According to point 7.1.6 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:

”The skin sensitisation test shall be carried out unless the active substances or co-formulants are known to have sensitising properties or the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, skin sensitisation properties of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the sensitising potential of the total mixture.”

The complete composition of the formulation with the classification of individual ingredients is available in part C.

Due to the fact, that all components of the formulation TERBUT 500 SC are known, the skin sensitisation test is not necessary.

Materials and methods

For consideration of sensitizing properties the following table applies:

Table 3.4.5

Generic concentration limits of ingredients of a mixture classified as either skin sensitisers or respiratory sensitisers that trigger classification of the mixture

Ingredient classified as:	Concentration triggering classification of a mixture as:		
	Skin Sensitiser	Respiratory Sensitiser	
	All physical states	Solid/Liquid	Gas
Skin Sensitiser Category 1	≥ 1,0 %	-	-
Skin Sensitiser Category 1A	≥ 0,1 %	-	-
Skin Sensitiser Category 1B	≥ 1,0 %		
Respiratory Sensitiser Category 1	-	≥ 1,0 %	≥ 0,2 %
Respiratory Sensitiser Category 1A	-	≥ 0,1 %	≥ 0,1 %
Respiratory Sensitiser Category 1B		≥ 1,0 %	≥ 0,2 %

Results and discussions

Only ingredient F₁ is classified as sensitizer at the concentration of 0.0225%. The content is lower than concentration triggering classification (C ≥ 0.05 %). Therefore the formulation is not classified as Skin Sens. 1, H317.

Conclusion

Only ingredient F₁ is classified as sensitizer at the concentration of 0.0225%. The content is lower than concentration triggering classification ($C \geq 0.05\%$). Therefore the formulation is not classified as Skin Sens. 1, H317.

A 1.7 Supplementary studies for combinations of plant protection products (KCP 7.1.7)

Not available.

A 1.8 Data on co-formulants (KCP 7.4)

A 1.8.1 Material safety data sheet for each co- formulant

Information regarding material safety data sheets of the co-formulants can be found in the confidential dossier of this submission (Registration Report - Part C).

A 1.8.2 Available toxicological data for each co-formulant

Available toxicological data for each co-formulant can be found in the confidential dossier of this submission (Registration Report - Part C).

A 1.9 Studies on dermal absorption (KCP 7.3)

Dermal absorption studies for Terbutyloazyna 500 SC have not been performed but based on Guidance on Dermal Absorption (EFSA Journal 2012;10(4):2665) it could be assumed that TERBUT 500 SC is closely related to formulation which was evaluated as representative product in the EU review of terbuthylazine. According to composition of TERBUT 500 SC and Terbuthylazine 500 SC provide in DAR, the properties of the composition are compatible . Namely, the amount of active substance in Terbuthylazine 500 SC is higher by 1% than TERBUT 500 SC and this products represents of the same type of formulation. Additionally, the both of formulation have the same amount of water (44%) and additives (9%). Based on this information, it is consider that the use of dermal absorption data stated in EFSA Journal 2011; 9(1):1969 (that is 0.1% for concentrate and 2.5% for dilution) is justified.

Table 6.6-9: Default dermal absorption rates for terbuthylazine

	Value	Justification for value	Acceptability of justification
Concentrate	0.10%	EFSA Journal 2011; 9(1):1969	yes
Dilution	2.50%	EFSA Journal 2011; 9(1):1969	yes

A 1.10 Other/Special Studies

A 1.10.1 Specific target organ toxicity

Comments of zRMS:	Based on the results of the calculation (for details check dRR part C) and in ac-
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	cordance with the provisions of the Regulation EC 1272/2008, the formulation TERBUT 500 SC requires classification in regards to specific target organ toxicity in case of repetitive exposure as STOT RE2, H373.
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Reference:	6.3
Report	Toxicological classification of product TERBUT 500 SC based on calculation method taking into consideration health hazards of constituent substances.; M. Kolodziej, 2019
Guideline(s):	Yes (methods used comparable to Regulation (EC) 1272/2008)
Deviations:	No
GLP:	No
Acceptability:	Yes
Duplication (if vertebrate study)	No

According to point 3.8.3 of Regulation (EC) No 1272/2008 as regards the data requirements for plant protection products:

” Mixtures are classified using the same criteria as for substances, or alternatively as described below. As with substances, mixtures shall be classified for specific target organ toxicity following single exposure. Where there is no reliable evidence or test data for the specific mixture itself, and the bridging principles cannot be used to enable classification, then classification of the mixture is based on the classification of the ingredient substances. In this case, the mixture shall be classified as a specific target organ toxicant (specific organ specified), following single exposure, when at least one ingredient has been classified as a Category 1 or Category 2 specific target organ toxicant and is present at or above the appropriate generic concentration limit as mentioned in Table 3.8.3 for Category 1 and 2 respectively”

Due to the fact, that all components of the formulation TERBUT 500 SC are known, the skin sensitisation test is not necessary.

