

FINAL REGISTRATION REPORT

Part B

Section 5

Analytical Methods

Detailed summary of the risk assessment

Product code: TERBUT 500 SC

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

Chemical active substance(s):

Terbutylazine, 500 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: PUH Chemirol Sp. z o.o.

Submission date: November 2019

Finalisation date: January 2021; June 2022

Version history

When	What
January 2021	RMS finalised dRR assessment
June 2022	Final Version after Commenting period

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5 Analytical methods

5.1 Conclusion and summary of assessment

Sufficiently sensitive and selective analytical methods are available for the active substance(s) and relevant impurities in the plant protection product.

Noticed data gaps are:

- None

Sufficiently sensitive and selective analytical methods are available for all analytes included in the residue definitions.

Noticed data gaps are:

- None

Commodity/crop	Supported/ Not supported
Maize	Supported

5.2 Methods used for the generation of pre-authorization data (KCP 5.1)

5.2.1 Analysis of the plant protection product (KCP 5.1.1)

5.2.1.1 Determination of active substance and/or variant in the plant protection product (KCP 5.1.1)

An overview on the acceptable methods and possible data gaps for analysis of terbuthylazine in plant protection product is provided as follows:

Comments of zRMS:	The proposed analytical method is suitable for the determination of active substances terbuthylazine in plant protection product Terbut 500 SC/La Zina 500 SC/Tekno 500 SC. The proposed analytical method has been fully validated in terms of specificity, linearity, repeatability, and accuracy. Proposed method fulfils the requirements of SANCO/3030/99 rev.4 and SANCO/3030/99 rev.5 guidance. The validation of the analytical method has been accepted.
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Reference:	KCP 5.1.1/01
Report	Terbut 500 SC Method development and validation for the determination of active substance and relevant impurities content in the formulation, Wołoszynowska, M., 2018, Study code: BA-07-18
Guideline(s):	SANCO/3030/99 rev.4.
Deviations:	No
GLP:	Yes
Acceptability:	Yes

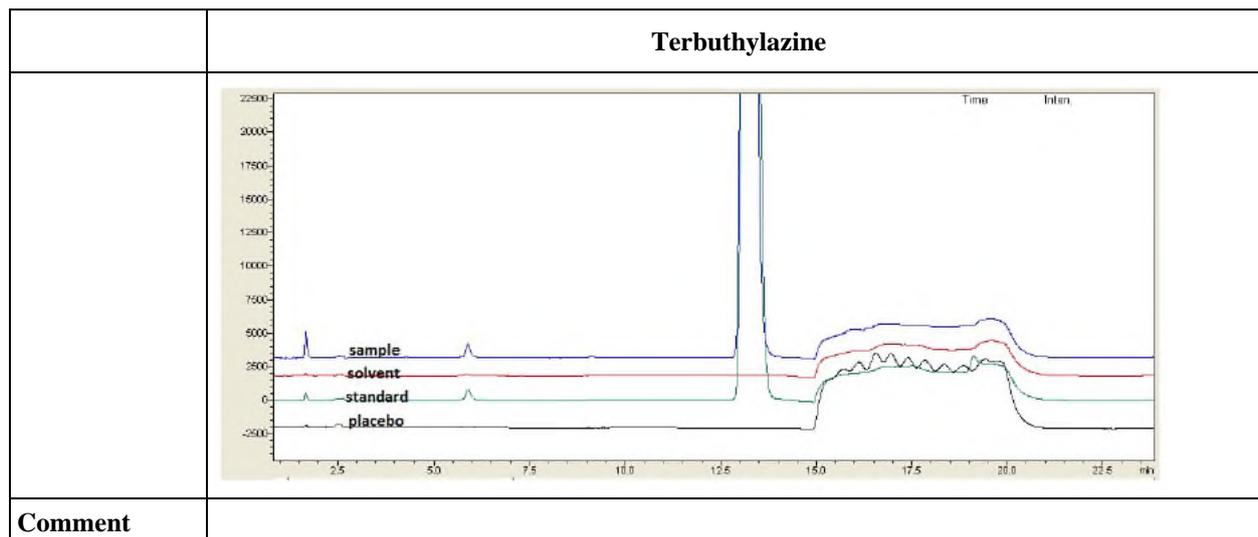
Materials and methods

Determination of active substance was performed by HPLC technique with UV/Vis detector using reversed phase column. The validated analytical methods are specific. There are no interferences between the analytes and other components of the specimen. The methods have good precision, accuracy and linearity and fulfil requirements of SANCO/3030/99 rev.4.

