FINAL REGISTRATION REPORT

Part B

Section 5

Analytical Methods

Detailed summary of the risk assessment

Product code: SHA 8500 A

Product name: MEPISHA

Chemical active substances:

Mepiquat chloride, 50 g/L

(Mepiquat 38 g/L)

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: Sharda Cropchem España S.L.

Submission date: February 2021

Finalisation date: 09/2021; 02/2022

Version history

When	What
09/2021	ZRMS Assessment
February 2022	Final version of RR

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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
High starch content (Winter wheat, winter barley, spring barley)	Supported
High oil content (Winter oilseed rape)	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 Mepiquat chloride in plant protection product is provided as follows:

Comments of zRMS:	**Conclusion** The analytical method (Ion chromatography) for the determination of Mepiquat Chloride in the formulation Mepisha has been submitted. The analytical method meets the criteria of specificity, linearity, precision and accuracy. The method for the determination of Mepiquat chloride is acceptable and validated according the requirements SANCO 3030/99 rev.4 and is suitable for determination of Mepiquat chloride in plant protection product Mepisha.

Reference:	KCP 5.1.1
Report	Accelerated storage stability test by heating at elevated temperature of Mepiquat Chloride 5.105% w/v equivalent to mepiquat ion 3.89% w/v SL. S. Srinivas, 2019, Report No. G16596
Guideline(s):	SANCO/3030/99 rev. 4
Deviations:	No

GLP: Yes

Acceptability: Yes

Materials and methods

The test item was analysed for its active ingredient content using Ion Chromatography. The analytical method for the determination of active ingredient content in test item was validated by establishing specifity, linearity, precision, LOD, LOQ and accuracy.

Linearity and Range of Detector Response
Accurately weighed 0.0104 g of Mepiquat Chloride reference standard into Tarson tube dissolved in about 5 mL of Milli-Q water, contents shaken well and made up to 10 mL with Milli-Q water. Later, varied volumes of aliquots from reference standard stock solution were taken into separate Tarson tubes and the volume was made up to the mark with Milli-Q water and solutions were shaken thoroughly to get the working standard solutions for detector linearity check.

Precision
About 0.10 of the test item in five replications was taken into separate Tarson Tubes and dissolved in about 10 mL of Milli-Q water, shaken well and the contents were then made up to 20 mL using Milli-Q water. These solutions were then analysed for the active ingredient content by inject to Ion Chromatography.

Accuracy
About 0.012 g blank matrix was weighed in triplicated at each of two fortification levels into Tarson tubes. From the stock solution of 0.50 mg/mL of Mepiquat Chloride standard, added an aliquot of 1.0 mL at lower fortification level and 2.0 mL at higher fortification level. Contents were shaken well and the contents made up to 20 mL with Milli-Q water. Fortification was done in triplicate. These fortified samples were analysed for active ingredient content using Ion Chromatography.

Specifity
Aliquots of solution from precision test (PR1), blank diluent (Milli-Q water) and working standard solution (DLC3) were injected into Ion Chromatography and checked for the absence of any interference at the retention time of the analyte.

Validation - Results and discussions

Table 5.2-1: Methods suitable for the determination of active substances mepiquat chloride in plant protection product MEPISHA/SHA 8500 A

	Mepiquat chloride
Author(s), year	S. Srinivas, 2019
Principle of method	Ion chromatography
Linearity (linear between mg/L / % range of the declared content) (correlation coefficient, expressed as r)	5 points 0.0400 mg/mL to 0.4997 mg/mL R = 0.9995 y=6.8382x-0.1136
Precision – Repeatability Mean n = 5 (%RSD)	%RSD = 1.20%
Accuracy	Overall mean recovery: 98.84 ±1.14%

	Mepiquat chloride
n = 6 **(% Recovery)**	
Interference/ Specificity	No interference the method is specific
Comment	LOD = 0.0176 mg/mL LOQ = 0.0198 mg/mL

Conclusion

According to SANCO/3030/99 rev.4 the method was successfully validated and is suitable for determination of mepiquat chloride content in the product MEPISHA/SHA 8500 A.

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

No method was submitted during the EU review of Mepiqat since the active substance has no relevant impurities.

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

Not relevant.

5.2.1.4 Applicability of existing CIPAC methods (KCP 5.1.1)

A CIPAC method No. 440 is available for Mepiquat.
A CIPAC method No. 440.302 is available for Mepiquat chloride

5.2.2 Methods for the determination of residues (KCP 5.1.2)

Please refer to post-registration methods.