Materials and methods

For consideration of specific target organ toxicity the following table applies:

Table 3.8.3

Generic concentration limits of ingredients of a mixture classified as a specific target organ toxicant that trigger classification of the mixture as Category 1 or 2.

Ingredient classified as:	Generic concentration limits triggering classification of the mixture as:	
	Category 1	Category 2
Category 1 Specific Target Organ Toxicant	Concentration $\geq 10\%$	$1,0\% \leq$ concentration $< 10\%$
Category 2 Specific Target Organ Toxicant		Concentration $\geq 10\%$ [(Note 1)]

Note 1

If a Category 2 specific target organ toxicant is present in the mixture as an ingredient at a concentration $\geq 1,0\%$ a SDS shall be available for the mixture upon request.

We also took into account the point 3.8.3.4.5.: “Care shall be exercised when extrapolating toxicity of a mixture that contains Category 3 ingredient(s). A generic concentration limit of 20 % is appropriate; however, it shall be recognised that this concentration limit may be higher or lower depending on the

Category 3 ingredient(s) and that some effects such as respiratory tract irritation may not occur below a certain concentration while other effects such as narcotic effects may occur below this 20 % value. Expert judgement shall be exercised.”

Results and discussions

The ingredient A is classified as STOT RE2. The concentration of the ingredient (45.86%) is significantly higher than concentration triggering classification 10%. According to point 3.8.3.4.5. CLP Regulation the formulation is classified as **STOT RE2, H373**.

Conclusion

Having considered risk to the human and animal health posed by ingredients of the preparation, the following classification of product TERBUT 500 SC 500 SC is proposed:

STOT RE2, H373

Classification	Hazard Statement	Pictogram	Signal Word
STOT RE2, H373	May cause damage to organs through prolonged or repeated exposure.		Warning

Appendix 3 Exposure calculations

A 3.1 Operator exposure calculations (KCP 7.2.1.1)

A 3.1.1 Calculations for terbuthylazine

Operator exposure for outdoor spray applications

Application rate of active substance	0.5 kg a.s./ha	<i>i_AppRate</i>
Assumed area treated	50 ha/day	<i>d_AreaTreated</i>
Amount of active substance applied	25 kg a.s./day	<i>i_AmountAS</i>
Dermal absorption of the product	0.10%	<i>i_AbsorpProduct</i>
Dermal absorption of in-use dilution	2.50%	<i>i_AbsorInuse</i>
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Indoor or Outdoor application	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Season	not relevant	

	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75 th centile	95 th centile		
Mixing and loading	Hands	57881	218196	AOEM	
	Body	34276	183491	AOEM	
	Head	1297	7114	AOEM	
	Protected hands (gloves)	280	4952	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	412	3656	AOEM	
	Protected head (hood and face shield)	21	403	AOEM	
	Inhalation	10	31	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Potential exposure		Incl. in AOEM model	
Head and respiratory PPE	None		1	1	
Water soluble bag	No		1		

	Exposure values	µg exposure/day applied		Reference	Comment
		75 th centile	95 th centile		
Application	Hands	3708	24212	AOEM	
	Body	2073	10688	AOEM	
	Head	98	296	AOEM	
	Protected hands (gloves)	243	4851	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	57	139	AOEM	
	Inhalation	5	19	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Potential exposure		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
Closed cab	No		vehicle mounted upward spraying only		

1. Total

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	0.2552809	0.2552809
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0042547	0.0042547
% of RVNAS	132.96%	132.96%

Operator exposure for outdoor spray applications

Application rate of active substance	0.5 kg a.s./ha	<i>i_AppRate</i>
Assumed area treated	50 ha/day	<i>d_AreaTreated</i>
Amount of active substance applied	25 kg a.s./day	<i>i_AmountAS</i>
Dermal absorption of the product	0.10%	<i>i_AbsorpProduct</i>
Dermal absorption of in-use dilution	2.50%	<i>i_AbsorInuse</i>
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Indoor or Outdoor application	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Season	not relevant	