Validation - Results and discussions

Table 5.2-1: Methods suitable for the determination of active substances terbuthylazine in plant protection product TERBUT 500 SC

	Terbuthylazine
Author(s), year	Wołoszynowska, M., 2018
Principle of method	HPLC
Linearity (linear between mg/L / % range of the declared content) (correlation coefficient, expressed as r)	<p>The linearity of the detector response was assessed using six standard solutions at the concentration range of terbuthylazine from 0.0233 mg/mL to 0.1867 mg/mL, which corresponds to the concentration range of 24% to 192% of terbuthylazine content in the preparation. All solutions were analysed twice.</p> <p>Correlation coefficient should be $R^2 \geq 0.99$ $y = 44\,800\,109x + 17\,765$ $R^2 = 0.9999$</p>
Precision – Repeatability Mean n = 6 (%RSD)	<p>The method repeatability was assessed on the basis of six independent determinations of active substance content in Terbut 500 SC preparation</p> <p>Acceptable relative standard deviation for main ingredient (~ 45%) is $RSDr \leq 1.51\%$. The obtained result 0.99% is acceptable.</p>
Accuracy n = 12 (% Recovery)	<p>Accuracy of active substance determination in Terbut 500 SC was assessed by recovery value at two levels of concentration. Each of twelve 10 mL volumetric flasks were charged with approximately 20 mg placebo and weighed. About 0.2 mL of the terbuthylazine standard solution at concentration of 1.1669 mg/mL was added to the each of the first six flasks and acetonitrile was added up to the volume. To each of the remaining six flasks 1.6 mL of terbuthylazine standard solution at the concentration of 0.7083 mg/mL was added and acetonitrile was added up to the volume. The flasks were put into the ultrasonic bath for 5 min. The concentration of analyte in each solution was calculated from the equation of the calibration curve. Obtained final concentrations were examined and the nominal and calculated contents were compared.</p> <p>For the main ingredient at concentration of > 10 % the average recovery value should be $100 \pm 2\%$. The obtained result of 100.05% is acceptable. For the level I the average recovery was 100.75%, RSD=0.37% For the level II the average recovery was 99.36%, RSD=0.95%</p>
Interference/ Specificity	The chromatograms of placebo, solvent, standard solution and the examined specimen solution were performed and superimposed.



Conclusion

The methods for determination of terbutylazine in Terbut 500 SC preparation are specific. The validation parameters for linearity, instrument precision, repeatability and accuracy are within the acceptance range. The content of active substance in Terbut 500 SC determined by developed and validated methods is, respectively:

Terbutylazine : $46.21 \pm 0.48\%$.

5.2.1.2 Description of analytical methods for the determination of relevant impurities (KCP 5.1.1)

An overview on the acceptable methods and possible data gaps for analysis of relevant impurities in plant protection product is provided as follows:

Comments of zRMS:	<p>The proposed analytical methods are suitable for the determination of relevant impurities atrazine, propazine and simazine in plant protection product Terbut 500 SC/La Zina 500 SC/Tekno 500 SC.</p> <p>The proposed analytical methods have been fully validated in terms of specificity, linearity, repeatability, and accuracy. The LOQs were determined.</p> <p>Proposed methods fulfil the requirements of SANCO/3030/99 rev.4 and SANCO/3030/99 rev.5 guidance.</p> <p>The validation of the analytical methods has been accepted.</p>
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Reference:	KCP 5.1.1/01
Report	Terbut 500 SC Method development and validation for the determination of active substance and relevant impurities content in the formulation, Wołoszynowska, M., 2018, Study code: BA-07-18
Guideline(s):	SANCO/3030/99 rev.4.
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Materials and methods

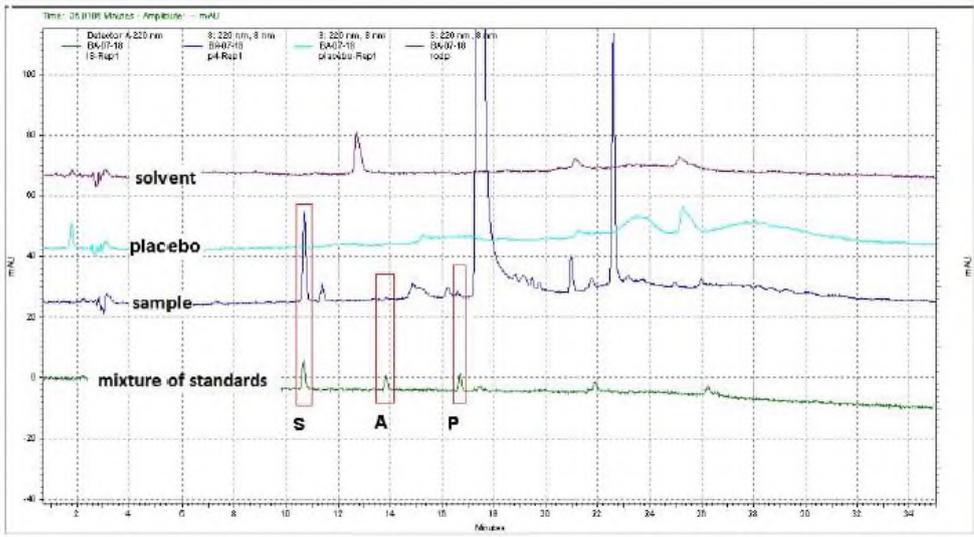
Determination of relevant impurities was performed by HPLC technique with UV/Vis detector using reversed phase column. The validated analytical methods are specific. There are no interferences between the analytes and other components of the specimen. The methods have good precision, accuracy and linearity and fulfil requirements of SANCO/3030/99 rev.4.

