FINAL REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: **TERBUT 500 SC**

Product names: **TERBUT 500 SC/**

TAZOPRYM 500 SC/ CORNAO 500 SC

Chemical active substance:

terbuthylazine, 500 g/L or g/kg

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

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

Submission date: 04/2020

MS Finalisation date: 10.2021; 03.2022; 05.2022

Version history

When	What
September 2021	New data on dermal absorption (Appendix 2).New exposure assessment (6.6.2; 6.6.3; 6.6.4; 6.6.5)
October 2021	Assessment by expert
March 2022	Final Registration Report
May 2022	Supplemented by expert

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6 Mammalian Toxicology (KCP 7)

6.1 Summary

Table 6.1-1: Information on TERBUT 500 SC *

Product name and code	TERBUT 500 SC/ TAZOPRYM 500 SC/ CORNAO 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 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 classes, categories	Acute Tox.4 Skin Sens.1 STOT RE 2
Hazard pictograms or Codes for hazard pictograms	GHS07, GHS08
Signal word	Warning
Hazard statements	H302 – Harmful if swallowed. H317 - May cause an allergic skin reaction H373 - May cause damage to organs (all organs) through prolonged or repeated exposure (oral and inhalation).
Precautionary statements	P260 – Do not breathe dust/fume/gas/mist/vapours/spray. P264 - Wash hand thoroughly after handling. P270 - Do not eat, drink or smoke when using this product. P272 - Contaminated work clothing should not be allowed out of the workplace. ~~P273 - Avoid release to the environment~~. P280 - Wear protective gloves/protective clothing/eye protection/face protection P301+P312 – IF SWALLOWED: Call a POISON CENTER/doctor if you feel unwell. P330 - Rinse mouth. P314 - Get medical advice/attention if you feel unwell. P302+P352- IF ON SKIN: Wash with plenty of water. P333+P313- If skin irritation or rash occurs: Get medical advice/ attention. P363- Wash contaminated clothing before reuse. P501 - Dispose of contents/ container to an approved waste disposal plant.
Additional labelling phrases	To avoid risks to man and the environment, comply with the instructions for use. [EUH401] **Bystander/Resident:** – After the treatment has been performed, place warning boards in visible places around the field, reading "No unauthorized access to the area treated with plant protection products". The boards should remain until the plants are harvested / the end of the growing season. ~~*(Po wykonanym zabiegu umieścić w widocznych miejscach wokół pola tablice ostrzegawcze o brzmieniu „Zakaz wstępu osobom postronnym na teren poddany zabiegom środkami ochrony roślin". Tablice powinny pozostać do czasu zbioru roślin/końca sezonu wegetacyjnego.)*~~ – During spraying, a buffer zone of at least 5 m from residential buildings / habitats and bystanders should be applied. ~~*(W czasie oprysku należy zastosować co najmniej 5 m strefę ochronną od zabudowań mieszkalnych/siedlisk oraz osób postronnych.)*~~ – During spraying, use techniques to reduce the drift of the product (drift-reduction nozzles, low vehicle speed, stable weather, etc.). ~~*(W czasie oprysku należy zastosować techniki zmniejszające znoszenie preparatu (dysze antyznoszeniowe, mała prędkość pojazdu, stabilna pogoda i inne)).*~~ – Do not use the product when the wind speed exceeds 4 m/s (recommended up to 2 m/s), ~~*(Środka nie stosować przy prędkości wiatru przekraczającej 4 m/s (zalecana do 2 m/s))*~~ – When using the PPP, do not allow drift of working liquid ~~*(Podczas stosowania środka nie dopuścić do znoszenia cieczy użytkowej)*~~ – Spray treatments under optimal conditions, preferably*:*

	• using only calibrated sprayers and sprayer booms set at a height not more than 50 cm above the sprayed soil surface*;* • with the fan turned off in the case of using sprayers with an auxiliary air stream; • at the sprayer's speed not exceeding 8 km/h; • using nozzles for medium-drop spraying at reduced pressure in order to obtain a greater amount of coarse droplets fraction. ~~*Zabiegi opryskiwania wykonywać w optymalnych warunkach, najlepiej:*~~ ~~• *z użyciem jedynie skalibrowanych opryskiwaczy oraz belek opryskiwacza ustawionych na wysokość nie większą niż 50 cm nad opryskiwaną powierzchnią gleby,*~~ ~~• *z wyłączonym wentylatorem w przypadku wykorzystywania opryskiwaczy z pomocniczym strumieniem powietrza,*~~ ~~• *przy prędkości opryskiwacza nie przekraczającej 7 km/h,*~~ ~~• *z użyciem końcówek do opryskuśredniokroplistego przy obniżonym ciśnieniu, celem uzyskania większej ilości frakcji kropel grubych.*~~ Period from application to the date when humans and animals may enter the area where the product has been applied (prevention period): Do not enter until the spray liquid is completely dry on the surface of the plants. ~~*(Okres od zastosowania środka do dnia, w którym na obszar, na którym zastosowano środek mogą wejść ludzie oraz zostać wprowadzone zwierzęta (okres prewencji): Nie wchodzić do czasu całkowitego wyschnięcia cieczy użytkowej na powierzchni roślin.)*~~

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	AOEM: Work wear (arms, body and legs covered) and Gloves - M/L and A.
Workers	Acceptable	~~AOEM: Work wear (arms, body and legs covered).~~ EUROPOEM II: Work wear (arms, body and legs covered).
Residents	Acceptable / Unacceptable	~~None~~ Martin S. et al. (2008): None AOEM: Additional phrases according to resident and bystander safety should be used on the label of the product.
Bystanders	Acceptable / Unacceptable	~~None~~ Martin S. et al. (2008): None AOEM: Additional phrases according to resident and bystander safety should be used on the label of the product..

No unacceptable risk for operators and workers 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.

No unacceptable risk for residents and bystanders was identified when the product is used as intended. ~~No specific PPE is necessary.~~ Additional phrases according to resident and bystander safety should be used on the label of the product (Table 6.1-2).

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 bystander exposure based on [EFSA model]**	**Acceptability of exposure assessment**			
			Method / Kind **(incl. application technique *****	**Max. number (min. interval between applications)** **a) per use** **b) per crop/ season**	**Max. application rate kg as/ha** **a) a.s. 1** **b) a.s. 2**	**Water L/ha** **min / max**			**Operator**	**Worker**	**Residents**	**Bystander**
1	Maize (BBCH)	F	Spraying, FCTM	1 ; 1	a) 0.500	200 - 300		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				

* 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

No Data gaps

Based on "Peer review of the pesticide risk assessment of the active substance Terbuthylazine", *EFSA Journal* 2019;17(9):5817. Noticed data gaps are:

- the specific toxicity of the groundwater metabolites LM3 and LM6 in order to conclude on the toxicological reference values to be used for the consumer risk assessment (relevant for all representative uses).

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 (ISO); N_2-tert-butyl-6-chloro-N_4-ethyl-1,3,5-triazine-2,4-diamine (IUPAC)
CAS-No.	5915-41-3

	Terbuthylazine
Classification and proposed labelling	
With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended)	Hazard classes, categories: Acute Tox.4 (H302) STOT RE 2 (H373) Code(s) for hazard pictogram(s): GHS07, GHS08 Signal word: Warning Hazard statements: H302 – Harmful if swallowed. H373 - May cause damage to organs (all organs) through prolonged or repeated exposure (oral and inhalation). Precautionary statements: P260 – Do not breathe vapours/ spray. P264 - Wash hand thoroughly after handling. P270 - Do not eat, drink or smoke when using this product. P272 - Contaminated work clothing should not be allowed out of the workplace. P273 - Avoid release to the environment. P301+P312+P330 – IF SWALLOWED: Call a POISON CENTER/doctor if you feel unwell. Rinse mouth. P391 - Collect spillage. P501 - Dispose of contents/ container to an approved waste disposal plant.
Additional C&L proposal	-
Agreed EU endpoints	
AOEL systemic	0.0032 mg/kg bw/d
Reference	Peer review of the pesticide risk assessment of the active substance Terbuthylazine, *EFSA Journal* 2011;9(1):1969,
Conditions to take into account/critical areas of concern with regard to toxicology	
According to Review Report/EFSA Conclusion for active substance *EFSA Journal* 2011;9(1):1969, *EFSA Journal* 2019;17(9):5817	Estimated operator exposure is below the AOEL for both representative formulations 'Terbuthylazine 500 SC' and 'Gardo® Gold®' when PPE (gloves during mixing and loading; gloves, coverall and sturdy footwear during application) is considered – according to the German Model. Estimated worker exposure is below the AOEL for the representative formulation 'Terbuthylazine 500 SC' when PPE (gloves, long sleeved shirt and long trousers) is worn.

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.

According to Regulation (EC) No 1107/2009 "The use of non-animal test methods and other risk assessment strategies should be promoted". Animal testing for the purposes of registration procedure should be minimized and tests on vertebrates should be undertaken as a last resort.
To avoid animal testing, skin corrosion/irritation and eye irritation or serious eye damage tests were performed based on alternative *in vitro* methods.

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)	300 <LD_{50} ≤2000 mg/kg bw	Yes	Acute Tox.4 (**H302**)	calculation
	Not submitted, not necessary. Justification presented in Appendix 2			
LD_{50} dermal, rat (calculation method)	>2000 mg/kg bw	Yes	None	calculation
	Not submitted, not necessary. Justification presented in Appendix 2			
LC_{50} inhalation, rat (calculation method)	-	Yes / No / Supplementary	None	
	Not submitted, not necessary. Justification presented in Appendix 2			
Terbut 500 SC: In Vitro Skin Corrosion: Transcutaneous Electrical Resistance Test (TER) (OECD 430)	Non-irritant	Yes	None	xxxx 2017
TERBUT 500 SCS: In vitro Skin Irritation: Reconstructed Human Epidermis Test Method (OECD 439)	Non-irritant	Yes	None	xxx., 2017
TERBUT 500 SC: Isolated Chicken Eye Test Method for Identifying i) Chemicals Inducing Serious Eye Damage and ii) Chemicals Not Requiring Classifications for Eye Irritation or Serious Eye Damage (OECD 438)	Non-irritant	Yes	None	xxx., 2017
Skin sensitisation (calculation method)	Sensitizer	Yes	**Skin Sens.1/H317**	-
	Justification presented in Appendix 2			
Supplementary studies for combinations of plant protection products	No data – not required			

Formulation does not contain any substances classified as:

- acute dermal toxicity,
- skin irritant,
- respiratory sensitizer,
- germ cell mutagenic,
- cancerogenic,
- toxic on reproduction,
- toxic on specific target organs (single exposure),
- aspiration hazard.

Thus according to points 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.10 of Regulation (EC) 1272/2008 product TERBUT 500 SC does not need to be classified in above mentioned categories.

TERBUT 500 SC contains the active substance – terbuthylazine, which is classified as STOT RE 2 with hazard statement H373. Its concentration in the product is equal to 50 %. This concentration is above concentration limit (10%) stated in Table 3.9.4 of Regulation (EC) 1272/2008, therefore the product is classified as **STOT RE 2** with hazard statement **H373**.

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 summarised in this document.

6.4.1 Metabolite 1 – Desethylterbuthylaznine (MT1)

An overview of the results of the accepted toxicological studies for groundwater metabolite **MT1** is given in the following table. All studies on the metabolite have previously been considered within an EU peer review process.

Toxicological relevance: No genotoxic potential. From the consumer exposure assessment point of view, the toxicological reference values of the parent are applicable to this metabolite. Intakes for MT1+MT13+MT14+LM2+LM4+LM5 account for 191% of the ADI (infant) and 127% of the ADI (toddler). Therefore, MT1 is considered a relevant metabolite in groundwater.