	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75 th centile	95 th centile		
Mixing and loading	Hands	57881	218196	AOEM	
	Body	34276	183491	AOEM	
	Head	1297	7114	AOEM	
	Protected hands (gloves)	280	4952	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	412	3656	AOEM	
	Protected head (hood and face shield)	21	403	AOEM	
	Inhalation	10	31	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	Yes		Incl. in AOEM model	
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied		Reference	Comment
		75 th centile	95 th centile		
Application	Hands	3708	24212	AOEM	
	Body	2073	10688	AOEM	
	Head	98	296	AOEM	
	Protected hands (gloves)	243	4851	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	57	139	AOEM	
	Inhalation	5	19	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Potential exposure		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	0.2552809	0.1638163
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0042547	0.0027303
% of RVNAS	132.96%	85.32%

Operator exposure for outdoor spray applications

Application rate of active substance	0.5 kg a.s./ha	<i>i_AppRate</i>
Assumed area treated	50 ha/day	<i>d_AreaTreated</i>
Amount of active substance applied	25 kg a.s./day	<i>i_AmountAS</i>
Dermal absorption of the product	0.10%	<i>i_AbsorpProduct</i>
Dermal absorption of in-use dilution	2.50%	<i>i_AbsorInuse</i>
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Indoor or Outdoor application	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Season	not relevant	

	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75 th centile	95 th centile		
Hands	57881	218196	AOEM		
Body	34276	183491	AOEM		
Head	1297	7114	AOEM		
Protected hands (gloves)	280	4952	AOEM		
Protected body (workwear or protective garment and sturdy footwear)	412	3656	AOEM		
Protected head (hood and face shield)	21	403	AOEM		
Inhalation	10	31	AOEM		
Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor	
Gloves	Yes		Incl. in AOEM model		
Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model		
Head and respiratory PPE	None		1	1	
Water soluble bag	No		1		

	Exposure values	µg exposure/day applied		Reference	Comment
		75 th centile	95 th centile		
Hands	3708	24212	AOEM		
Body	2073	10688	AOEM		
Head	98	296	AOEM		
Protected hands (gloves)	243	4851	AOEM		
Protected body (workwear or protective garment and sturdy footwear)	57	139	AOEM		
Inhalation	5	19	AOEM		
Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor	
Gloves	Yes		Incl. in AOEM model		
Clothing	Potential exposure		Incl. in AOEM model		
Head and respiratory PPE	None		1	1	
Closed cab	No		vehicle mounted upward spraying only		

1. Total

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	0.2552809	0.0771985
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0042547	0.0012866
% of RVNAS	132.96%	40.21%

A 3.2 Worker exposure calculations (KCP 7.2.3.1)

A 3.2.1 Calculations for terbuthylazine

WORKER EXPOSURE		EUROPOEM II MODEL		
form		Re-entry in the field		
a.s.	terbuthylazine			
Parameter	Value	Unit	References, comments	
Re-entry activities in the field				
AR	Application rate	0.5	kg a.s./ha	summary of intended uses
Worker				
Duration				
T		8	hours / day	default: 6 h (Europeem II)
Inhalation Exposure				
	no model available	-		w ithout PPE
Dermal Exposure				
DFR	Dislodgeable foliar residue	30	mg a.s./m2/kg a.s./ha	default (Europeem II)
TC	Transfer coefficient	0.25	m2/ hour	vegetable (field): 0.25; ornamentals: 0.5; small fruit: 0.3; large fruit: 0.45 (Europeem II)
	Dermal Exposure	30	mg a.s./ day	DE = DFR x AR x TC x T
Internal exposure				
DA	Dermal Absorption	2.5	%	
	PPE-factor dermal	5		gloves*
	AOEL	0.192	mg a.s./ day	based on 70 kg bw
		Without PPE	With PPE	
	Internal exposure	[mg a.s./ day]	[mg a.s./ day]	
	Inhalation	-	-	no model available
	Dermal	0.750	0.150	DE(int) = DE x (DA/100)
	Total	0.750	0.150	sum
	% AOEL			
	Inhalation	-	-	no model available
	Dermal	391	78	%AOEL = 100 x DE(int) / AOEL
	Total	391	78	sum

* It is assumed in the used TC values, that body exposure is already reduced by (protective) clothing. The use of gloves will result in an extra reduction factor of 5.