Validation - Results and discussions

Table 5.2-2: Methods suitable for the determination of the relevant impurities in plant protection product (PPP) TERBUT 500 SC

	Atrazine max. 10 g/kg 1 g/kg	Propazine max. 1 g/kg 10 g/kg	Simazine max. 30 g/kg
Author(s), year	Wołoszynowska, M., 2018 and Wołoszynowska, M., 2020		
Principle of method	HPLC		
Linearity (linear between mg/L) (correlation coefficient, expressed as r)	<p>The linearity of the detector response was assessed using six standard solutions at the concentration range of atrazine from 0.000021 mg/mL to 0.00062 mg/mL, at the concentration range of propazine from 0.000028 mg/mL to 0.00071 mg/mL and at the concentration range of simazine from 0.00063 mg/mL to 0.0025 mg/mL. All solutions were analysed twice.</p> <p>$y = 114\ 118\ 235x - 419$ $R^2 = 0.9983$ Correlation coefficient should be $R^2 \geq 0.99$. The obtained result is acceptable</p>	<p>The linearity of the detector response was assessed using six standard solutions at the concentration range of atrazine from 0.000021 mg/mL to 0.00062 mg/mL, at the concentration range of propazine from 0.000028 mg/mL to 0.00071 mg/mL and at the concentration range of simazine from 0.00063 mg/mL to 0.0025 mg/mL. All solutions were analysed twice.</p> <p>$y = 171\ 529\ 773x - 16\ 679$ $R^2 = 0.9989$ Correlation coefficient should be $R^2 \geq 0.99$. The obtained result is acceptable.</p>	<p>The linearity of the detector response was assessed using six standard solutions at the concentration range of atrazine from 0.000021 mg/mL to 0.00062 mg/mL, at the concentration range of propazine from 0.000028 mg/mL to 0.00071 mg/mL and at the concentration range of simazine from 0.00063 mg/mL to 0.0025 mg/mL. All solutions were analysed twice.</p> <p>$y = 167824326x - 28459$ $R^2 = 0.9982$ Correlation coefficient should be $R^2 \geq 0.99$. The obtained result is acceptable.</p>
Precision – Repeatability Mean n = 6 (%RSD)	<p>The method repeatability was assessed on the basis of six independent determinations of relevant impurities content in Terbut 500 SC preparation. Because peak of atrazine was not detected above either of the LOQ values in any of the solutions, six weights of placebo (approximately 100 mg) were fortified with atrazine at 10LOQ level (0.00010 mg/mL) were analyzed to determine reproducibility</p> <p>Acceptable relative standard</p>	<p>The method repeatability was assessed on the basis of six independent determinations of relevant impurities content in Terbut 500 SC preparation. Because peak of atrazine propazine was not detected above either of the LOQ values in any of the solutions, six weights of placebo (approximately 100 mg) were fortified with atrazine propazine at 10LOQ level (0.00010 0.0002 mg/mL) were analyzed to determine reproducibility</p>	<p>The method repeatability was assessed on the basis of six independent determinations of relevant impurities content in Terbut 500 SC preparation. Because peak of atrazine was not detected above either of the LOQ values in any of the solutions, six weights of placebo (approximately 100 mg) were fortified with atrazine at LOQ level (0.00010 mg/mL) were analyzed to determine reproducibility</p>