Table 6.4-1: Summary of the results of toxicity studies for MT1

Type of test, species (Guideline)	Result	Acceptability	Reference*
Acute oral toxycity (rat) (OECD 425)	Acute oral LD_{50} (rats): 236 mg/kg bw	Yes	xxxx 2003
Acute oral toxycity (rat) (OECD 423)	Acute oral LD_{50} (rats): 300-500 mg/kg bw	Yes	xxxx., 2004
Bacterial mutagenicity	Mutagenicity in bacterial cells: negative.	Yes	xxxx 2003
Reverse Mutation Assay (OECD 471)	Mutagenicity in bacterial cells: negative.	Yes	xxxxx 2004
Clastrogenicity in vitro (OECD 473; EEC B.10)	Clastogenicity in CHO cells: negative.	Yes	xxxx., 2003
Cell Mutation Assay at the thymidine kinase locus (Tk +/-) in mouse lymphoma L5178Y cell. (OECD 476)	Gene Mutation Assay: weakly positive	Yes	xxx., 2004
In vivo rat bone marrow micronucleus test (OECD 474)	Rat micronucleus assay: negative: negative	Yes	xxx 2006
In vivo rat liver unscheduled DNA synthesis assay (OECD 486)	*in vivo* unscheduled DNA synthesis: negative	Yes	xxx 2006
90 day oral toxicity study in rats (diet)	90 rat day study: Reduced body weight gain. Total WBC reduced.	Yes	xxx al., 1971

* indicates that a study was reviewed at EU level

6.4.2 Metabolite 2 – 2-hydroxyterbuthylazine (MT 13)

An overview of the results of the accepted toxicological studies for groundwater metabolite **MT13** is given in the following table. All studies on the metabolite have previously been considered within an EU peer review process.

Toxicological relevance: No genotoxic potential. From the consumer exposure assessment point of view, the toxicological reference values of the parent are applicable to this metabolite. Intakes for MT1+MT13+MT14+LM2+LM4+LM5 account for 191% of the ADI (infant) and 127% of the ADI (toddler). Therefore, MT13 is considered a relevant metabolite in groundwater.

Table 6.4-2: Summary of the results of toxicity studies for MT13

Type of test, species (Guideline)	Result	Acceptability	Reference*
Acute oral toxycity (rat) (OECD 401; EEC B.1)	LD_{50}> 2000 mg/kg bw	Yes	xxxx 2001
90-day toxicity in the rat (OECD 408; EEC B.26)	90 day dietary rats: NOAEL and LOAEL of 3.4 and 10.3 mg/kg bw, based on changes in haematology and clinical chemistry parameters.	Yes	xxxx., 2002
Bacterial mutagenicity (OECD 471 ; EEC B.13/14)	Mutagenicity in bacterial cells: negative.	Yes	xxxx 2001
Mammalian cell mutagenicity (OECD 476 ; EEC B.17)	Mutagenicity in L5178Y cells: negative	Yes	xxx., 2001
Clastrogenicity in vitro (OECD 473; EEC B.10)	Clastogenicity in CHO cells: negative.	Yes	xxx., 2002

* indicates that a study was reviewed at EU level

6.4.3 Metabolite 3 – desethyl-2-hydroxyterbuthylazine (MT 14)

An overview of the results of the accepted toxicological studies for groundwater metabolite **MT14** is given in the following table. All studies on the metabolite have previously been considered within an EU peer review process.

Toxicological relevance: No genotoxic potential. From the consumer exposure assessment point of view, the toxicological reference values of the parent are applicable to this metabolite. Intakes for MT1+MT13+MT14+LM2+LM4+LM5 account for 191% of the ADI (infant) and 127% of the ADI (toddler). Therefore, MT14 is considered a relevant metabolite in groundwater.

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

Type of test, species (Guideline)	Result	Acceptability	Reference*
Acute oral toxycity (rat) (OECD 401; EEC B.1)	LD_{50}> 2000 mg/kg bw	Yes / No / Supplementary	xxxx., 2000
90-day toxicity in the rat (OECD 408; EEC B.26)	90 dietary rats: NOAEL and LOAEL of 10.3 and 45.7 mg/kg bw, based on increased mortality and water consumption, changes in haematology, clinical chemistry and urinalysis parameters and increased	Yes	xxxx., 2001

Type of test, species (Guideline)	Result	Acceptability	Reference*
	kidney weight secondary to chronic renal failure.		
Bacterial mutagenicity (OECD 471; EEC B.13/14)	Mutagenicity in bacterial cells: negative.	Yes	xxx 2000
Mammalian cell mutagenicity (OECD 476; EEC B.17)	Negative.	Yes	xxx 2000
Clastrogenicity in vitro (OECD 473; EEC B.10)	Clastogenicity in CHO cells: negative.	Yes	xxxxx 2001

* indicates that a study was reviewed at EU level

6.4.4 Metabolite 4 – amino-dihydroxytriazine (LM1; MT24)

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).
LM1 also known as ammelide is a mammalian metabolite of melamine. 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). Melamine was found to have no toxicological relevance for groundwater according to the guidance document on groundwater metabolites.

Toxicological relevance: No genotoxic potential.

6.4.5 Metabolite 5 – 2-(4-aminbo-6-hydroxy-[1,3,5]triazin-2-yl-amino)-2-methyl-propionic acid (LM 2; MT28)

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 present 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.

Toxicological relevance: No genotoxic potential. From the consumer exposure assessment point of view, the toxicological reference values of the parent are applicable to this metabolite. Intakes for MT1+MT13+MT14+LM2+LM4+LM5 account for 191% of the ADI (infant) and 127% of the ADI (toddler). Therefore, LM2 is considered a relevant metabolite in groundwater.

6.4.6 Metabolite:6–2,6-dihydroxy-7,7-dimethyl-7,8-dihydro-6H-imidazo[1,2-a][1,3,5]triazin-4-one (LM 3)

An overview of the results of the accepted toxicological studies for groundwater metabolite **LM3** is given in the following table. All studies on the metabolite have previously been considered within an EU peer review process.
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.

Toxicological relevance: No genotoxic potential. Reference values for consumer risk assessment could not be derived. Therefore, the relevance of LM3 in groundwater cannot be concluded.

Table 6.4-4: Summary of the results of toxicity studies for LM3

Type of test, species (Guideline)	Result	Acceptability	Reference*
Reverse Mutation Assay (OECD 471)	Mutagenicity in bacterial cells: negative	Yes	xxxxx 2009
In vitro Chromosome Aberration study in human lymphocytes (OECD 473)	*In vitro* Chromosome Aberration: negative	Yes	xxx., 2009

* indicates that a study was reviewed at EU level

6.4.7 Metabolite 7 – 2-(4-ethylamino-6-hydroxy-[1,3,5]triazin-2-ylamino)-2-methyl-propionic acid (LM 4)

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.

Toxicological relevance: No genotoxic potential. From the consumer exposure assessment point of view, the toxicological reference values of the parent are applicable to this metabolite. Intakes for MT1+MT13+MT14+LM2+LM4+LM5 account for 191% of the ADI (infant) and 127% of the ADI (toddler). Therefore, LM4 is considered a relevant metabolite in groundwater.

6.4.8 Metabolite 8 – t-butylamino-dihydroxy-triazine (LM 5; MT23)

An overview of the results of the accepted toxicological studies for groundwater metabolite **LM5** is given in the following table. All studies on the metabolite have previously been considered within an EU peer review process.
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). It can be reasonably predicted that the toxicity of metabolite LM5 is less than that of terbuthylazine.

Toxicological relevance: No genotoxic potential. From the consumer exposure assessment point of view, the toxicological reference values of the parent are applicable to this metabolite. Intakes for MT1+MT13+MT14+LM2+LM4+LM5 account for 191% of the ADI (infant) and 127% of the ADI (toddler). Therefore, LM5 is considered a relevant metabolite in groundwater.

Table 6.4-5: Summary of the results of toxicity studies for LM5

Type of test, species (Guideline)	Result	Acceptability	Reference*
Reverse Mutation Assay (OECD 471)	Mutagenicity in bacterial cells: negative	Yes	xxxxx., 2009

* indicates that a study was reviewed at EU level

6.4.9 Metabolite 9 – 4-tert-butylamino-6-hydroxy-1-methyl-1H-[1,3,5]triazin-2-one (LM 6)

An overview of the results of the accepted toxicological studies for groundwater metabolite **LM6** is given in the following table. All studies on the metabolite have previously been considered within an EU peer review process.
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.

Toxicological relevance: No genotoxic potential. Reference values for consumer risk assessment could not be derived. Therefore, the relevance of LM6 in groundwater cannot be concluded.

Table 6.4-6: Summary of the results of toxicity studies for LM6

Type of test, species (Guideline)	Result	Acceptability	Reference*
Reverse Mutation Assay (OECD 471)	Mutagenicity in bacterial cells: negative	Yes	xxxx., 2009
Cell Mutation Assay at the thymidine kinase locus (Tk +/-) in mouse lymphoma L5178Y cell. (OECD 476)	Gene Mutation Assay: positive at cytotoxic level	Yes	xxx 2009
In vitro Chromosome Aberration study in human lymphocytes (OECD 473)	*In vitro* Chromosome Aberration: negative	Yes	xxx 2009
In vivo rat bone marrow micronucleus test (OECD 474)	Rat micronucleus assay: negative	Yes	xxx., 2006

* indicates that a study was reviewed at EU level

6.5 Dermal Absorption (KCP 7.3)

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	~~0.1%~~ 4.5 %	~~1. Peer review of the pesticide risk assessment of the active substance Terbuthylazine *EFSA Journal* 2011; 9(1):1969.~~ 2. Egron, 2021, Study code: S21-01424
Dilution	2.5 % 22 %	

6.5.1 Justification for proposed values - terbuthylazine

Data on dermal absorption for Terbuthylazine in TERBUT 500 SC is available.

~~Justifications for default are presented below. 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.~~

~~Taking into account, that:~~

- ~~TERBUT 500 SC is not classified as irritant in the case of skin and eyes, based on toxicological studies;~~
- ~~TERBUT 500 SC does not contain any synergist and safener;~~
- ~~the absorption rate for the concentrate was very slowly, based on data presented in the *EFSA Journal* 2011; 9(1):1969;~~
- ~~SC formulation is water-based formulation;~~

~~it is consider that the use of dermal absorption data presented in *EFSA Journal* 2011; 9(1):1969 for the formulation TERBUT 500 SC (0.1 % for concentrate and 2.5% for dilution) is appropriate and justified.~~

~~Proposed dermal absorption rates for terbuthylazine are based on dermal absorption studies on a formulation closely related to TERBUT 500 SC. Full summaries of studies on the dermal absorption have been evaluated within an EU peer review process and are described in detail in Additional Report to the DAR for terbuthylazine (Vol. 3, Annex B, part 2, B.6, 2010).~~
~~In Additional Report to the DAR for terbuthylazine (2010) values for dermal absorption taken to risk assessment were: 0.1 % for concentration and 2.5 % spray dilution. These values were proposed based on experimental data for terbuthylazine 500 g/L SC in *vitro* absorption through human epidermis. In this case the high dose level was 500 g a.s./L and the low doses were selected as 3.75 g a.s./L.~~

~~These values of 0.1% and 2.5% of dermal absorption was used to predicted exposure after application of Terbuthylazine 500 SC (Oxon): "worse case"- 0.850 kg terbuthylazine/ha in an application volume 200 L/ha. In this case undiluted concentration is 500 g a.s./L and for in-field solution concentration is 4.25 g a.s./L(in "worse case").~~

~~In the case of TERBUT 500 SC, containing 500 g/L, undiluted concentration is 500 g a.s./L (as in the case of Terbuthylazine 500 g/L SC (Oxon) formulation) and for in-field solution concentration is 3.75 g a.s./L ("wore case").~~

Proposed dermal absorption rates for terbuthylazine are based on dermal absorption studies on a formulation TERBUT 500 SC (Appendix 2). The study results are summarized in the below table (Table 6.5-2).
The values for dermal absorption taken to risk assessment are: 4.5 % for concentration and 22 % spray dilution (1:301). These values are proposed based on experimental data for the TERBUT 500 SC (terbuthylazine 500 g/L) in *vitro* absorption through human epidermis. In this case the high dose level was 500 g a.s./L and the low doses were selected as 1.66 g a.s./L.
These values of 4.5 % and 22% of dermal absorption was used to predicted exposure after application of TERBUT 500 SC: "worse case"- 0.500 kg terbuthylazine/ha in an application volume 300 L/ha. In this case undiluted concentration is 500 g a.s./L and for in-field solution concentration is 1.66 g a.s./L (in "worse case").