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

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 Mepiquat (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 water content	Mepiquat (sum of mepiquat and its salts, expressed as Mepiquat chloride)	0.02 mg/kg	~~Reg. (EU) No. 2019/1791~~ Reg. (EU) 2021/976
Plant, high acid content		0.02 mg/kg	~~Reg. (EU) No. 2019/1791~~ Reg. (EU) 2021/976
Plant, high protein/high starch content (dry commodities)		0.02 mg/kg	~~Reg. (EU) No. 2019/1791~~ Reg. (EU) 2021/976
Plant, high oil content		0.02 mg/kg	~~Reg. (EU) No. 2019/1791~~ Reg. (EU) 2021/976
Plant, difficult matrices (hops, spices, tea)		0.02 mg/kg	~~Reg. (EU) No. 2019/1791~~ Reg. (EU) 2021/976
Muscle	Mepiquat (sum of mepiquat and its salts, expressed as Mepiquat chloride)	0.05 mg/kg	~~Reg. (EU) No. 2019/1791~~ Reg. (EU) 2021/976
Milk		0.07 mg/kg	~~Reg. (EU) No. 2019/1791~~ Reg. (EU) 2021/976
Eggs		0.07 mg/kg	~~Reg. (EU) No. 2019/1791~~ Reg. (EU) 2021/976
Fat		0.05 mg/kg	~~Reg. (EU) No. 2019/1791~~ Reg. (EU) 2021/976
Liver, kidney		0.05 mg/kg	~~Reg. (EU) No. 2019/1791~~ Reg. (EU) 2021/976
Soil (Ecotoxicology)	The sum of mepiquat and its salts expressed as Mepiquat chloride	0.05 mg/kg	common limit
Drinking water (Human toxicology)	The sum of mepiquat and its salts expressed as Mepiquat chloride	0.1 µg/L	general limit for drinking water
Surface water (Ecotoxicology)	The sum of mepiquat and its salts expressed as Mepiquat chloride	2600 µg/L	Lowest E_bC_{50} for *Lemna giba*
Air	The sum of mepiquat and its salts expressed as Mepiquat chloride	90 µg/m^3	AOEL sys: 0.3 mg/kg bw/d
Tissue (meat or liver)		Not required.	Not classified as T / T+
Body fluids		Not required.	Not classified 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 mepiquat in plant matrices is given in the following tables.

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: Mepiquat (sum of Mepiquat and its salts, expressed as Mepiquat chloride)				
Matrix type	**Method type**	**Method LOQ**	**Principle of method (i.e. GC-MS or HPLC-UV)**	**Author(s), year / missing / EU agreed**
High water content	Primary	0.05 mg/kg	HPLC-MS/MS	A. Lehman, C. Mackenroth, 2003 Report No. 2003/1001373 Belgium 2006 EU Agreed
	ILV	0.05 mg/kg	HPLC-MS/MS	H. Schultz, 2003b Report No. 2003/1001272 Belgium, 2006 EU agreed
	Confirmatory (if required)	-	-	LC/MS/MS is highly specific method and no confirmation is required.
High acid content	Primary	0.05 mg/kg	HPLC-MS/MS	A. Lehman, C. Mackenroth, 2003 Report No. 2003/1001373 Belgium 2006 EU Agreed
	ILV	0.05 mg/kg	HPLC-MS/MS	H. Schultz, 2003b Report No. 2003/1001272 Belgium, 2006 EU agreed
	Confirmatory (if required)	-	-	LC/MS/MS is highly specific method and no confirmation is required.
High oil content	Primary	0.05 mg/kg	HPLC-MS/MS	A. Lehman, C. Mackenroth, 2003 Report No. 2003/1001373 Belgium 2006 EU Agreed
	ILV	0.05 mg/kg	HPLC-MS/MS	H. Schultz, 2003b Report No. 2003/1001272 Belgium, 2006 EU agreed
	Confirmatory (if required)	-	-	LC/MS/MS is highly specific method and no confirmation is required.
High protein/high starch content (dry)	Primary	0.05 mg/kg	HPLC-MS/MS	A. Lehman, C. Mackenroth, 2003 Report No. 2003/1001373 Belgium 2006 EU Agreed
	ILV	0.05 mg/kg	HPLC-MS/MS	H. Schultz, 2003b Report No. 2003/1001272

Component of residue definition: Mepiquat (sum of Mepiquat and its salts, expressed as Mepiquat chloride)				
Matrix type	**Method type**	**Method LOQ**	**Principle of method (i.e. GC-MS or HPLC-UV)**	**Author(s), year / missing / EU agreed**
				Belgium, 2006 EU agreed
	Confirmatory (if required)	-	-	LC/MS/MS is highly specific method and no confirmation is required.