	Atrazine max. 10 g/kg 1 g/kg	Propazine max. 1 g/kg 10 g/kg	Simazine max. 30 g/kg
	deviation for analyte (~ 0.0015%) is RSDr ≤ 10.07% 7.13%. The obtained result 6.37% is acceptable.	Acceptable relative standard deviation for analyte (~ 0.0018%) is RSDr ≤ 9.85%. The obtained result 7.08% is acceptable. Because the RSD value for propazine while detrmining repeatability of the method for six measurements was higher than the acceptable, in accordance with SANCO document, one of the extreme value was rejected and the RSD for five measurements was claculated. The results obtained was RSD=3.79% and is lower than the acceptable relative standard deviation for analyte (~ 0.0018%) RSDr ≤ 6.97%.	Acceptable relative standard deviation for analyte (~ 0.038%) is RSDr ≤ 4.37%. The obtained result 2.76 2.21% is acceptable.
Accuracy n = 12 (% Recovery)	Accuracy of impurities determination in Terbut 500 SC was assessed by recovery value at two levels of concentration. Each of twelve 10 mL volumetric flasks were charged with approximately 20 mg placebo and weighed. About 0.1 mL of the atrazine standard solution at concentration of 0.0272 mg/mL, of the propazine standard solution at concentration of 0.0222 mg/mL and of the simazine standard solution at concentration of 0.0242 mg/mL were added to the each of the first six flasks and acetonitrile was added up to the volume. To each of the remaining six flasks 0.2 mL of standards solution at the same concentration were added and acetonitrile was added up to the volume. The flasks were put into the ultrasonic bath for 5 min. The concentration of analytes in each solution was calculated from the equation of the calibration curve. Obtained final concentrations were examined and the nominal and calculated contents were compared. For the level I the average	Accuracy of impurities determination in Terbut 500 SC was assessed by recovery value at two levels of concentration. Each of twelve 10 mL volumetric flasks were charged with approximately 20 mg placebo and weighed. About 0.1 mL of the atrazine standard solution at concentration of 0.0272 mg/mL, of the propazine standard solution at concentration of 0.0222 mg/mL and of the simazine standard solution at concentration of 0.0242 mg/mL were added to the each of the first six flasks and acetonitrile was added up to the volume. To each of the remaining six flasks 0.2 mL of standards solution at the same concentration were added and acetonitrile was added up to the volume. The flasks were put into the ultrasonic bath for 5 min. The concentration of analytes in each solution was calculated from the equation of the calibration curve. Obtained final concentrations were examined and the nominal and calculated contents were compared. For the level I the average	Accuracy of impurities determination in Terbut 500 SC was assessed by recovery value at two levels of concentration. Each of twelve 10 mL volumetric flasks were charged with approximately 20 mg placebo and weighed. About 0.1 mL of the atrazine standard solution at concentration of 0.0272 mg/mL, of the propazine standard solution at concentration of 0.0222 mg/mL and of the simazine standard solution at concentration of 0.0242 mg/mL were added to the each of the first six flasks and acetonitrile was added up to the volume. To each of the remaining six flasks 0.2 mL of standards solution at the same concentration were added and acetonitrile was added up to the volume. The flasks were put into the ultrasonic bath for 5 min. The concentration of analytes in each solution was calculated from the equation of the calibration

	Atrazine max. 10 g/kg 1 g/kg	Propazine max. 1 g/kg 10 g/kg	Simazine max. 30 g/kg
	recovery was 101.92%, RSD=1.58% For the level II the average recovery was 97.23%, RSD=1.15% Average recovery was 99.57%	recovery was 97.97%, RSD=2.14% For the level II the average recovery was 93.98%, RSD=0.98% Average recovery was 95.97%	curve. Obtained final concentrations were examined and the nominal and calculated contents were compared. For the level I the average recovery was 123.09%, RSD=0.58% For the level II the average recovery was 80.39%, RSD=0.37% Average recovery was 101.74%
Interference/ Specificity	The chromatograms of placebo, solvent, mixture of standards solutions and the examined specimen solution were performed and superimposed		
			
LOQ	The limit of quantification (LOQ) was defined as the lowest quantity of standard (approximately the height of the peak is a 10-fold amount of the baseline noise) ie. 0.0000119 mg/mL for atrazine For the impurities at concentration of > 0.1 % the average recovery value should be 100 ± 25 %. The obtained result of 99.57% is acceptable.	The limit of quantification (LOQ) was defined as the lowest quantity of standard (approximately the height of the peak is a 10-fold amount of the baseline noise) ie. 0.0000215 mg/mL for propazine For the impurities at concentration of > 0.1 % the average recovery value should be 100 ± 25 %. The obtained result of 95.97% is acceptable.	The limit of quantification (LOQ) was defined as the lowest quantity of standard (approximately the height of the peak is a 10-fold amount of the baseline noise) ie. 0.0000242 mg/mL for simazine For the impurities at concentration of > 0.1 % the average recovery value should be 100 ± 25 %. The obtained result of 98.36% 101.74% is acceptable.
Comment	Acceptable	Acceptable	Acceptable

Conclusion

The methods for determination of atrazine, propazine and simazine in Terbut 500 SC preparation are specific. The validation parameters for linearity, instrument precision, repeatability and accuracy are within the acceptance range. The content of relevant impurities in Terbut 500 SC determined by developed and validated methods is, respectively:

Atrazine: < LOQ it means below 0.0002% = 2ppm,

Propazine: < LOQ it means below 0.0004% = 4ppm,

Simazine: 0.0387 ± 0.0009%.

5.2.1.3 Description of analytical methods for the determination of formulants (KCP 5.1.1)

Please refer to PART C – Confidential data.

5.2.1.4 Applicability of existing CIPAC methods (KCP 5.1.1)

Analytical methods for determination of Terbutylazine impurities and relevance of CIPAC methods in TERBUT 500 SC were not evaluated as part of the EU review of any of active substances. Therefore, all relevant data are provided and are considered adequate.

5.2.1.5 Methods for the determination of residues (KCP 5.1.2)

An overview on the acceptable methods and possible data gaps for analysis of residues of terbuthylazine for the generation of pre-authorization data is given in the following table. For the detailed evaluation of new/ additional studies it is referred to Appendix 2.