A 3.3 Resident and bystander exposure calculations (KCP 7.2.2.1)

A 3.3.1 Calculations for terbuthylazine

Resident exposure for					
Croptype		Cereals			
Application method		Downward spraying			
Application equipment		Vehicle-mounted			<i>i_AppEquip</i>
Formulation type		Soluble concentrates, emulsifiable concentrate, etc.			<i>i_FormVal</i>
Buffer strip		2-3 m			<i>i_Buffer</i>
Application rate of the product		0.5 kg a.s./ha			<i>i_AppRate</i>
Concentration of active substance (in-use dilution for liquid applications)		2.5 g a.s./l			<i>d_ConcAS</i>
Dermal absorption of product		0.10%			<i>i_AbsorpProduct</i>
Dermal absorption of in-use dilution		2.50%			<i>i_AbsorpInuse</i>
Oral absorption		100.00%			<i>i_AbsorpOrallnuse</i>
Dislodgeable foliar residue (<i>i_AppRate</i> * <i>i_DFR</i>)		1.5 µg a.s./cm ²			<i>d_DFR</i>
Vapour pressure of in-use dilution		low volatile substances having a vapour pressure of <5*10 ⁻³ Pa	Pa		<i>i_Volat</i>
Concentration in air		0.001 mg/m ³			<i>d_AirCon</i>
Resident dermal spray drift exposure 75th percentile - adult		0.47 ml spray dilution/person			
Resident dermal spray drift exposure 75th percentile - child		0.327 ml spray dilution/person			
Resident inhal. spray drift exposure 75th percentile - adult		0.00010 ml spray dilution/person			
Resident inhal. spray drift exposure 75th percentile - child		0.00022 ml spray dilution/person			
Resident dermal spray drift exposure mean - adult		0.22318 ml spray dilution/person			
Resident dermal spray drift exposure mean - child		0.18 ml spray dilution/person			
Resident inhal. spray drift exposure mean - adult		0.00009 ml spray dilution/person			
Resident inhal. spray drift exposure mean - child		0.00017 ml spray dilution/person			
Exposure duration dermal		2 hours			<i>d_ReExpDur</i>
Exposure duration inhalation		24 hours			<i>d_ReExpDurInhal</i>
Exposure duration entry into treated crops		0.25 hours			<i>d_ExpDurTreatCrop</i>
Light clothing adjustment factor		18.0%			<i>d_ClothAF</i>
Breathing rate adult		0.23 m ³ /day/kg			<i>d_BreathRAAd</i>
Breathing rate child (1-3 year old)		1.07 m ³ /day/kg			<i>d_BreathRCh</i>
Drift percentage on surface (75th percentile)		5.60%			
Drift percentage on surface (mean)		4.10%			
Turf transferable residues percentage		5.00%			<i>d_Turf</i>
Transfer coeff. of surface deposits-adult		7300 cm ² /hour			<i>d_ReTCAd</i>
Transfer coeff. of surface deposits-child (1-3 year old)		2600 cm ² /hour			<i>d_ReTCCh</i>
Saliva extraction percentage		50.00%			<i>d_SalExt</i>
Surface area of hands mouthed		20 cm ²			<i>d_AreaHM</i>
Frequency of hand to mouth activity		9.5 events/hour			<i>d_ReFreqHM</i>
Ingestion rate for mouthing of grass per day		25 cm ²			<i>d_MouthGrass</i>
Dislodgeable residues percentage transferability for object to mouth		20.00%			<i>d_DRP</i>
Transfer coefficient for entry into treated crops (75th percentile) - adult		7500 cm ² /h			<i>d_TcEntryAd</i>
Transfer coefficient for entry into treated crops (75th percentile) - child		2250 cm ² /h			<i>d_TcEntryCh</i>
Transfer coefficient for entry into treated crops (mean) - adult		5980 cm ² /h			<i>d_TcEntryAd</i>
Transfer coefficient for entry into treated crops (mean) - child		1794 cm ² /h			<i>d_TcEntryCh</i>
1. Total					
1.1 1-3 year old child					
	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0173088	0.0107000	0.0058800	0.0210938	0.0414738
Total systemic exposure per kg body weight (mg a.s./day/kg)	0.0017309	0.0010700	0.0005880	0.0021094	0.0041474
% of RVNAS	54.09%	33.44%	18.38%	65.92%	129.61%
1.2 Adult					
	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0243375	0.0138000	0.0051100	0.0703125	0.0852667
Total systemic exposure per kg body weight (mg a.s./day/kg)	0.0004056	0.0002300	0.0000852	0.0011719	0.0014211
% of RVNAS	12.68%	7.19%	2.66%	36.62%	44.41%