Table 5.3-3: Statement on extraction efficiency

	Method for products of plant origin
Required, available from:	U. Rabe, H. Schleuter, 2003 Report No. 1992/5069

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

An overview on the acceptable methods and possible data gaps for analysis of mepiquat in animal matrices is given in the following tables.

Table 5.3-4: Validated methods for food and feed of animal origin (if appropriate)

Component of residue definition: Mepiquat (sum of Mepiquat and its salts, expressed as Mepiquat chloride)				
Matrix type	**Method type**	**Method LOQ**	**Principle of method (*i.e.* GC-MS or HPLC-UV)**	**Author(s), year / missing**
Milk	Primary	0.05 mg/kg	IC	U. Schepers, 1990 Report No. 1990/0147 Belgium, 2006
	ILV	0.05 mg/kg	IC	D. J. Burkey, D. S. Malinsky, 1992 Report No. 1992/5130 Belgium, 2006
	Confirmatory (if required)	0.05 mg/kg	GC-NPD	W. Horton, R. Huber, B. Schwemmer, 1977 Report No. 1977/5025 and 1979/5040
Eggs	Primary	0.05 mg/kg	IC	U. Schepers, 1990 Report No. 1990/0147 Belgium, 2006
	ILV	0.05 mg/kg	IC	D. J. Burkey, D. S. Malinsky, 1992 Report No. 1992/5130 Belgium, 2006
	Confirmatory (if required)	0.05 mg/kg	GC-NPD	W. Horton, R. Huber, B. Schwemmer, 1977 Report No. 1977/5025 and

Component of residue definition: Mepiquat (sum of Mepiquat and its salts, expressed as Mepiquat chloride)				
Matrix type	**Method type**	**Method LOQ**	**Principle of method (*i.e.* GC-MS or HPLC-UV)**	**Author(s), year / missing**
				1979/5040
Muscle	Primary	0.05 mg/kg	IC	U. Schepers, 1990 Report No. 1990/0147 Belgium, 2006
	ILV	0.05 mg/kg	IC	D. J. Burkey, D. S. Malinsky, 1992 Report No. 1992/5130 Belgium, 2006
	Confirmatory (if required)	0.05 mg/kg	GC-NPD	W. Horton, R. Huber, B. Schwemmer, 1977 Report No. 1977/5025 and 1979/5040
Fat	Primary	0.05 mg/kg	IC	U. Schepers, 1990 Report No. 1990/0147 Belgium, 2006
	ILV	0.05 mg/kg	IC	D. J. Burkey, D. S. Malinsky, 1992 Report No. 1992/5130 Belgium, 2006
	Confirmatory (if required)	0.05 mg/kg	GC-NPD	W. Horton, R. Huber, B. Schwemmer, 1977 Report No. 1977/5025 and 1979/5040
Kidney, liver	Primary	0.05 mg/kg	IC	U. Schepers, 1990 Report No. 1990/0147 Belgium, 2006
	ILV	0.05 mg/kg	IC	D. J. Burkey, D. S. Malinsky, 1992 Report No. 1992/5130 Belgium, 2006
	Confirmatory (if required)	0.05 mg/kg	GC-NPD	W. Horton, R. Huber, B. Schwemmer, 1977 Report No. 1977/5025 and 1979/5040
	Primary	0.05 mg/kg	LC – MS/MS	H. Schultz, 2005 Report No. 2005/1026539 Addendum to the DAR, UK, 2008 EU Agreed
	ILV	0.05 mg/kg	LC – MS/MS	A. Richter, 2005 Report No. 2005/1026624 Addendum to the DAR, UK, 2008 EU Agreed
	Confirmatory (if required)			LC/MS/MS is highly specific method and no confirmation is required.

Table 5.3-5: Statement on extraction efficiency

	Method for products of animal origin
Required, available from:	-
Not required, because:	Not presented in the DAR/EU review of Mepiquat.