Table 5.2-3: Validated methods for the generation of pre-authorization data

Component of residue definition: Terbuthylazine				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
Food/feed of plant origin (Residues)	Primary	0.02 mg/kg	GC-NPD	Diertelre, 1993 II A 4.2.1, IIIA 5.2 DAR Terbuthylazine – Additional report, B.5: Methods of analysis January 2010. EU agreed EFSA Journal 2011; 9(1):1969
	Confirmatory (if required)	0.02 mg/kg	HPLC MS/MS	Ferguson, 2009 II A 4.2.1, IIIA 5.2 DAR Terbuthylazine – Additional report, B.5: Methods of analysis January 2010. EU agreed EFSA Journal 2011; 9(1):1969
Animal products, food of animal origin (Residues)	Primary	According to the EFSA Journal 2011; 9(1):1969, no methods required as MRLs for animal tissues have not been set.		
	Confirmatory (if required)			

Component of residue definition: Terbutylazine				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
Soil (Environmental fate)	Primary	0.02 mg/kg	GC-MS	Lutolf W., 1995 II A 4.2.2 to 4.2.4, IIIA 5.2 DAR Terbutylazine – Additional report, B.5: Methods of analysis January 2010. EU agreed EFSA Journal 2011; 9(1):1969
	Confirmatory (if required)	0.01 mg/kg	HPLC-MS/MS	Figueiredo J, 2003 II A 4.2.2 to 4.2.4, IIIA 5.2 DAR Terbutylazine – Additional report, B.5: Methods of analysis January 2010. EU agreed EFSA Journal 2011; 9(1):1969
Water (surface, ground and drinking water) (Environmental fate)	Primary	0.1 mg/kg	RP HPLC-MS/MS	Robinson.,2004 II A 4.2.2 to 4.2.4, IIIA 5.2 DAR Terbutylazine – Additional report, B.5: Methods of analysis January 2010. EU agreed EFSA Journal 2011; 9(1):1969
	Confirmatory (if required)	Not required		
Air (Environmental fate)	Primary	1µg/m ³	GC-NPD	Tribolet.,1992 II A 4.2.2 to 4.2.4, IIIA 5.2 DAR Terbutylazine – Additional report, B.5: Methods of analysis January 2010. EU agreed EFSA Journal 2011; 9(1):1969
	Confirmatory (if required)	1µg/m ³	GC-MS	Tribolet.,1992 II A 4.2.2 to 4.2.4, IIIA 5.2 DAR Terbutylazine – Additional report, B.5: Methods of analysis January 2010. EU agreed EFSA Journal 2011; 9(1):1969
Soil, water,... (Efficacy)	Primary	Not required		
	Confirmatory (if required)			
Feed, body fluids,... (Toxicology)	Primary	No data submitted or required as terbutylazine is not classified as toxic or very toxic		
	Confirmatory (if required)			
Body fluids, air, (Exposure)	Primary	No data submitted or required as terbutylazine is not classified as toxic or very toxic		
	Confirmatory (if required)			
Soil, water.	Primary	All data was evaluated during Annex I inclusion , and new studies are		

Component of residue definition: Terbutylazine				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
(Ecotoxicology)	Confirmatory (if required)	necessary. All methods are described separately in DAR Vol3 B9 Ecotoxicology 2007. Please refer to the DAR Vol 3 B9 2007. No general analytical methods were developed for risk assessment apart those reported as specific in studies in support of ecotoxicological studies.		

5.3 Methods for post-authorization control and monitoring purposes (KCP 5.2)

Data provided on Annex I inclusion is sufficient for post-authorizations methods. No new methods are necessary since all data is described and presented in Table 5.2-3 in point KCP 5.1.2.

5.3.1 Analysis of the plant protection product (KCP 5.2)

Analytical methods for the determination of the active substance and relevant impurities in the plant protection product shall be submitted, unless the applicant shows that these methods already submitted in accordance with the requirements set out in point 5.2.1 can be applied.

5.3.2 Description of analytical methods for the determination of residues of Terbutylazine (KCP 5.2)

5.3.2.1 Overview of residue definitions and levels for which compliance is required

Compared to the residue definition proposed in the Draft Assessment Report (incl. its addenda) the current legal residue definition is identical.

Table 5.3-1: Relevant residue definitions for monitoring/enforcement and levels for which compliance is required

Matrix	Residue definition	MRL / limit	Reference for MRL/level Remarks
Plant, high protein/high starch content (dry commodities) –Maize	Terbutylazine	LOQ 0.02 mg/kg	EFSA Journal 2011; 9(1):1969
Muscle	Not necessary for the representative uses.	EFSA Journal 2011; 9(1):1969	EFSA Journal 2011; 9(1):1969
Milk			
Eggs			
Fat			
Liver, kidney			
Soil (Ecotoxicology)	Terbutylazine (MT0) plus desethyl-terbutylazine (MT1) plus hydroxyl-terbutylazine (MT13)	LOQ 0.01 mg/kg	EFSA Journal 2011; 9(1):1969