Resident exposure for						
Croptype	Cereals					
Application method	Downward spraying					
Application equipment	Vehicle-mounted-Drift Reduction					<i>i_AppEquip</i>
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.					<i>i_FormVal</i>
Buffer strip	5 m					<i>i_Buffer</i>
Application rate of the product	0.5 kg a.s./ha					<i>i_AppRate</i>
Concentration of active substance (in-use dilution for liquid applications)	2.5 g a.s./l					<i>d_ConcAS</i>
Dermal absorption of product	0.10%					<i>i_AbsorpProduct</i>
Dermal absorption of in-use dilution	2.50%					<i>i_AbsorpInuse</i>
Oral absorption	100.00%					<i>i_AbsorpOrallnuse</i>
Dislodgeable foliar residue (<i>i_AppRate</i> * <i>i_DFR</i>)	1.5 µg a.s./cm ²					<i>d_DFR</i>
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10 ⁻³ Pa					<i>i_Volat</i>
Concentration in air	0.001 mg/m ³					<i>d_AirCon</i>
Resident dermal spray drift exposure 75th percentile - adult	0.23798 ml spray dilution/person					
Resident dermal spray drift exposure 75th percentile - child	0.2175 ml spray dilution/person					
Resident inhal. spray drift exposure 75th percentile - adult	0.00009 ml spray dilution/person					
Resident inhal. spray drift exposure 75th percentile - child	0.00017 ml spray dilution/person					
Resident dermal spray drift exposure mean - adult	0.12278 ml spray dilution/person					
Resident dermal spray drift exposure mean - child	0.12 ml spray dilution/person					
Resident inhal. spray drift exposure mean - adult	0.00008 ml spray dilution/person					
Resident inhal. spray drift exposure mean - child	0.00014 ml spray dilution/person					
Exposure duration dermal	2 hours					<i>d_ReExpDur</i>
Exposure duration inhalation	24 hours					<i>d_ReExpDurInhal</i>
Exposure duration entry into treated crops	0.25 hours					<i>d_ExpDurTreatCrop</i>
Light clothing adjustment factor	18.0%					<i>d_ClothAF</i>
Breathing rate adult	0.23 m ³ /day/kg					<i>d_BreathRAAd</i>
Breathing rate child (1-3 year old)	1.07 m ³ /day/kg					<i>d_BreathRCh</i>
Drift percentage on surface (75th percentile)	2.30%					
Drift percentage on surface (mean)	1.80%					
Turf transferable residues percentage	5.00%					<i>d_Turf</i>
Transfer coeff. of surface deposits-adult	7300 cm ² /hour					<i>d_ReTCAd</i>
Transfer coeff. of surface deposits-child (1-3 year old)	2600 cm ² /hour					<i>d_ReTCCh</i>
Saliva extraction percentage	50.00%					<i>d_SalExt</i>
Surface area of hands mouthed	20 cm ²					<i>d_AreaHM</i>
Frequency of hand to mouth activity	9.5 events/hour					<i>d_ReFreqHM</i>
Ingestion rate for mouthing of grass per day	25 cm ²					<i>d_MouthGrass</i>
Dislodgeable residues percentage transferability for object to mouth	20.00%					<i>d_DRP</i>
Transfer coefficient for entry into treated crops (75th percentile) - adult	7500 cm ² /h					<i>d_TcEntryAd</i>
Transfer coefficient for entry into treated crops (75th percentile) - child	2250 cm ² /h					<i>d_TcEntryCh</i>
Transfer coefficient for entry into treated crops (mean) - adult	5980 cm ² /h					<i>d_TcEntryAd</i>
Transfer coefficient for entry into treated crops (mean) - child	1794 cm ² /h					<i>d_TcEntryCh</i>
1. Total						
1.1 1-3 year old child						
	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)	
Total systemic exposure (mg a.s./day)	0.0057859	0.0107000	0.0012075	0.0210938	0.0317138	
Total systemic exposure per kg body weight (mg a.s./day/kg)	0.0005786	0.0010700	0.0001208	0.0021094	0.0031714	
% of RVNAS	18.08%	33.44%	3.77%	65.92%	99.11%	
1.2 Adult						
	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)	
Total systemic exposure (mg a.s./day)	0.0062107	0.0138000	0.0010494	0.0703125	0.0739300	
Total systemic exposure per kg body weight (mg a.s./day/kg)	0.0001035	0.0002300	0.0000175	0.0011719	0.0012322	
% of RVNAS	3.23%	7.19%	0.55%	36.62%	38.51%	

Appendix 4 Detailed evaluation of exposure and/or DFR studies relied upon (KCP 7.2, KCP 7.2.1.1, KCP 7.2.2.1, KCP 7.2.3.1)