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 mepiquat in soil is given in the following tables.

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

Component of residue definition: The sum of Mepiquat and its salts expressed as Mepiquat chloride			
Method type	**Method LOQ**	**Principle of method (*i.e.* GC-MS or HPLC-UV)**	**Author(s), year / missing**
Primary	0.01 mg/kg	IC	C. Grote, 2003a Report No. 2001/1014998 Belgium, 2006 EU Agreed
Confirmatory	0.01 mg/kg	LC-MS/MS	C. Grote, 2003a Report No. 2001/1014998 Belgium, 2006 EU Agreed

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 mepiquat in surface and drinking water is given in the following tables.

Table 5.3-7: Validated methods for water (if appropriate)

Component of residue definition: The sum of Mepiquat and its salts expressed as Mepiquat chloride				
Matrix type	**Method type**	**Method LOQ**	**Principle of method (i.e. GC-MS or HPLC-UV)**	**Author(s), year / missing**
Drinking water	Primary	0.05 µg/L	IC	C. Grote, 2003c Report No. 2001/1014999 Belgium, 2006 EU agreed
	ILV	-	-	Not provided during EU review.
	Confirmatory	0.05 µg/L	HPLC-MS/MS	C. Grote, 2003c Report No. 2001/1014999 Belgium, 2006 EU agreed
Surface water	Primary	0.05 µg/L	IC	C. Grote, 2003c Report No. 2001/1014999 Belgium, 2006 EU agreed

Component of residue definition: The sum of Mepiquat and its salts expressed as Mepiquat chloride				
Matrix type	**Method type**	**Method LOQ**	**Principle of method (i.e. GC-MS or HPLC-UV)**	**Author(s), year / missing**
	Confirmatory	0.05 µg/L	HPLC-MS/MS	C. Grote, 2003c Report No. 2001/1014999 Belgium, 2006 EU agreed

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 mepiquat in air is given in the following tables.

Table 5.3-8: Validated methods for air (if appropriate)

Component of residue definition: The sum of Mepiquat and its salts expressed as Mepiquat chloride			
Method type	**Method LOQ**	**Principle of method (i.e. GC-MS or HPLC-UV)**	**Author(s), year / missing**
Primary	0.016 µg/m^3	IC	W. Zengmeister, 2002, 2003 Report No. 2002/1000200 and No. 2003/1005457 Belgium, 2006 EU Agreed
Confirmatory	0.016 µg/m^3	HPLC-MS/MS	W. Zengmeister, 2002, 2003 Report No. 2002/1000200 and No. 2003/1005457 Belgium, 2006 EU Agreed

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

Not required as Mepiquat chloride is not classified as toxic or highly toxic (EFSA Scientific Report (2008) 146, 1-73)

5.3.2.8 Other studies/ information

Not relevant.

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	S. Srinivas	2019	Accelerated storage stability test by heating at elevated temperature of mepiquat chloride 5.105% w/v equivalent to mepiquat ion 3.89% w/v SL. Eurofins Advinus Limited Report No. G16596 GLP Unpublished	N	Sharda Cropchem Limited

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

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

The following tables are to be completed by MS

List of data submitted by the applicant and not relied on

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

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

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

A 2.1 Analytical methods for mepiquat

A 2.1.1 Methods used for the generation of pre-authorization data (KCP 5.1)

No new or additional studies have been submitted

A 2.1.2 Methods for post-authorization control and monitoring purposes (KCP 5.2)

A 2.1.2.1 Description of analytical methods for the determination of residues in plant matrices (KCP 5.2)

No new or additional studies have been submitted

A 2.1.2.2 Description of analytical methods for the determination of residues in animal matrices (KCP 5.2)

No new or additional studies have been submitted

A 2.1.2.3 Description of Methods for the Analysis of Soil (KCP 5.2)

No new or additional studies have been submitted

A 2.1.2.4 Description of Methods for the Analysis of Water (KCP 5.2)

No new or additional studies have been submitted

A 2.1.2.5 Description of Methods for the Analysis of Air (KCP 5.2)

No new or additional studies have been submitted

A 2.1.2.6 Description of Methods for the Analysis of Body Fluids and Tissues (KCP 5.2)

No new or additional studies have been submitted

A 2.1.2.7 A.2.A.9 Other Studies/ Information

No new or additional studies have been submitted