Matrix	Residue definition	MRL / limit	Reference for MRL/level Remarks
Drinking water (Human toxicology)	Terbutylazine (MT0) plus desethyl-terbutylazine (MT1) plus hydroxy-terbutylazine (MT13) plus desethyl-hydroxy-terbutylazine (MT14) plus LM1, LM2, LM3, LM4, LM5 and LM6	0.1 µg/L	general limit for drinking water
Surface water (Ecotoxicology)	Terbutylazine (MT0) plus desethyl-terbutylazine (MT1) plus hydroxyl-terbutylazine (MT13)	12 µg a.s/L	EFSA Journal 2011; 9(1):1969
Air	Terbutylazine	1 µg/m ³	AOEL sys/AOEL inhal: 0.0032 mg/kg bw/d
Tissue (meat or liver)	Terbutylazine	Not required	notclassified as T / T+
Body fluids		Not required	notclassified as T / T+

5.3.2.2 Description of analytical methods for the determination of residues in plant matrices (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of Terbutylazine in plant matrices is given in the following tables. For the detailed evaluation of additional studies it is referred to Appendix 2.

zRMS comment

EFSA Journal 2020;18(1):5980:

Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs):

Dry and high-water content matrices:

GC-NPD, LOQ 0.02mg/kg (DFG S19) for terbutylazine in cereal grain, ILV considered acceptable (EFSA, 2011). This method was reported validated for maize whole plant during the peer however an ILV and confirmatory methods are missing (United Kingdom, 2007; Spain, 2018)

High oil content matrices:

LC-MS/MS method for terbutylazine, MT1 and MT14 with an individual LOQ of 0.02 mg/kg; ILV and confirmatory method are missing (United Kingdom, 2010a; Spain, 2018)

EURLs (EURLs, 2018) provided for routine analyses the following methods for terbutylazine:

High water, acid content commodities and high oil commodities: •LC-MS/MS method (QuEChERS-method EN 15662:2008) with a LOQ 0.01 mg/kg, validated in tomato, orange, almonds and avocado; Dry matrices: •LC-QqQ-MS/MS method (QuEChERS-method EN 15662:2008) with a LOQ 0.01 mg/kg validated in wheat, oat, rice and rye; Special matrices: •LC-MS/MS method (QuEChERS-method EN 15662:2008) with a LOQ 0.01 mg/kg, validated in green tea.

Table 5.3-2: Validated methods for food and feed of plant origin (required for all matrix types, “difficult” matrix only when indicated by intended GAP)

Component of residue definition: Terbutylazine (MT0)				
Matrix type	Method type	Method LOQ	Principle of method	Author(s), year / missing / EU agreed
High protein/high starch content (dry) Maize	Primary	0.02 mg/kg	GC-NPD	Syngenta : Diertelrle, 1993. EU agreed Oxon: Freschi 2002c, EU agreed
	ILV	0.02mg/kg	LC MS/MS	Syngenta: Ferguson 2009 EU agreed OXON: not available
	Confirmatory (if required)		Not required	

Table 5.3-3: Statement on extraction efficiency

	Method for products of plant origin
Required, available from:	DAR 2010 (additional report) Vol3 B5
Not required, because:	No new studies necessary since all studies described in DAR are sufficient.

5.3.2.3 Description of analytical methods for the determination of residues in animal matrices (KCP 5.2)

According to the EFSA Journal 2011; 9(1):1969 for all representative uses in maize, there is no requirement for presenting methods for methods for food and feed of animal origin. There is no residue definition for monitoring purposes.

zRMS comment

EFSA Journal 2020;18(1):5980:

*Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs):
 LC–MS/MS multi-residue QuEChERS method (EN 15662:2009-02) for terbutylazine in animal matrices;
 LOQ 0.01mg/kg; confirmatory method and ILV available for milk, meat, egg, liver, fat and kidney; LOD <0.00125 mg/kg (Spain, 2018)
 Analytical method for enforcement of MT1 in milk, not available and required.
 GC-NPD, LOQ 0.02mg/kg (DFG S19) for terbutylazine in animal matrices; confirmatory method missing and ILV available (United Kingdom, 2007)
 EURLs (EURLs, 2018) provided for routine analyses of food of animal origin for terbutylazine an:
 •LC–MS–Q–TOF QuEChERS with a screening detection limit (SDL) of 0.0025 mg/kg for terbutylazine, validated in milk and milk products; meat (red and white), fish (high and low fat), various honeys
 •LC–MS/MS QuEChERS EN-15662 method for monitoring terbutylazine and MT1 with an individual LOQ of 0.01 mg/kg in milk (EURLs, 2018)*

5.3.2.4 Description of methods for the analysis of soil (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of Terbutylazine in soil is given in the following tables. No new methods are necessary.

Table 5.3-4: Validated methods for soil (if appropriate)

Component of residue definition: Terbutylazine (MT0) plus desethyl-terbutylazine (MT1) plus hydroxyl-terbutylazine (MT13)			
Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Primary	LOQ=0.01 mg/kg	LC MS/MS	REM 148.11.: Figueriredo J, 2003; Trobolet R., 2003 EU Approved
Confirmatory	Not required		

5.3.2.5 Description of methods for the analysis of water (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of terbutylazine in surface and drinking water is given in the following tables. No new method is necessary.