~~**Justification is presented in the Confidential part of this submission (Registration Report – Part C).**~~

Table 6.5-2: Summary of the results of submitted dermal absorption studies for terbutylazine

Test	Concentrate	Spray dilution (1:301)	Formulation in study	Acceptability of study	Justification provided on representativity of study formulation for current product	Acceptability of justification	Reference*
In vitro (human)	4.5 %	22 %	Terbut 500 SC	Yes	Not required	Justification accepted. Endpoint can be used for current product. Endpoint cannot be used for current product.	xxx 2021, Study code: S21-01424

~~**Table 6.5-3: Default dermal absorption rates for terbuthylazine**~~

	~~**Value**~~	~~**Justification for value**~~	~~**Acceptability of justification**~~
~~Concentrate~~	~~0.1%~~	~~In the absence of any supporting dermal absorption data, it is proposed a dermal absorption value from EFSA Journal 2011; 9(1):1969 established for the representative formulation (500 g/L SC formulation).~~	~~text~~
~~Dilution~~	~~2.5%~~		

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	Suspension concentrate [SC]
Category	Herbicide
Active substance (incl. content)	**Terbuthylazine (**500 g/L)
AOEL systemic	0.0032 mg/kg bw/d
Inhalation absorption	100%
Oral absorption	100%
Dermal absorption	Concentrate: ~~0.1%~~ 4.5 % Dilution: ~~2.5%~~ 22 %

6.6.1 Selection of critical use 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)

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 is presented in Table 6.6-2. The outcome of the estimation is presented in Table 6.6-3 (longer term exposure). Detailed calculations are in Appendix 3.

Table 6.6-2: Exposure models for intended uses

Critical use	Maize (max. 1.0 L product/ha)
1st 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

Table 6.6-3: Estimated operator exposure (longer term exposure)

		Terbuthylazine	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Tractor mounted boom spray application outdoors (downward spraying)			
Application rate		1 x 0.50 kg a.s./ha	
~~**Spray application** (AOEM**;** 75th percentile) Body weight: 60 kg Application volume: 200 L/ha Area treated: 50 ha/day~~	~~No PPE~~	~~0.0043~~	~~133 %~~
	~~Gloves: M/L and A.~~	~~0.0019~~	~~**57.8 %**~~
	~~Gloves, Protective garment + sturdy footwear: M/L and A.~~	~~0.00045~~	~~**14 %**~~
Application rate		1 x 0.50 kg a.s./ha	
Spray application (AOEM**;** 75th percentile) Body weight: 60 kg Application volume: 200 L/ha Area treated: 50 ha/day	No PPE	0.0919	2871.7 %
	Gloves, Protective garment + sturdy footwear: M/L and A.	0.0032	100 %
	Tractor mounted boom spray – Drift reduction		
	No PPE	0.3303	2416.2 %
	Gloves, Protective garment + sturdy footwear: M/L and A.	0.002	**59.3 %**

According to the model calculations, it can be concluded that the risk for the operator using TERBUT 500 SC on maize is acceptable when:

- personal protective equipment (gloves) and
- tractor mounted boom spray with drift reduction

is used.

Comment:
According to the EFSA AOEM Model, it can be concluded that the risk for the operator is acceptable with use of gloves, protective garment + sturdy footwear: M/L and A.
It can be concluded that according to the EFSA calculations and comparing the estimated exposure to the AOEL for terbuthylazine the risk for the operator using TERBUT 500 SC with vehicle-mounted (downward spraying - tractor mounted boom spray with drift reduc-tio) on professional uses is acceptable when personal protective equipment is used (gloves during mixing/loading and application process; work wear (arms, body and legs covered) during application process
Implication for labelling: P280: Wear protective gloves, protective clothing

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)

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 (longer term exposure). Detailed calculations are in Appendix 3.

Table 6.6-4: Exposure models for intended uses

Critical use(s)	Maize (max. 1.0 ~~1.5~~ L product/ha)
~~1st 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~~
2nd Model	**EUROPOEM II**

Table 6.6-5: Estimated worker exposure (longer term exposure)

		Terbuthylazine	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Field Crop, Trctor Mounted Interval between treatments: 365 days			
Number of applications and application rate		1 x 0.500 kg a.s./ha	
~~**AOEM**~~ ~~Outdoor~~ ~~Work rate: 2 hours/day,~~ ~~DT_{50}: 30 days~~ ~~Initial DFR: 3 µg/cm²/kg a.s./ha~~ ~~Body weight: 60 kg~~	~~Potential~~ ~~TC: 12500 cm²/person/h~~	~~0.0156~~	~~488.3 %~~
	~~Work wear (arms, body and legs covered)~~ ~~TC: 1400 cm²/person/h~~	~~0.00175~~	~~**54.7 %**~~
EUROPOEM II Outdoor Work rate: 2 hours/day, DT_{50}: 30 days Initial DFR: 3 µg/cm²/kg a.s./ha Body weight: 60 kg	Potential TC: 12500 cm²/person/h	0.0132	**412.5 %**
	Work wear (arms, body and legs covered) TC: 1400 cm²/person/h	0.00263	**82.5 %**

There is no unacceptable risk for the worker wearing adequate work wear (arms, body and legs covered) (with PPE), when re-entering crops treated with TERBUT 500 SC.
It should be mentioned on the label that treated crops should not be re-entered before spray deposits on leaf surfaces have completely dried.

Comment:
According to the EUROPOEM II Model, it can be concluded there is no unacceptable risk anticipated for the worker wearing adequate work wear (gloves and work wear when handling treated crops). ~~arms, body and legs covered~~ 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.

P280: Wear protective gloves, protective clothing

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)

6.6.4.1 Estimation of resident and 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 Table 6.6-7 (longer term resident exposure). Detailed calculations are in Appendix 3.

Table 6.6-6: Exposure models for intended uses

Critical use(s)	Maize (max. 1.5 L product/ha)
Model	Martin S. et al. (2008) [Guidance for Exposure and Risk Evaluation for Bystanders and Residents Exposed to Plant Protection Products During and After Application; J. Verbr. Lebensm. 3 (2008): 272-281 Birkhäuser Verlag Basel] and Bundesanzeiger (BAnz), 06 January 2012, Issue No. 4, pp. 75-76.
	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 6.6-7: Estimated resident exposure according to Martin S. model

	Terbuthylazine	
Model data	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Field crops, Tractor mounted, outdoor application to low crop		
Application rate:	1 x 0.500 kg a.s./ha	
~~Bystanders (adult)~~	~~0.00177~~	~~55.4 %~~

~~Drift rate: 8.5% (2-3 m)~~ ~~Body weight: 60 kg~~		
~~Bystanders (children)~~ ~~Drift rate: 8.5% (2-3 m)~~ ~~Body weight: 16.15 kg~~	~~0.00139~~	~~**43.3 %**~~
~~Residents (adult)~~ ~~Drift rate: 8.5% (2-3 m)~~ ~~Body weight: 60 kg~~	~~0.00013~~	~~**4 %**~~
~~Residents (children)~~ ~~Drift rate: 8.5% (2-3 m)~~ ~~Body weight: 16.15 kg~~	~~0.00083~~	~~**25.9 %**~~
Bystanders (adult) Drift rate: 0.905% (5 m) Body weight: 60 kg	0.00167	**51.9 %**
Bystanders (children) Drift rate: 0.905% (5 m) Body weight: 16.15 kg	0.00130	**40.6 %**
Residents (adult) Drift rate: 0.905% (5 m) Body weight: 60 kg	0.00012	**3.8 %**
Residents (children) Drift rate: 0.905% (5 m) Body weight: 16.15 kg	0.00023	**7.2 %**

Table 6.6-8:Estimated resident exposure according to AOEM

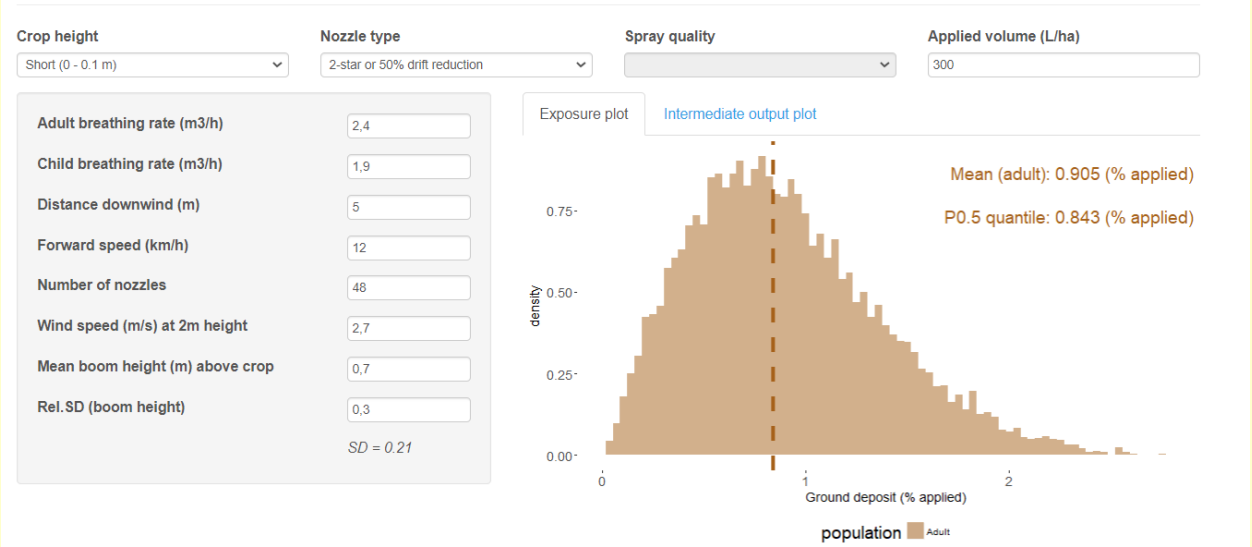
AOEM		Total absorbed dose (mg/kg/day)	% of systemic AOEL
Resident - child	Spray drift (75th percentile) mg/kg bw/day	0.0033	102.62%
	Vapour (75th percentile) mg/kg bw/day	0.0011	33.44%
	Surface deposits (75th percentile) mg/kg bw/day	0.0004	12.88%
	Entry into treated crops (75th percentile) mg/kg bw/day	0.0145	452.46%
	All pathways (mean) mg/kg bw/day	0.0148	461.02%
Resident - adult	Spray drift (75th percentile) mg/kg bw/day	0.0006	18.67%
	Vapour (75th percentile) mg/kg bw/day	0.0002	7.19%
	Surface deposits (75th percentile) mg/kg bw/day	0.0002	4.81%
	Entry into treated crops (75th percentile) mg/kg bw/day	0.0080	251.37%
	All pathways (mean) mg/kg bw/day	0.0071	221.02%

The ecotoxicology evaluation for terbuthylazine includes an arithmetic mean DT_{50} of 2.8 days for foliar deposits on maize (see Additional Repart Anex B.9; B.9.1.3.3.2.i). This can be taken into account assuming that workers will realistically not enter treated crops until the day following application. DFR after 1 day can be estimated as follows:

$$DFR\ (t) = DFR \times e^{(-\ln(2)/DT50) \times t} = 2.34\ \mu g/cm^2/kg\ a.s./ha$$

Using **Martin S. et al. (2008)** approach, there is no an unacceptable health risk to the public based on estimations of bystander and resident exposure (adults and children) for TERBUT 500 SC, using the criti-

cal uses. Drift rate used in the model (Martin S. et al. (2008) approach) was calculated using BREAM2 (version 23.07.2020), calculator developed for bystander and resident exposure to pesticide spray drift from agricultural applications by a boom sprayer. It differs from the original BREAM calculator in the way that the relationship between airborne spray and potential dermal exposure, following additional research. The uncertainty in this relationship is reduced and the variability is more accurately captured in this version. A statistical comparison between the new model and field data shows that BREAM2 is a better predictor than BREAM of potential dermal exposures. The predicted 75th and 95th percentiles of potential dermal exposure are reduced compared with BREAM under normal operating conditions.
To calculate ground deposit (% applied), BREAM calculator unput data was applied (Table 15, Guidance on Pesticides Exposure Assessment of Operator, Worker, Resident and Bystander, *EFSA Journal 2014; 12 (10):3874*).
According to assumption from operator risk assessment, 50 % drift reduction (nozzle type) was assumed, in this case. Received value of drift deposit was equal 0.905%.