Table 5.3-5: Validated methods for water (if appropriate)

Component of residue definition: Terbutylazine (MT0) plus desethyl-terbutylazine. (MT1) plus hydroxy-terbutylazine (MT13) plus desethyl-hydroxy-terbutylazine (MT14) plus LM1, LM2, LM3, LM4, LM5 and LM6				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Drinking water	Primary	LOQ= 0.1 µg/L for parent, MT1, MT13, MT14 LOQ=0.05 µg/L for LM5, LM6, LM3	Reverse phase HPLC-MS/MS	DAR(additional report) 2010, IIA 4.2.2 to 4.2.4, IIIA 5.2 Syngenta: RAM 426/01 Robinson N.J, 2004 Glanzel, A. 2005 Syngenta HPLC MS/MS method Zietz, E. 2009 OXON: Todd,N.,2002
	ILV		Not available	
	Confirmatory		Not required	
Surface water	Primary	LOQ= 0.1 µg/L for parent, MT1, MT13, MT14 LOQ=0.05 µg/L for LM5, LM6, LM3		Syngenta: REM 148.05:Lutolf W., 1995a REM 148.11.:Figueriredo J, 2003; Trobolet R., 2003 Oxon: Todd M, 2002a Gillis N.A, 1997 Todd M., 1999

Component of residue definition: Terbutylazine (MT0) plus desethyl-terbutylazine. (MT1) plus hydroxy-terbutylazine (MT13) plus desethyl-hydroxy-terbutylazine (MT14) plus LM1, LM2, LM3, LM4, LM5 and LM6				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
	Confirmatory		Not required	

5.3.2.6 Description of methods for the analysis of air (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of terbutylazine in air is given in the following tables. No new method necessary.

Table 5.3-6: Validated methods for air (if appropriate)

Component of residue definition: terbutylazine			
Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Primary	1 µg/m ³	GC-NPD	Syngenta: Tribolet R, 1992 Oxon: Schulz M, and Ullrich-Mitzel A., 1995
Confirmatory		Not required	

For any special comments or remarkable points concerning the analytical methods for air it is referred to Appendix 2.

5.3.2.7 Description of methods for the analysis of body fluids and tissues (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of terbutylazine in body fluids and tissues is given in the following table. No new methods are necessary.

No methods are necessary, since no MRLs for animal tissues have not been set. No data submitted or required as terbutylazine is not classified as toxic or very toxic.

5.3.2.8 Other studies/ information

No other studies are provided.

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 5.1.1/01	M. Wołoszynowska	2018	Terbut 500 SC Method development and validation for the determination of active substance and relevant impurities content in the formulation Study code: BA-07-18 INSTITUTE OF INDUSTRIAL ORGANIC CHEMISTRY, Analytical Department, 6 Annopol Str., 03-236 Warsaw GLP Unpublished	N	Letter of access from Synthos Agro Sp. z o.o.
KCP 5.1.1/02	M. Wołoszynowska	2020	Ammendment No. 1 to Final Report: Terbut 500 SC Method development and validation for the determination of active substance and relevant impurities content in the formulation Study code: BA-07-18 INSTITUTE OF INDUSTRIAL ORGANIC CHEMISTRY, Analytical Department, 6 Annopol Str., 03-236 Warsaw GLP Unpublished	N	Letter of access from Synthos Agro Sp. z o.o.

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

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 5.1.2/01	Dieterle, R.	1993	GS13529, Applicability of Multiresidue Method DFG S 19 for determination of GS 13529 in maize(grain and whole plant) Company Report No: 121-92 Novartis Crop Protection AG Basel, Switzerland/Ciba-Geigy Ltd.,Basel Switzrland GLP Unpublished	N	Syngenta
KCP 5.1.2/02	Ferguson, L.	2009	Terbuthylazine – Independent Laboratory validation of analytical method no. REM 201.01 for the determination of terbuthylazine (GS 13529) and its Metabolites GS26379 and GS28620 in whole Maize Plants and Rape seed. Company Report No: GS13529_10121 Syngenta-Jealott Hill Bracknell UK, Oxon Italia S.p.A.,Pero, Italy Charles River Laboratories, Edinburgh, UK, 30377 GLP Unpublished	N	Syngenta/ Oxon
KCP 5.1.2/03	Luetolf, W.	1995a	Determination of residues of parent compund by gas chromatography (GC), Soil Company Report No: REM 148.05 Novartis Crop Protection AG Basel, Switzerland/Ciba-Geigy Ltd.,Basel Switzrland GLP Unpublished	N	Syngenta
KCP 5.1.2/04	Figueiredo J	2003	Determination of GS13529 (Terbuthylazine) and its metabolites GS26379, GS28620 and GS23158 in soil by LC-MS/MS.REM 148.11 Report No: REM 148.11 Syngenta Crop Protection,AG, Basel GLP no Unpublished	N	Syngenta
KCP 5.1.2/05	Robinson,N.	2004	Residue analytical method for the determiation of residues of terbuthylazine (GS 13529), GS23158, GS26379 and GS28620 in Water Report No: REM 426/01 Syngenta Crop Protection,AG, Basel,Switzerland	N	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, Jealotts Hill, UK GLP Unpublished		
KCP 5.1.2/06	Tribolet, R.	1992	Sampling of air and determination of residues of parent compound by gas chromatography Company Report No: REM 148-03 Novartis Crop Protection AG Basel, Switzerland/Ciba-Geigy Ltd.,Basel Switzerland GLP Unpublished	N	Syngenta
KCP 5.1.2/07	Tribolet, R.	1996	Validation by analysis of fortified specimens and determination of recoveries. Validation of method REM 148.03 in air Company Report No: 140/95 Novartis Crop Protection AG Basel, Switzerland/Ciba-Geigy Ltd.,Basel Switzerland GLP Unpublished	N	Syngenta
KCP 5.2/01	Dieterle, R.	1993	GS13529, Applicability of Multiresidue Method DFG S 19 for determination of GS 13529 in maize(grain and whole plant) Company Report No: 121-92 Novartis Crop Protection AG Basel, Switzerland/Ciba-Geigy Ltd.,Basel Switzerland GLP Unpublished	N	Syngenta
KCP 5.2/02	Ferguson, L.	2009	Terbuthylazine – Independent Laboratory validation of analytical method no. REM 201.01 for the determination of terbuthylazine (GS 13529) and its Metabolites GS26379 and GS28620 in whole Maize Plants and Rape seed. Company Report No: GS13529_10121 Syngenta-Jealott Hill Bracknell UK, Oxon Italia S.p.A.,Pero, Italy Charles River Laboratories, Edinburgh, UK, 30377 GLP Unpublished	N	Syngenta/ Oxon
KCP	Luetolf, W.	1995a	Determination of residues of parent compound by gas chromatography (GC), Soil	N	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
5.2/03			Company Report No: REM 148.05 Novartis Crop Protection AG Basel, Switzerland/Ciba-Geigy Ltd.,Basel Switzzland GLP Unpublished		
KCP 5.2/04	Figueiredo J	2003	Determination of GS13529 (Terbutylazine) and its metabolites GS26379, GS28620 and GS23158 in soil by LC-MS/MS.REM 148.11 Report No: REM 148.11 Syngenta Crop Protection,AG, Basel GLP no Unpublished	N	Syngenta
KCP 5.2/05	Todd M.	1999	Validation and determination of residues in soil samples generated from field dissipation trials held in northern Europe. Huntingdon Life Science limited, UK Oxon ItaliaS.P.A, Pero, Italy Report No OXN 228/993260 GLP Unpublished	N	Oxon
KCP 5.2/06	Todd M.	2002	Terbutylazine: Validation od methodology for the determination of residues of terbutylazine and its two major metabolites desethylterbutylazineand 2-hydroxyterbutylazine in soil Oxon ItaliaS.P.A, Pero, Italy Report No OXN 229/024125 GLP Unpublished	N	OXON
KCP 5.2/07	Todd M.	2002	Terbutylazine: Validation od methodology for the determination of residues of terbutylazine and its two major metabolites desethylterbutylazineand 2-hydroxyterbutylazine in drinking and surface water Oxon ItaliaS.P.A, Pero, Italy Report No OXN 229/024126 GLP Unpublished	N	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
KCP 5.2/08	Robinson,N.	2004	Residue analytical method for the determination of residues of terbuthylazine (GS 13529), GS23158, GS26379 and GS28620 in Water Report No: REM 426/01 Syngenta Crop Protection,AG, Basel,Switzerland Syngenta, Jealotts Hill, UK GLP Unpublished	N	Syngenta
KCP 5.2/09	Tribolet, R.	1992	Sampling of air and determination of residues of parent compound by gas chromatography Company Report No: REM 148-03 Novartis Crop Protection AG Basel, Switzerland/Ciba-Geigy Ltd.,Basel Switzerland GLP Unpublished	N	Syngenta
KCP 5.2/10	Tribolet, R.	1996	Validation by analysis of fortified specimens and determination of recoveries. Validation of method REM 148.03 in air Company Report No: 140/95 Novartis Crop Protection AG Basel, Switzerland/Ciba-Geigy Ltd.,Basel Switzerland GLP Unpublished	N	Syngenta
KCP 5.2/11	Schulz M, and Ullrich-Mitzel A	1995	Analytical method for the determination of terbuthylazine in air RCC AG Itingen, Switzerland Oxon Italia S.P.A, Pero Italy Report no: 385615 GLP Unpublished	N	Oxon

The following tables are to be completed by MS

List of data submitted by the applicant and not relied on

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

List of data relied on not submitted by the applicant but necessary for evaluation

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

Appendix 2 Detailed evaluation of submitted analytical methods

Not required.