According to the **AOEM calculator** results of the exposure estimations suggest that the use of TERBUT 500 SC according to the intended uses presented in GAP, causes unacceptable health risk for resident (adult and child). The exposure (all pathways) was 461 % and 221 % of AOEL for child and adult, respectively (buffer zone: 5m; 50 % drift reduction). The majority of the exposure is supposed to occur if a resident and bystander enters into the treated area.

Four pathways of exposure are considered (Guidance on Pesticides Exposure Assessment of Operator, Worker, Resident and Bystander, *EFSA Journal 2014; 12 (10):3874*):

- spray drift (at the time of application),
- vapour (may occur after the PPP has been applied),
- surface deposits,
- entry into treated crops (walking in treated field).

Summing all the exposure pathways, each one being conservative (considering high percentiles of exposure), would result in an overly conservative and unrealistic result.
Resident represents the worst case scenario. The four estimated exposures are presented separately because, it is unlikely and unrealistic that all the different exposures from the different pathways will occur contemporaneously in the case of bystanders or resident. It should be noted that the majority of the exposure is supposed to occur if a resident and bystander enters into the treated area (according to the AOEM).

It should be taking into account that TERBUT 500 SC can be applied preemergence (BBCH 00) to the soil or early post emergence (BBCH12-16), when maize is low. In both cases the risk to exposure to TERBUT 500 SC is limited, especially in the case of entry into treated crop (dermal exposure), resident and bystander do not have possibility to dermal (physical) contact with crop/ weed which was treated by TERBUT 500 SC.
Corn sowing begins in mid-April, when the average temperature is 8-12°C in Poland, so it is unlikely that bystanders or resident will not have clothes or a covered body in mid-April or early May in climatic codition of Poland.
In the case of TERBUT 500 SC application time, enters into the treated area is not a main pathways of exposure. It seems that spray drift and surface deposits, which may occur after the PPP application are more realistic pathways of exposure. In this case, mean sum of the exposure is equal 115 % (child) and 23.5 % (adult) according to the AOEM.

In the case of early post emergence application (BBCH 12-16), maize is low crop. According to the practice, maize is not hay densely, but in rows with an appropriate spacing of 70 cm, sowing density of 7-8 plants per m^2 (depended on soil condition). Main goals of the application of TERBUT 500 SC is to fight weeds between the maize. Main amount of TERBUT 500 SC is applied on soil and weeds with the use of a special nozzels type with drift reduction.

The re-entry exposure of residents (adult/child) according to the AOEM is over-estimates considering the height of the crop (BBCH scale) and the clothes worn by the resident at this period of the year.

According to Ecotoxicological protection, as well for pre-emergence use as a post-emergence use to protect aquatic organisms and non-target terrestrial plants respect a buffer zone and drift reduction nozzle should be used (50 % or 75%). AOEM do not assume higher drift reduction that 50 %. Application of the boom sprayer with 75 % drift reduction nozzle, in the significant way reduce the systemic exposure, what was presented in Table 6.6-9.

Table 6.6-9:Estimated resident exposure according to AOEM, comparison of the effect of the application drift reduction nozzles.

	Drift reduction nozzle					
	No		**50 %**		**75%**	
	Systemic exposure [mg a.s./kg bw/ day]	**% of systemic AOEL**	**Systemic exposure [mg a.s./kg bw/ day]**	**% of systemic AOEL**	**Systemic exposure [mg a.s./kg bw/ day]**	**% of systemic AOEL**
1-3 year old child						
Spray drift	0.006568	205.24 %	0.0032839	102.62 %	0.0018157	51.31 %
Vapour	0.00107	33.44 %	0.001070	33.44 %	0.00107	33.44 %
Surface deposits	0.0008246	25.77 %	0.000412	12.88 %	0.0000206	6.44 %
- dermal	0.0006578		0.0003289		0.000165	
- hand to mouth	0.000109		0.0000546		0.0000273	
- object to mouth	0.0000575		0.00002875		0.0000144	
Enter into treated crops	0.0145	452.46 %	0.0145	452.46 %	0.0145	452.46 %
- dermal	0.0145		0.0145		0.0145	
- hand to mouth						
- object to mouth						
Adult						
Spray drift	0.001195	37.35 %	0.000598	18.67 %	0.0003087	9.34 %
Vapour	0.00023	7.19 %	0.00023	7.19 %	0.00023	7.19 %
Surface deposits (dermal)	0.000308	9.62 %	0.000154	4.81 %	0.0001205	2.40 %
Enter into treated crops (dermal)	0.00804	251.37 %	0.00804	251.37 %	0.00804	251.37 %

Risk for a resident and bystander can by minimalize if:

- min. 5-meter buffer zone is kept during spraying,
- drift-reduction nozzles (min. 50 %) are used,

- warning boards preventing from resident/bystander entry into treated area are installed and remain until the plants are harvested / the end of the growing season “No unauthorized access to the area treated with plant protection products” ~~(“Zakaz wstępu osobom postronnym na teren poddany zabiegom środkami ochrony roślin”).~~

In this case, the incidental short-time exposure of bystander and resident (children and adult) to terbuthylazine can be acceptable.
It is worth to mention that also spray drift and surface deposits can be successfully reduced by the application of the PPP according to Good Plant Protection Practice

Following sentence regarding the use of risk mitigation measures is recommended to be placed in the section of precautions for the bystander/resident:

- After the treatment has been performed, place warning boards in visible places around the field, reading "No unauthorized access to the area treated with plant protection products". The boards should remain until the plants are harvested / the end of the growing season.
  ~~*(Po wykonanym zabiegu umieścić w widocznych miejscach wokół pola tablice ostrzegawcze o brzmieniu „Zakaz wstępu osobom postronnym na teren poddany zabiegom środkami ochrony roślin”. Tablice powinny pozostać do czasu zbioru roślin/końca sezonu wegetacyjnego.)*~~
- During spraying, a buffer zone of at least 5 m from residential buildings / habitats and bystanders should be applied.
  ~~*(W czasie oprysku należy zastosować co najmniej 5 m strefę ochronną od zabudowań mieszkalnych/siedlisk oraz osób postronnych.)*~~
- During spraying, use techniques to reduce the drift of the product (drift-reduction nozzles, low vehicle speed, stable weather, etc.).
  ~~*(W czasie oprysku należy zastosować techniki zmniejszające znoszenie preparatu (dysze antyznoszeniowe, mała prędkość pojazdu, stabilna pogoda i inne)).*~~
- Do not use the product when the wind speed exceeds 4 m/s (recommended up to 2 m/s),
  ~~*(Środka nie stosować przy prędkości wiatru przekraczającej 4 m/s (zalecana do 2 m/s))*~~
- When using the PPP, do not allow drift of working liquid.
  ~~*(Podczas stosowania środka nie dopuścić do znoszenia cieczy użytkowej)*~~
- Spray treatments under optimal conditions, preferably*:*
  - using only calibrated sprayers and sprayer booms set at a height not more than 50 cm above the sprayed soil surface*;*
  - with the fan turned off in the case of using sprayers with an auxiliary air stream;
  - at the sprayer's speed not exceeding 8 km/h;
  - using nozzles for medium-drop spraying at reduced pressure in order to obtain a greater amount of coarse droplets fraction.

  ~~*Zabiegi opryskiwania wykonywać w optymalnych warunkach, najlepiej:*~~
  - ~~*z użyciem jedynie skalibrowanych opryskiwaczy oraz belek opryskiwacza ustawionych na wysokość nie większą niż 50 cm nad opryskiwaną powierzchnią gleby,*~~
  - ~~*z wyłączonym wentylatorem w przypadku wykorzystywania opryskiwaczy z pomocniczym strumieniem powietrza,*~~
  - ~~*przy prędkości opryskiwacza nie przekraczającej 7 km/h,*~~
  - ~~*z użyciem końcówek do oprysku średniokroplistego przy obniżonym ciśnieniu, celem uzyskania większej ilości frakcji kropel grubych.*~~

Period from application to the date when humans and animals may enter the area where the product has been applied (prevention period): Do not enter until the spray liquid is completely dry on the surface of the plants.

~~*(Okres od zastosowania środka do dnia, w którym na obszar, na którym zastosowano środek mogą wejść ludzie oraz zostać wprowadzone zwierzęta (okres prewencji): Nie wchodzić do czasu całkowitego wyschnięcia cieczy użytkowej na powierzchni roślin.)*~~

Comment: Considering all the above mentioned risk mitigation measures, the exposure of residents / bystanders is acceptable according to Martin S. model Calculated exposure of people living (adults and children) near the fields where TERBUT 500 SC is used is below of the AOEL for terbuthylazine, therefore the product does not pose an unacceptable health risk to the public. Bufor zone 5 m
Implication for labelling: P280: Wear protective gloves, protective clothing

According to the AOEM calculator results of the exposure estimations suggest that the use of TERBUT 500 SC according to the intended uses presented in GAP, causes unacceptable health risk for resident (adult and child).

6.6.4.2Measurement 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 terbuthylazine 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 7.1.4	xxx.	2017	Terbyt 500 SC: In Vitro Skin Corrosion: Transcutaneous Electrical Resistance Test (TER) Study code: OES-17/17 Institute of Industrial Organic Chemistry, Branch Pszczyna GLP Unpublished	N	Synthos Agro Sp z.o.o Oświęcim
KCP 7.1.4	xxx	2017	TERBUT 500 SC: *In vitro* Skin Irritation: Reconstructed Human Epidermis Test Method. Krakowian D., 2019. Study code: SIT-3/17. Institute of Industrial Organic Chemistry, Branch Pszczyna GLP Unpublished	N	Synthos Agro Sp z.o.o Oświęcim
KCP 7.1.5	xxxxx.	2017	Terbyt 500 SC: Isolated Chicken Eye Test Method for Identifying i) Chemicals Inducing Serious Eye Damage and ii) Chemicals Not Requiring Classifications for Eye Irritation or Serious Eye Damage. Study code: ICE-12/17. Institute of Industrial Organic Chemistry, Branch Pszczyna GLP Unpublished	N	Synthos Agro Sp z.o.o Oświęcim
KCP 7.3	xxx	2021	*In-vitro* human skin penetration of terbuthylazine in TERBUT 500 SC Study code: S21-014 Eurofins Agroscience Services Chem SAS GLP	N	Synthos Agro Sp z.o.o Oświęcim

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
			Unpublished 24		

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
KIIA 5.8.1	xxxxx	2003	GS26379: Acute Oral Toxicity Study in the Rat – Up and Down Procedure Syngenta Crop Protection AG, Basell Report No CTL/AR7315 GLP Not published Syngenta File N GS26379/0020	Y	SYNGENTA
KIIA 5.8.1	xxxx	2004	Assesment of acute oral toxicity with terbuthylazine-desethyl in the rat (acute class method) Oxon Italia S. p. A.	Y	OXON
KIIA 5.8.1	xxxxx	2003	GS26379: Bacterial Mutation Assay in *S. typhimurium* and *E. coli* Syngenta Crop Protection AG, Basell Report No CTL/YV6393 GLP Not published Syngenta File N GS26379/0021	Y	SYNGENTA
KIIA 5.8.1	xxxx	2004	Evaluationof the mutagenic activity of terbuthylazine-desethyl in the Salmonella typhimurium reverse mutation assay and the Escherichia coli reverse mutation assay (with independent repeat) Oxon Italia S. p. A. GLP Not published	Y	OXON

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
			File GS13529_10044		
KIIA 5.8.1	xxxxx.	2003	GS26379: *In vitro* Cytogeenetic assay in human lymphocytes Syngenta Crop Protection AG, Basell Report No CTL/SV1196 GLP Not published Syngenta File N GS26379/0022	Y	SYNGENTA
KIIA 5.8.1	xxxx	2004	GS26379:L5178Y TK+/- Mouse lymphoma mutation assay Syngenta Crop Protection AG, Basell Report No VV0297-REG GLP Not published File No GS26379/0024	Y	SYNGENTA
KIIA 5.8.1	xxxxx	2006	GS26379: rat bone marrow micronucleus test Syngenta Crop Protection AG, Basell GLP Not published File No GS26379/0026	Y	SYNGENTA
KIIA 5.8.1	xxxx	2006	GS26379: in vivo rat liver unscheduled DNAsynthesis assay Syngenta Crop Protection AG, Basell GLP Not published File No GS26379/0025	Y	SYNGENTA
KIIA 5.8.1	xxxxx	1971	90-day subacute oral toxicity study with GS 26379 technical in albino rats Novartis Crop Protection AG, Basell Not GLP Not published File No GS26379/0001	Y	SYNGENTA
KIIA	xxxxx	2001	GS23158 tech. (metabolite of GS13529): Acute Oral Toxicity in the Rat (limit test)	Y	SYNGENTA

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
5.8.1			Syngenta Crop Protection AG, Basell Report No 20011053 GLP Not published Syngenta File N GS23158/0020		
KIIA 5.8.1	xxxxxx	2002	GS23158 tech. (metabolite of GS13529): 90-days acute oral toxicity study in the rat (administration in food) Syngenta Crop Protection AG, Basell Report No 20011053 GLP Not published Syngenta File N GS23158/0010	Y	SYNGENTA
KIIA 5.8.1	xxxxx	2001	GS23158 tech. (metabolite of GS13529): *Salmonella* and *Escherichia*/ mammmalian microsome mutagenicity test Syngenta Crop Protection AG, Basell Report No 20011054 GLP Not published Syngenta File N GS23158/0012	Y	SYNGENTA
KIIA 5.8.1	xxxxx	2001	GS23158 tech. (metabolite of GS13529): L5178Y TK+/- mouse lymphoma mutation assay Syngenta Crop Protection AG, Basell Report No 20011054 GLP Not published Syngenta File N GS23158/0012	Y	SYNGENTA
KIIA 5.8.1	xxxx	2002	GS23158: *In vitro* Cytogeenetic assay in human lymphocytes Syngenta Crop Protection AG, Basell Report No CTL/SV1087 GLP Not published	Y	SYNGENTA

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
			Syngenta File N GS23158/0013		
KIIA 5.8.1	xxxxx., 2000	2000	GS28620 tech. (metabolite of GS13529): Acute Oral Toxicity in the Rat (limit test) Syngenta Crop Protection AG, Basell Report No 20001004	Y	SYNGENTA
KIIA 5.8.1	xxxx	2001	GS28620 tech. (metabolite of GS13529): 90-days acute oral toxicity study in the rat (administration in food) Syngenta Crop Protection AG, Basell Report No 20001005	Y	SYNGENTA
KIIA 5.8.1	xxxxx	2000	GS28620 tech. (metabolite of GS13529): *Salmonella* and *Escherichia*/ mammmalian microsome mutagenicity test Syngenta Crop Protection AG, Basell Report No 252/268-D5140/ 20001002	Y	SYNGENTA
KIIA 5.8.1	xxxxx.	2000	GS28620 tech. (metabolite of GS13529): Mutation at the thymidine kinase (TK) locus of mouse lymphoma L5178Y cells (MLA) using the microtitre fluctuation Syngenta Crop Protection AG, Basell Report No 252/268-D5140/ 20001002	Y	SYNGENTA
KIIA 5.8.1	xxxx	2001	GS28620 tech. (metabolite of GS13529): Induction of chromosome aberrations in cultured chinese hamsternovary (CHO) cells Report No 252/268-D6171/ 20001003	Y	SYNGENTA
KIIA 5.8.1	xxxx.	2009	CSCD692760/LM3 *Salmonella typhimurium* and *Escherichi coli* reverse mutation assay Syngenta Crop Protection AG, Basell GLP Not published File No GS13529_10139	Y	OXON/ SYNGENTA
KIIA 5.8.1	xxxxxx.	2009	CSCD692760/LM3 Chromosome aberration test in human lymphocytes *in vitro* Syngenta Crop Protection AG, Basell GLP Not published	Y	SYNGENTA

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
			File No GS13529_10142		
KIIA 5.8.1	xxxx.	2009	GS16984/LM5 *Salmonella typhimurium* and *Escherichi coli* reverse mutation assay Syngenta Crop Protection AG, Basell GLP Not published File No SYN545666_10000	Y	SYNGENTA/ OXON
KIIA 5.8.1	xxxxxx.	2009	CSCD648241/LM6 *Salmonella typhimurium* and *Escherichi coli* reverse mutation assay Syngenta Crop Protection AG, Basell GLP Not published File No GS13529_10005	Y	SYNGENTA
KIIA 5.8.1	xxxxx.	2009	CSCD648241/LM6 Cell mutation assay at the thymidine kinase locus (TK+/-) in mouse lymphoma L5178Y cells Syngenta Crop Protection AG, Basell GLP Not published File No SYN545666_10002	Y	SYNGENTA
KIIA 5.8.1	xxxx	2009	CSCD648241/LM6 Chromosome aberration test in human lymphocytes in vitro Syngenta Crop Protection AG, Basell GLP Not published File No GS13529_10140	Y	SYNGENTA
KIIA 5.8.1	xxxx	2006	CSCD648241/LM6 Micronucleus test in the mouse Syngenta Crop Protection AG, Basell Oxon Italia S. p. A. GLP Not published File No GS13529_10141	Y	SYNGENTA

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
KCP					

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
KCP					

Appendix 2 Detailed evaluation of the studies relied upon

A 2.1 Statement on bridging possibilities

A 2.2 Acute oral toxicity (KCP 7.1.1)

Comments of zRMS:	**The estimated value ATE_{mix} of acute oral toxicity for TERBUT 500 SC is higher than 300 mg/kg bw, but lower than 2000 mg/kg bw.** **Therefore, classification is required according to Regulation (EC) No. 1272/2008. TERBIT 500 SC is classified Acute Tox 4 / H302.**

TERBUT 500 SC contains:

- one component (terbuthylazine) which is classified as Acute Tox. 4 with hazard statement H302. Terbuthylazine concentration in the product is equal to 46 %.

Acute oral toxicity value (ATE_{mix}) for TERBUT 500 SC can be estimated according to principles of Regulation (EC) 1272/2008, formula in section 3.1.3.6.1 (additivity formula) as follows:

$$\frac{100}{ATE_{mix}} = \sum_n \frac{C_i}{ATE_i}$$

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.

Therefore, ATE_{mix} value is equal to:

$$ATE_{mix} = \frac{100}{\frac{46}{500}} = 1087\ mg/kg\ bw$$

The estimated value ATE_{mix} of acute oral toxicity for TERBUT 500 SC is higher than 300 mg/kg bw, but lower than 2000 mg/kg bw. Thus, classification is required according to Regulation (EC) No. 1272/2008. TERBIT 500 SC can be classified to **category 4 (Acute Tox 4 (H302))**.

A 2.3 Acute percutaneous (dermal) toxicity (KCP 7.1.2)

Comments of zRMS:	**TERBUT 500 SC does not contain any component which is classified as acute dermal toxicity, therefore the product is unclassified**

TERBUT 500 SC does not contain any component which is classified as acute dermal toxicity, therefore the product will not be classified as acute dermal toxicity.
Therefore, no classification is required.

A 2.4 Acute inhalation toxicity (KCP 7.1.3)

Comments of zRMS:	**TERBUT 500 SC does not contain any component which is classified as acute inhalation toxicity, therefore the product is unclassified**

No data on acute inhalation toxicity for terbuthylazine in TERBUT 500 SC is available.

The recommended way of spraying formulation TERBUT 500 SC results in production of medium drops size. TERBUT 500 SC contains active substances with a vapour pressure below 1×10^{-2} Pa (vapour pressure terbuthylazine: 1.52×10^{-4} Pa at 22 °C (>99%, OXON); 9.0×10^{-5} Pa at 25 °C (99.4%,Syngenta)). TERBUT 500 SC will not be used as a fumigant or an aerosol.

TERBUT 500 SC does not contain any component which is classified as acute inhalation toxicity, therefore the product will not be classified as acute inhalation toxicity.
Therefore, no classification is required.

A 2.5 Skin irritation (KCP 7.1.4)

Comments of zRMS:	**Under the experimental (study 1 and 2) conditions, TERBUT 500 SC is not a skin irritant. Thus, no classification is required according to Regulation (EC) No. 1272/2008**

A 2.5.1 Study 1

Reference	KCP 7.1.4
Report	Terbut 500 SC: *In Vitro* Skin Corrosion: Transcutaneous Electrical Resistance Test (TER), xxxx., 2016. Study code: OES-17/17
Guideline(s)	OECD Guideline No. 430 (2015)/ EU Method B.40. Council Regulation (EC) No. 440/2008
Deviations	No
GLP	Yes
Acceptability	Yes

Materials and methods

Test material (Lot/Batch No.)	Terbut 500 SC (Batch No. 7/17)
Species	Rat, WISTAR (outbred)
No. of animals (group size)	2 females
Initial test using one animal	No
Exposure	150 µL, 24 hours
Vehicle/Dilution	None
Post exposure observation period	Immediately
Remarks	None

Results and discussions

Table A 1: Skin irritation of TERBUT 500 SC

Animal No.	Mean TER value ± SD (kΩ)
1	13.33
2	15.03

The mean TER values for the test item were higher than 5 kΩ.

Clinical signs:	No clinical signs of toxicity were observed.

Conclusion

Under the experimental conditions, TERBUT 500 SC is **not a skin irritant**. Thus, no classification is required according to Regulation (EC) No. 1272/2008.

A 2.5.2 Study 2

Reference	KCP 7.1.4
Report	TERBUT 500 SCS: *In vitro* Skin Irritation: Reconstructed Human Epidermis Test Method. xxxxx., 2018. Study code: SIT-3/17.
Guideline(s)	OECD 439 (2015)/EU Methods B.46
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	Terbut 500 SC (Batch No. 7/17)
Test sytem	EpiDerm™ tissues (human reconstructed epidermis model)
No. of inserts	3 inserts with tissues of the human skin model EpiDerm
Initial test using one animal	No
Exposure	Topical exposure; 30 µL liquid test item will be applied without preparation(60 min.)
Negative control	DPBS buffer
Positive control	5 % SDS
Viability Test	MTT Viability Test
Vehicle/Dilution	None
Remarks	None

Results and discussions

Table A 2: Tissue viability [%]

	Negative control	Positive control	DIFLUD 050 FS
Tissue no. 1 viability	99.0	1.7	102.7
Tissue no. 2 viability	102.2	1.7	97.2
Tissue no. 3 viability	98.7	2.0	102.2
Mean Tissue viability	**100.0**	**1.8**	**100.7**
SD (±)	2.1	0.2	3.2

Conclusion

After the treatment with the test item, the mean value of relative tissue viability was equal to 128.1 %. This value is above the threshold for skin irritation potential (≤ 50%).
TERBUT 500 SC, is considered to be **non-irritating to skin** (no category) in the Reconstructed human Epidermis (RhE) Test Method.

Test according to the OECD Guideline No. 439 is able to reliably discriminate non-irritating chemicals from irritating / corrosive to the skin and can therefore be used for to classify skin irritation risk according to the GHS System adopted by the OECD.

Under the experimental conditions, TERBUT 500 SC is **not a skin irritant**. Thus, no classification is required according to Regulation (EC) No. 1272/2008.

A 2.6 Eye irritation (KCP 7.1.5)

Comments of zRMS:	**Under the experimental conditions, product TERBUT 500 SC is not an eye irritant.** **Thus, no classification is required according to Regulation (EC) No. 1272/2008.**

A 2.6.1 Study 1

Reference	KCP 7.1.5
Report	TERBIT 500 SC: Isolated Chicken Eye Test Method for Identifying i) Chemicals Inducing Serious Eye Damage and ii) Chemicals Not Requiring Classifications for Eye Irritation or Serious Eye Damage. xxxx., 2017, Study code: ICE-12/17.
Guideline(s)	OECD Guideline No 438 (2018)/ EU Method B.48. Council Regulation (EC) No. 440/2008
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	TERBUT 500 SC (Batch No.7/17)
Species	Chickens, eyeballs
No. of animals (group size)	9 eyeballs
Initial test using one animal	No
Exposure	0.03 mL (single instillation) for 10 sec.
Irrigation (time point)	10 sec., physiological salt
Post exposure observation period	4 hours
Remarks	None

Results and discussions

Table A 3: Eye irritation of product TERBUT 500 SC

Observation after time (min.)	Corneal opacity		Corneal swelling (%)		Fuorescein retention	
	Mean scores	ICE class	Mean scores	ICE class	Mean scores	ICE class
30 min.	0.2	I	-0.8	I	0.3	I
75 min.	0.2	I	-1.0	I	-	-
120 min.	0.2	I	0.8	I	-	-
180 min.	0.2	I	1.6	I	-	-
240 min.	1.0	II	1.7	I	-	-

Table A 4: Eye irritation of TERBUT 500 SC – Summary of the results

	Maximal ICE Class			
	Fuorescein retention	Corneal opacity	Corneal swelling	UN GHS Classification
TERBUT 500 SC	I	II	I	No category
Positive control	IV	IV	IV	Category 1
Negative control	I	I	I	No category

Clinical signs:	No changes of the corneal surface were observed. Histopathological examinations revealed: slight cell erosions of the superficial layer of the anterior corneal epithelium (one eyeball).

Conclusion

Under the experimental conditions, product TERBUT 500 SC is **not an eye irritant**. Thus, no classification is required according to Regulation (EC) No. 1272/2008.

A 2.7 Skin sensitisation (KCP 7.1.6)

Comments of zRMS:	**TERBUT 500 SC contains two components which concentration is above concentration limit, hence TERBUT 500 SC therefore the product is classified as Skin Sens. 1/ H317**

Calculation method (Regulation (EC) No 1272/2008)

TERBUT 500 SC does not contain any component which is classified as respiratory sensitizer with hazard statement H334, therefore the product will not be classified as respiratory sensitizer with hazard statement H334.

TERBUT 500 SC contains two components which are classified as Skin Sens. 1 with hazard statement H317:

- the concentration of the first component in TERBUT 500 SC is equal to 0.01%. This concentration is below concentration limit for this substance (0.05%) presented in Table 3.1 of Annex VI to of Regulation 1272/2008.
- the concentration of the second component in TERBUT 500 SC is equal to 0.01%. This concentration is above concentration limit for this substance (0.0015%) presented in Table 3.1 of Annex VI to of Regulation 1272/2008.

The total amount of substances which are classified as Skin Sens.1 in TERBUT 500 SC is equal 0.02%. This concentration is below concentration limit (1%) stated in Table 3.4.5 of Regulation 1272/2008.
Nevertheless, the product contains substance which concentration is above concentration limit, hence TERBUT 500 SC should be classified as **Skin Sens. 1** with hazard statement **H317**.

A 2.8 Supplementary studies for combinations of plant protection products (KCP 7.1.7)

A 2.9 Data on co-formulants (KCP 7.4)

A 2.9.1 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 2.9.2 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 2.10 Studies on dermal absorption (KCP 7.3)

According requirements from Reg. No. 284/2013/WE the study shall be conducted when dermal exposure is a significant exposure route and no acceptable risk is estimated using default absorption value.

Use of plant protection product TERBUT 500 SC is safe for operator, taking into account proposed dose of product, type of usage, type of personal protective equipment (gloves, protective garment and sturdy footwear). Using tractor mounted boom sprayer and maintain general rules of safety and hygiene of work-

ing with plant protection products and comply with requirements enclosed in label, risk during employ TERBUT 500 SC is acceptable, absorbed dose of terbuthylazine has safe value, below AOEL for this active ingredients.
~~According to above there isn't necessity to do tests of dermal absorption for TERBUT 500 SC.~~

A 2.10.1 Study 1 – Active substance 1 in product code/name

Comparative dermal absorption, in vitro using rat and human skin

Comments of zRMS:	**The dermal penetration of terbutylazine formulated as TERBUT 500 SC through human dermatomed skin was determined *in vitro* is acceptable.** **The dermal penetration estimates to be used for risk assessment were set at 4.5% and 22% for the formulation concentrate and the 1:301 spray dilution based on the EFSA guidance criteria**

Reference	KCP 7.3
Report	*In-vitro* human skin penetration of terbuthylazine in TERBUT 500 SC, C. xxxx, 2021, Study code: S21-01424
Guidelines	Guidance on Dermal Absorption, EFSA Journal 2017; 15(6): 4873. OECD guideline for the testing of chemicals: Test No. 428: Skin Absorption: *in vitro* Method (13 April 2004). OECD guidance document for the conduct of skin absorption studies, OECD series on testing and assessment. Number 28, 05-Mar-2004 (ENV/JM/MONO(2004)2). OECD Guidance notes on dermal absorption, 18 August 2011 (ENV/JM/MONO(2011)36).
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material	Name (Lot/Batch No.)	[Ring-U-^{14}C]-terbuthylazine (Batch XXV/2/E/2)
	Test preparation	Spiking
	Specific activity	153.13 µCi/mg
	Radiochemical purity	100 %
Product	Name (Lot/Batch No.)	TERBUT 500 SC (Batch No. SNS-H-11-01)
	Company code	TERBUT 500 SC
	Concentration a.s.	503.4 [g/L]
	Formulation type	SC
Blank product	Name (Lot/Batch No.)	TERBUT 500 SC Blank formulation (Batch No.SNS-H-11-02)
	Concentration a.s.	0 [g/L]

Test system		
Diffusion cell	Cell type	Dynamic, Flow-through diffusion cells

	(if dynamic) Flow rate	1.5 mL/h
	Exposed skin area	1 cm²
	Cover	Unoccluded
Membrane	Skin type	Dermatomed, 1 cm x 1 cm sections
	Skin thickness range	314-400 µm
	Skin donors age	36 to 48 years old
	Skin donors sex	f
	Location	abdomen
	Source	ex vivo (Human skin samples were obtained from abdominal surgery of four donors)
	Integrity test	Yes, TEWL measurement
Receptor	Receptor medium	Ethanol/water 50/50 v/v
	Solubility in receptor medium	Yes
Sample Time	Exposure time	8h (to mimic contact during a normal working day)
	Observation time	24h
Sampling	Sample intervals	7 sampling times: 1h, 2h, 4h, 8h, 12h, 18h, 24h
Washing		post exposure
Final Procedure	Tape stripping	Yes
	TS1-2 analysed separately	Yes
Remarks: None		

Tested doses	Concentrate	Spray dilution 1
Target concentration [mg/ml]	500	1.66
Area dose [µg/cm²]	5000	16.6
Total dose [µg/cell]	4907.89	16.82
Specific activity [kBq/ml]	1179	1133
No. of donors	4	4
No of cells used/valid cells*	12/12	12/12

* Justification for excluded cells, if applicable

Results and discussions

Table A 5: In-vitro dermal penetration of active substance 1 formulated as product code/name through human skin - Recovery data

Dose group	**High dose**		**Low dose**	
	(Formulation concentrate)		(Spray dilution 1:301)	
Target concentration [mg/mL]	500		1.66	
Target dose [µg/cm²]	5000		16.6	
Mean actual applied dose [µg/cm²]	4907.89		16.82	
	Recovery [%]		Recovery [%]	
	Mean	S.D.	Mean	S.D.
Dislodgeable dose				
Skin washing after 8 h	93.53	4.34	76.15	7.93
Donor chamber wash	2.29	0.77	0.74	0.55
Dose associated to skin				
Tape strips: 1st sample, strips 1 + 2	0.68	0.22	5.98	5.88
Tape strips: 2nd sample; strips 3 - n	0.94	0.41	4.28	2.42
Skin preparation	1.75	1.55	6.51	5.83
Absorbed dose				
Receptor fluid	0.44	0.16	5.46	2.93
Receptor chamber wash	0.16	0.13	0.08	0.07
Total recovery[1]	99.78	3.53	99.22	2.64

Absorption essentially complete at end of study (>75% absorption within half the study duration) [%Absorption at $t_{0.5}$]	No [63.98% ±6.30]		No [68.58% ±6.15]	
If no: Absorption estimates = absorbed dose + skin preparation + tape strips sample 2)[2]	3.28	1.87	16.34	8.26
If yes: Absorption estimates = absorbed dose + skin preparation	N/A	N/A	N/A	N/A
Absorption estimates used for risk assessment[5]	**4.5**		**21.6**	

1 Values may not calculate exactly due to rounding of figures

2 In accordance with the EFSA Guidance on Dermal Absorption (EFSA Journal 2017;15(6):4873), the radioactivity in the second tape-strip pool (3rd to nth tape strip) is considered potentially absorbable if less than 75% of the absorption occurred in the first half of the study.

3 In accordance with the EFSA Guidance on Dermal Absorption (EFSA Journal 2017;15(6):4873), total absorption = mean + k*SD, where k= 0.64 based on the number of replicates employed (n=12).

BLQ : below the limit of quantification

NC: not calculated

N/A: not applicable

SD: standard deviation

Remarks
No applicable.

Conclusion/endpoint:

The dermal penetration of terbutylazine formulated as TERBUT 500 SC through human dermatomed skin was determined *in vitro*. The amount of applied dose penetrating within 24 hours was determined to be 4.5 %(mean ± k*standard deviation) and 22% for the formulation concentrate and the 1:301 spray dilution, respectively.
The dermal penetration estimates to be used for risk assessment were set at 4.5% and 22% for the formulation concentrate and the 1:301 spray dilution based on the EFSA guidance criteria.

A 2.11 Other/Special Studies

Appendix 3 Exposure calculations

A 3.1 Operator exposure calculations (KCP 7.2.1.1)

A 3.1.1 Calculations for terbuthylazine

Table A 6: Input parameters considered for the estimation of operator exposure

Formulation type	SC		Crop type	Cereals
Application rate (AR)	0.50	kg a.s./ha	Application method	Downward spraying
Area treated per day (A)	50	ha	Application equipment	Vehicle-mounted
Dermal absorption (DA)	0.1	% (concentr.)	Indoor/outdoor	Outdoor
	2.5	% (dilution)	Closed cabin	Yes
Inhalation absorption (IA)	100	%	Drift reduction	Yes
Body weight (BW)	60	kg/person	Cultivation	Normal
AOEL	0.0032	mg/kg bw/d	Water soluble bag	No

Table A 7: Estimation of operator exposure towards terbuthylazine according to EFSA guidance – with PPE (gloves)

Operator exposure for Terbut 500 S.C. outdoor spray applications

Application rate of active substance	0,5	kg a.s./ha	*i_AppRate*
Assumed area treated	50	ha/day	*d_AreaTreated*
Amount of active substance applied	25	kg a.s./day	*i_AmoutAS*
Dermal absorption of the product	0,10%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	2,50%		*i_AbsorInuse*
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
		75th centile	95th 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	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
		75th centile	95th 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	Yes		Incl. in AOEM model	
	Clothing	Potential exposure		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	Yes		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	0,1110618
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0,0042547	0,0018510
% of RVNAS	132,96%	57,84%

Table A 8: Estimation of operator exposure towards terbuthylazine according to EFSA guidance – with PPE (gloves and work wear)

Operator exposure for Terbut 500 S.C. outdoor spray applications

Application rate of active substance	0,5	kg a.s./ha	*i_AppRate*
Assumed area treated	50	ha/day	*d_AreaTreated*
Amount of active substance applied	25	kg a.s./day	*i_AmoutAS*
Dermal absorption of the product	0,10%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	2,50%		*i_AbsorInuse*
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
		75th centile	95th 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
		75th centile	95th 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	Yes		Incl. in AOEM model	
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	Yes		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	0,0267874
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0,0042547	0,0004465
% of RVNAS	132,96%	13,95%

Application rate of active substance	0,5	kg a.s./ha	*i_AppRate*
Assumed area treated	50	ha/day	*d_AreaTreated*
Amount of active substance applied	25	kg a.s./day	*i_AmoutAS*
Dermal absorption of the product	4,50%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	22,00%		*i_AbsorInuse*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted-Drift Reduction		
Season	not relevant		

OutdoorSoluble concentrates, emulsifiable concentrate, etc.Downward sprayingVehicle-mounted-Drift Red

	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75th centile	95th 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
		75th centile	95th centile		
Application	Hands	1569	5926	AOEM	
	Body	322	328	AOEM	
	Head	13	27	AOEM	
	Protected hands (gloves)	19	78	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	11	13	AOEM	
	Inhalation	5	9	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
	Closed cab	Yes		vehicle mounted upward spraying only	

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	4,6390788	0,1137654
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0,0773180	0,0018961
% of RVNAS	2416,19%	59,25%

A 3.2 Worker exposure calculations (KCP 7.2.3.1)

A 3.2.1 Calculations for terbuthylazine

Table A 9: Input parameters considered for the estimation of worker exposure

Intended use(s)	Cereals, outdoor		Dislodgeable foliar residue (DFR)	3	µg/cm²/kg a.s./ha
Application rate (AR)	0.50	kg a.s./ha	Dermal absorption (DA)	2.5	% (worst case)
Number of applications (NA)	1		Inhalation absorption (IA)	100	%
Interval between applications	365	days	Work rate per day (WR)	2	h/d
Half-life of active substance	30	days	TC dermal (potential)	12500	cm²/h
Multiple application factor (MAF)	1		TC dermal (work wear)	1400	cm²/h
Body weight (BW)	60	kg/person	TC dermal (work wear, gloves)	-	cm²/h
AOEL	0.0032	mg/kg bw/d	Task specific factor inhalation	-	ha/h x 10^{-3}

Crop type	Cereals	
Indoor or outdoor	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Worker's task	Inspection, irrigation	
Main body parts in contact with foliage	Hand and body	
Application rate of active substance	0,5	kg a.s./ha
Number of applications	1	
Interval between multiple applications	365	days
Half-life of active substance	30	days
Multiple application factor	1,0	
Dermal absorption of the product	0,10%	
Dermal absorption of the in-use dilution	2,50%	
Dislodgeable foliar residue (i_AppRate*i_DFR)	1,5	µg a.s./cm²
Working hours	2	hr
Dermal transfer coefficient - Total potential exposure	12500	cm²/hr
Dermal transfer coefficient - arms, body and legs covered	1400	cm²/hr
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment	cm²/hr
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10^(-3)

Table A 10: Estimation of longer term worker exposure towards terbuthylazine according to EFSA guidance

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves
Total systemic exposure (mg a.s./day)	0,9375000	0,1050000	no TC available for this assessment
Total systemic exposure per kg body weight (mg/kg bw/day)	0,0156250	0,0017500	
% of RVNAS	488,28%	54,69%	

WORKER EXPOSURE — EUROPOEM II MODEL

form: S.C.
a.s.: Terbuthylazine

Re-entry in the field

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	2	hours / day	default: 6 h (Europoem II)
Inhalation Exposure			without PPE
no model available	-		

Dermal Exposure				
DFR	Dislodgeable foliar residue	30	mg a.s./m2/kg a.s./ha	default (Europoem II)
TC	Transfer coefficient	0,14	m2/ hour	vegetable (field): 0.25; ornamentals: 0.5; small fruit: 0.3; large fruit: 0.45 (Europoem II)
	Dermal Exposure	**4,2**	mg a.s./ day	DE = DFR x AR x TC x T
Internal exposure				
DA	Dermal Absorption	22	%	
	PPE-factor dermal	5		gloves*
	AOEL	0,0032	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	0,924	0,185	DE(int) = DE x (DA/100)
Total	**0,924**	**0,185**	**sum**
% AOEL			
Inhalation	-	-	no model available
Dermal	28875	5775	%AOEL = 100 x DE(int) / AOEL
Total	**28875**	**5775**	**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.

	Total absorbed dose (mg/kg bw/day)	**% of systemic AOEL**
No PPE	0.0132	**412.5 %**
With PPE	0.00263	**82.5 %**

A.3.3. Resident and bystander exposure calculations (KCP 7.2.2.1)

A 3.3.1 Calculations for terbuthylazine

Table A 11: Input parameters considered for the estimation of bystander exposure

Intended use(s):	Maize		**Drift (D):**	0,91	% (FCTM, 1 m)
Application rate (AR):	0,5	kg a.s./ha	**Exposed Body Surface Area (BSA):**	1	m² (adults)
				0,21	m² (children)
Body weight (BW):	60	kg/person (adults)	**Specific Inhalation Exposure (I*A):**	0,001	mg/kg a.s. (6 hours, adults)
	16,15	kg/person (children)		0,00057	mg/kg a.s. (6 hours, children)
Dermal absorption (DA):	~~2,50~~ 22 %	% ('worst case')	**Area Treated (A):**	20	ha/d (based on Field Crops, Tractor Mounted (FCTM))
Inhalation absorption (IA):	100	%	**Exposure duration (T):**	5	min
AOEL:	0,0032	mg/kg bw/d			

Table A 12: Estimation of bystander exposure towards Terbuthylazine

Adults			**Children**		
Bystander: Dermal exposure after application in Maize (via spray drift)					
SDE_B = (AR x D x BSA x DA) / BW			SDE_B = (AR x D x BSA x DA) / BW		
(50 x 8,5% x 1 x 2,5%) / 60			(50 x 8,5% x 0,21 x 2,5%) / 16,15		
External exposure	4,25	mg/person	External exposure	0,8925	mg/person
External exposure	0,0708333	mg/kg bw/d	External exposure	0,0552632	mg/kg bw/d
Absorbed dose:	**0,0017708**	**mg/kg bw/d**	**Absorbed dose:**	**0,0013816**	**mg/kg bw/d**
Bystander: Inhalation exposure after application in Maize					
SIE_B = (I^*_A x AR x A x T x IA) / BW			SIE_B = (I^*_A x AR x A x T x IA) / BW		
(0,001 / 360 x 0,5 x 20 x 5 x 100%) / 60			(0,001 / 360 x 0,5 x 20 x 5 x 100%) / 16,15		
External exposure	0,0001389	mg/person	External exposure	7,982E-05	mg/person
External exposure	2,315E-06	mg/kg bw/d	External exposure	4,942E-06	mg/kg bw/d
Absorbed dose:	**0,0000023**	**mg/kg bw/d**	**Absorbed dose:**	**0,0000049**	**mg/kg bw/d**
Total systemic exposure: $SE_B = SDE_B + SIE_B$			Total systemic exposure: $SE_B = SDE_B + SIE_B$		
Total systemic exposure (absorbed dose)	0,1063889	mg/person	Total systemic exposure (absorbed dose)	0,0223923	mg/person
Total systemic exposure (absorbed dose)	**0,0017731**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0,0013865**	**mg/kg bw/d**
% of AOEL:	**55,41**	**%**	**% of AOEL:**	**43,33**	**%**

Bystander exposure towards Terbuthylazine					
Adults			**Children**		
Bystander: Dermal exposure after application in Maize (via spray drift)					
SDE_B = (AR x D x BSA x DA) / BW			SDE_B = (AR x D x BSA x DA) / BW		
(50 x 0,905% x 1 x 22%) / 60			(50 x 0,905% x 0,21 x 22%) / 16,15		
External exposure	0,4525	mg/person	External exposure	0,095025	mg/person
External exposure	0,0075417	mg/kg bw/d	External exposure	0,0058839	mg/kg bw/d
Absorbed dose:	**0,0016592**	**mg/kg bw/d**	**Absorbed dose:**	**0,0012945**	**mg/kg bw/d**
Bystander: Inhalation exposure after application in Maize					
SIE_B = (I^*_A x AR x A x T x IA) / BW			SIE_B = (I^*_A x AR x A x T x IA) / BW		
(0,001 / 360 x 0,5 x 20 x 5 x 100%) / 60			(0,001 / 360 x 0,5 x 20 x 5 x 100%) / 16,15		
External exposure	0,0001389	mg/person	External exposure	7,982E-05	mg/person
External exposure	2,315E-06	mg/kg bw/d	External exposure	4,942E-06	mg/kg bw/d
Absorbed dose:	**0,0000023**	**mg/kg bw/d**	**Absorbed dose:**	**0,0000049**	**mg/kg bw/d**
Total systemic exposure: $SE_B = SDE_B + SIE_B$			Total systemic exposure: $SE_B = SDE_B + SIE_B$		
Total systemic exposure (absorbed dose)	0,0996889	mg/person	Total systemic exposure (absorbed dose)	0,0209853	mg/person
Total systemic exposure (absorbed dose)	**0,0016615**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0,0012994**	**mg/kg bw/d**
% of AOEL:	**51,92**	**%**	**% of AOEL:**	**40,61**	**%**

Table A 13: Input parameters considered for the estimation of resident exposure

Intended use(s):	Maize	**Drift (D):**	0,91	% (FCTM, 1 m)

Application rate (AR):	0,5	kg a.s./ha	**Transfer coefficient (TC):**	7300	cm^2/h (adults)
				2600	cm^2/h (children)
Number of applications (NA):	1		**Turf Transferable Residues (TTR):**	5	%
Body weight (BW):	60	kg/person (adults)	**Exposure Duration (H):**	2	h
	16,15	kg/person (children)	**Airborne Concentration of Vapour (ACV):**	none	
Dermal absorption (DA):	~~2,50~~ 22	% ('worst case')	**Inhalation Rate (IR):**	16,57	m^3/d (adults),
Inhalation absorption (IA):	100	%		8,31	m^3/d (children)
Oral absorption (OA)	100	%	**Saliva Extraction Factor (SE):**	50	%
AOEL	0,0032	mg/kg bw/d	**Surface Area of Hands (SA):**	20	cm^2
			Frequency of Hand to Mouth (Freq):	20	events/h
			Dislodgeable foliar residues (DFR):	20	%
			Ingestion Rate for Mouthing of Grass/Day (IgR):	25	cm^2/d

Table A 14: Estimation of resident exposure towards terbuthylazine

Adults			**Children**		
Residents: Dermal exposure after application in Maize (via deposits caused by spray drift)					
SDE_R = (AR x NA x D x TTR x TC x H x DA) / BW			SDE_R = (AR x NA x D x TTR x TC x H x DA) / BW		
(0,005 x 1 x 2,77% x 5% x 7300 x 2 x 2,5%) / 60			(0,005 x 1 x 2,77% x 5% x 2600 x 2 x 2,5%) / 16,15		
External exposure	0,31025	mg/person	External exposure	0,1105	mg/person
External exposure	0,0051708	mg/kg bw/d	External exposure	0,0068421	mg/kg bw/d
Absorbed dose:	**0,0001293**	**mg/kg bw/d**	**Absorbed dose:**	**0,0001711**	**mg/kg bw/d**
Residents: Inhalation exposure to vapour					
SIE_R = (AC_V x IR x IA) / BW			SIE_R = (AC_V x IR x IA) / BW		
(0 x 16,57 x 100%) / 60			(0 x 8,31 x 100%) / 16,15		
External exposure		mg/person	External exposure		mg/person
External exposure		mg/kg bw/d	External exposure		mg/kg bw/d
Absorbed dose:		**none**	**Absorbed dose:**		**none**
			Residents: Oral exposure (hand-to-mouth transfer)		
			SOE_H = (AR x NA x D x TTR x SE x SA x Freq x H x OA) / BW		
			(0,005 x 1 x 2,77% x 5% x 50% x 20 x 20 x 2 x 100%) / 16,15		
			External exposure	0,0085	mg/person
			External exposure	0,0005263	mg/kg bw/d
			Absorbed dose	**0,0005263**	**mg/kg bw/d**
			Residents: Oral exposure (object-to-mouth transfer)		
			SOE_O = (AR x NA x D x DFR x IgR x OA) / BW		
			FAŁSZ		
			External exposure	0,002125	mg/person

			External exposure	0,0001316	mg/kg bw/d
			Absorbed dose	**0,0001316**	**mg/kg bw/d**
Total systemic exposure: $SE_R = SDE_R + SIE_R$			Total systemic exposure: $SE_R = SDE_R + SIE_R + SOE_H + SOE_O$		
Total systemic exposure (absorbed dose)	0,0077563	mg/person	Total systemic exposure (absorbed dose)	0,0133875	mg/person
Total systemic exposure (absorbed dose)	**0,0001293**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0,0008289**	**mg/kg bw/d**
% of AOEL:	**4,04**	**%**	**% of AOEL:**	**25,90**	**%**

Resident exposure towards Terbuthylazine					
Adults			**Children**		
Residents: Dermal exposure after application in Maize (via deposits caused by spray drift)					
$SDE_R = (AR \times NA \times D \times TTR \times TC \times H \times DA) / BW$			$SDE_R = (AR \times NA \times D \times TTR \times TC \times H \times DA) / BW$		
(0,005 x 1 x 0,57% x 5% x 7300 x 2 x 22%) / 60			(0,005 x 1 x 0,57% x 5% x 2600 x 2 x 22%) / 16,15		
External exposure	0,0330325	mg/person	External exposure	0,011765	mg/person
External exposure	0,0005505	mg/kg bw/d	External exposure	0,0007285	mg/kg bw/d
Absorbed dose:	**0,0001211**	**mg/kg bw/d**	**Absorbed dose:**	**0,0001603**	**mg/kg bw/d**
Residents: Inhalation exposure to vapour					
$SIE_R = (AC_V \times IR \times IA) / BW$			$SIE_R = (AC_V \times IR \times IA) / BW$		
(0 x 16,57 x 100%) / 60			(0 x 8,31 x 100%) / 16,15		
External exposure		mg/person	External exposure		mg/person
External exposure		mg/kg bw/d	External exposure		mg/kg bw/d
Absorbed dose:		**none**	**Absorbed dose:**		**none**
			Residents: Oral exposure (hand-to-mouth transfer)		
			$SOE_H = (AR \times NA \times D \times TTR \times SE \times SA \times Freq \times H \times OA) / BW$		
			(0,005 x 1 x 0,57% x 5% x 50% x 20 x 20 x 2 x 100%) / 16,15		
			External exposure	0,000905	mg/person
			External exposure	5,604E-05	mg/kg bw/d
			Absorbed dose	**0,0000560**	**mg/kg bw/d**
			Residents: Oral exposure (object-to-mouth transfer)		
			$SOE_O = (AR \times NA \times D \times DFR \times IgR \times OA) / BW$		
			FAŁSZ		
			External exposure	0,0002263	mg/person
			External exposure	1,401E-05	mg/kg bw/d
			Absorbed dose	**0,0000140**	**mg/kg bw/d**
Total systemic exposure: $SE_R = SDE_R + SIE_R$			Total systemic exposure: $SE_R = SDE_R + SIE_R + SOE_H + SOE_O$		
Total systemic exposure (absorbed dose)	0,0072672	mg/person	Total systemic exposure (absorbed dose)	0,0037196	mg/person
Total systemic exposure (absorbed dose)	**0,0001211**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0,0002303**	**mg/kg bw/d**
% of AOEL:	**3,78**	**%**	**% of AOEL:**	**7,20**	**%**

Table A 15: Input parameters considered for the estimation of resident exposure

Croptype	Cereals	
Application method	Downward spraying	
Application equipment	Vehicle-mounted-Drift Reduction	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Buffer strip	5	m
Application rate of the product	0,5	kg a.s./ha
Concentration of active substance (in-use dilution for liquid applications)	1,666666667	g a.s./l
Dermal absorption of product	4,50%	
Dermal absorption of in-use dilution	22,00%	
Oral absorption	100,00%	
Dislodgeable foliar residue (i_AppRate*i_DFR)	1,17	µg a.s./cm^2
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa
Concentration in air	0,001	mg/m^3
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
Exposure duration inhalation	24	hours
Exposure duration entry into treated crops	0,25	hours
Light clothing adjustment factor	18,0%	
Breathing rate adult	0,23	m^3/day/kg
Breathing rate child (1-3 year old)	1,07	m^3/day/kg
Drift percentage on surface (75th percentile)	2,30%	
Drift percentage on surface (mean)	1,80%	
Turf transferable residues percentage	5,00%	
Transfer coeff. of surface deposits-adult	7300	cm^2/hour
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm^2/hour
Saliva extraction percentage	50,00%	
Surface area of hands mouthed	20	cm^2
Frequency of hand to mouth activity	9,5	events/hour
Ingestion rate for mouthing of grass per day	25	cm^2
Dislodgeable residues percentage transferability for object to mouth	20,00%	
Transfer coefficient for entry into treated crops (75th percentile) - adult	7500	cm^2/h
Transfer coefficient for entry into treated crops (75th percentile) - child	2250	cm^2/h
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm^2/h
Transfer coefficient for entry into treated crops (mean) - child	1794	cm^2/h

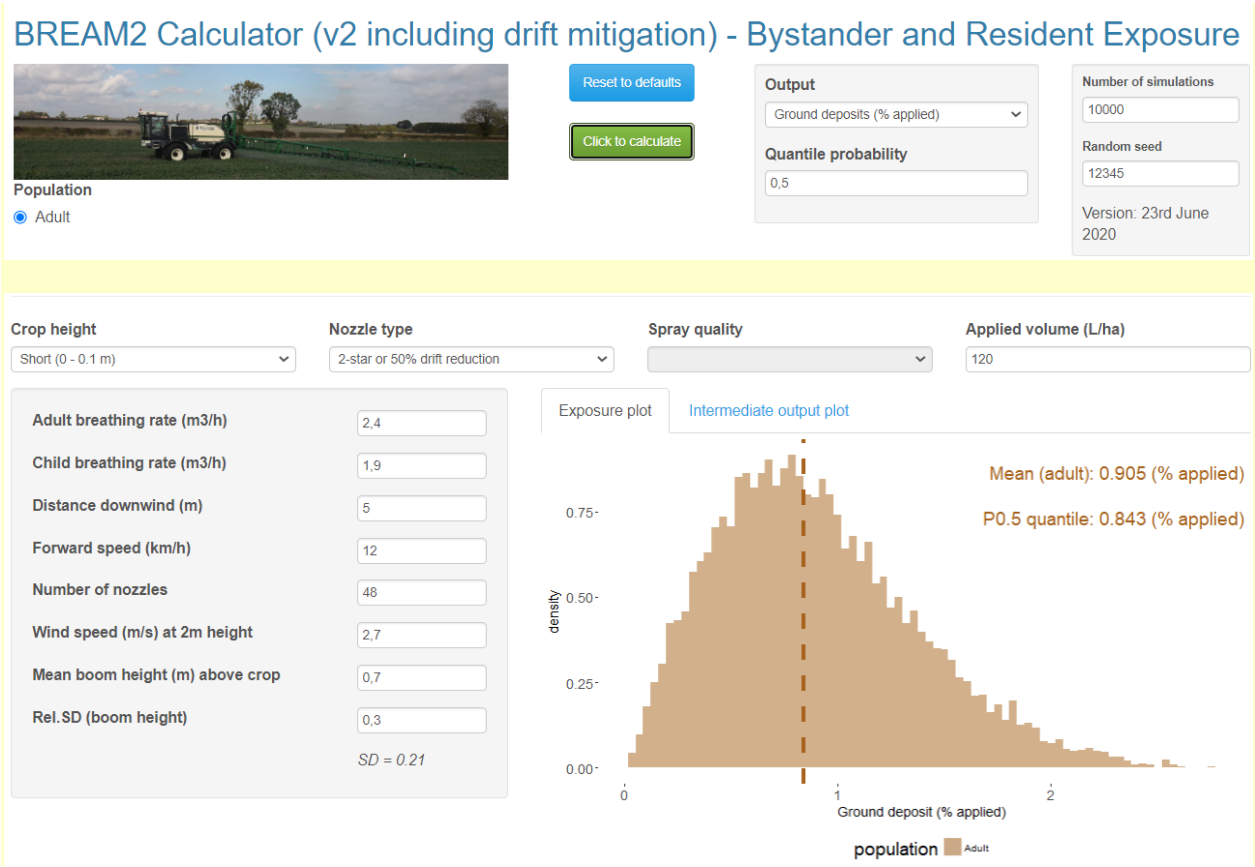
Table A 16: Estimation of resident exposure towards terbuthylazine – AOEM

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)	**0,0328392**	**0,0107000**	**0,0041228**	**0,1447875**	**0,1475271**
Total systemic exposure per kg body weight (mg/kg bw/day)	**0,0032839**	**0,0010700**	**0,0004123**	**0,0144788**	**0,0147527**
% of RVNAS	**102,62%**	**33,44%**	**12,88%**	**452,46%**	**461,02%**
1.2 Adult					
	Spray drift	**Vapour**	**Surface deposits**	**Entry into treated crops**	**All pathways (mean)**
Total systemic exposure (mg a.s./day)	**0,0358513**	**0,0138000**	**0,0092345**	**0,4826250**	**0,4243646**

Total systemic exposure per kg body weight (mg/kg bw/day)	0,0005975	0,0002300	0,0001539	0,0080438	0,0070727
% of RVNAS	18,67%	7,19%	4,81%	251,37%	221,02%

	Systemic exposure [mg a.s. /day]	Systemic exposure [mg a.s./kg bw/day]
1-3 year old child		
Spray drift	0,0181567	0,0018157
Vapour	0,0107000	0,0010700
Surface deposits		
Dermal	0,0025740	0,0002574
Hand to mouth	0,0004275	0,0000428
Object to mouth	0,0002250	0,0000225
Entry into treated crops		
Dermal	0,1154439	0,0115444
Hand to mouth		
Object to mouth		
Adult		
Spray drift	0,0185246	0,0003087
Vapour	0,0138000	0,0002300
Surface deposits (dermal)	0,0072270	0,0001205
Entry into treated crops (dermal)	0,3848130	0,0064136

Table A 17: Ground deposit calculation - BREAM 2 calculator



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)