FINAL REGISTRATION REPORT

Part B

Section 5

Analytical Methods

Detailed summary of the risk assessment

Product code: SHA 6800 A

Product name(s): DUKES

Chemical active substance(s):

Dithianon, 700 g/kg

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

Applicant: Sharda Cropchem España S.L.

Submission date: September 2020

MS Finalisation date: May 2021; December 2021

Version history

When	What
05/2021	Assessment
December 2021	Final registration report 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 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:

- ILV method for drinking water. Method should be provided at renewal of the product.
- Statement on the extraction efficiency of methods for determining residues in plant matrices should be provided at renewal of the product.

Commodity/crop	Supported/ Not supported
Pome fruits	**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 Dithianon in plant protection product is provided as follows:

Comments of zRMS:	The proposed analytical method is suitable for the determination of active substance dithianon in plant protection product Dukes. 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.

Reference:	KCP 5.1.1
Report	Physico-Chemical Characterization of Dithianon 70% WG, Jose Angel Escudero, 2016, 15-4150-07
Guideline(s):	Yes (SANCO/3030/99 rev.4)
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Materials and methods

The determination of Dithianon content in DITH (Dithianon 70% WG) was determined using reversed phase HPLC using UV detection at 225 nm and external standardisation. Confirmation of the identity of the analyte is performed by comparing the spectra of the analyte peak in the sample of test item with a corresponding reference product. Spectra were registered in the range between 200 and 300 nm. Peak purity was also be reported in each chromatogram.

Test Item

Name:	Dithianon 70% WG
Active substance:	Dithianon
CAS:	3347-22-6
A.i. content:	70% w/w
Batch number:	SWEPL-48752
Date of expiry:	07/01/2017

Reference item:

Commercial name:	Dithianon Pestanal Fluka Ref. 45462
Purity:	96.6%
Batch number:	SZBD326XV
CAS:	3347-22-6
Date of expiry:	22.11.2018

Analytical conditions:

Column:	Lichrospher 100 RP18 5µm, 250x4mm
Column temperature	25°C
Eluent:	70% Acetonitrile/30% Water
Flow rate:	1.4 ml/min
Wavelength:	225 nm
Injection volume:	10 µl
Retention:	3.4 min
Run time:	10 min

Validation - Results and discussions

Specificity

Method is specific for dithianon in Dithianon 70% WG. There are no interferences from other substances present in the formulation. Representative chromatograms are provided.

Linearity

The analytical method shows an excellent correlation between response and analytical concentration over the range 20.2-404.0 mg/l dithianon. The correlation coefficient (R) was 0.99992.

Precision (Repeatability)

The average of five replicate sample determinations is 72.2 ± 0.4% w/w, dithianon. Relative standard deviation %RSD= 0.5 and is lower than % RSD based on the Horwitz equation (1.41%), so it shows an excellent repeatability of the analytical method.

Accuracy

Determination of accuracy is based on the recovery of known amounts of analyte from a representative sample matrix.

The analytical method was validated by spiking the test item solution with dithianon at level of 80% of the certified value, and at level of 120% of the certified value. The average recovery is 99.9 ± 0.6 % (RSD% = 0.6) for dithianon. This result shows that the recovery value is adequate because it is in the confidence interval 98-102%.

Table 5.2-1: Methods suitable for the determination of Dithianon in plant protection product DITH (Dithianon 70% WG)

	Dithianon
Author, year	Jose Angel Escudero, 2016
Principle of method	Reverse phase HPLC using UV detection at 225 nm
Linearity (linear between mg/L / % range of the declared content) (correlation coefficient, expressed as r)	Linear between 20.2 and 404.0 mg/l R = 0.99992 (n=6) y=26363x-76313
Precision – Repeatability Mean n = 5 (%RSD)	0.5
Accuracy n = 3 (% Recovery)	99.9 ± 0.6 %
Interference/ Specificity	There are no interference from other substance present in the formualtion. Representative chromatograms are provided.
Comment	-

Conclusion

The method is suitable to determine the Dithianon content in Dithianon 70% WG.

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

Not relevant, not necessary.

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

Not relevant, not necessary.

5.2.1.4 Applicability of existing CIPAC methods (KCP 5.1.1)

A CIPAC method are available: 153/TC/(M) 153/WP/(M), 153/SC/(M)

5.2.2 Methods for the determination of residues (KCP 5.1.2)

Please refer to the post-registration method.

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

No new methods are necessary since all data is described in EU approved documents for Dithi-anon–

DAR Vol 3 B5 (2006) and Additional report 2010.

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 Dithianon (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	Dithianon	0.01 mg/kg	EFSA, 2010
Plant, high acid content		0.01 mg/kg	EFSA, 2010
Plant, high protein/high starch content (dry commodities)		0.01 mg/kg	EFSA, 2010
Plant, high oil content		0.01 mg/kg	EFSA, 2010
Plant, difficult matrices (hops, spices, tea)		1.00 mg/kg	EFSA, 2010
Muscle	Dithianon	0.01 mg/kg	EFSA, 2010
Milk		0.01 mg/kg	EFSA, 2010
Eggs		0.01 mg/kg	EFSA, 2010
Fat		0.01 mg/kg	EFSA, 2010
Liver, kidney		0.01 mg/kg	EFSA, 2010
Soil (Ecotoxicology)	Dithianon	0.05 mg/kg	Common limit
Drinking water (Human toxicology)	Dithianon	0.1 µg/L	general limit for drinking water
Surface water (Ecotoxicology)	Dithianon	0.46 µg/L	Lowest NOEC – O. mykiss
Air	Dithianon	4.05 µg/m^3	AOEL sys: 0.0135 mg/kg bw/d
Tissue (meat or liver)	Not required	Not classified as T / T+	Not classified as T / T+
Body fluids	Not required	Not classified as T / T+	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 Dithianon in plant matrices is given in the following tables (please refer to the EFSA Journal 2010; 8 (11): 1904).

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: Dithianon				
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	0.01 mg/kg	LC-MS/MS	EU agreed (This method is specific, validated on two mass transitions, so confirmatory is not required)
	ILV	0.01 mg/kg	LC-MS/MS	EU agreed
	Confirmatory (if required)	-	-	-
High acid content	Primary	0.01 mg/kg	LC-MS/MS	EU agreed (This method is specific, validated on two mass transitions, so confirmatory is not required)
	ILV	0.01 mg/kg	LC-MS/MS	EU agreed
	Confirmatory (if required)	-	-	-
High oil content	Primary	0.01 mg/kg	LC-MS/MS	EU agreed (This method is specific, validated on two mass transitions, so confirmatory is not required)
	ILV	0.01 mg/kg	LC-MS/MS	EU agreed
	Confirmatory (if required)	-	-	-
High protein/high starch content (dry)	Primary	0.01 mg/kg	LC-MS/MS	EU agreed (This method is specific, validated on two mass transitions, so confirmatory is not required)
	ILV	0.01 mg/kg	LC-MS/MS	EU agreed
	Confirmatory (if required)	-	-	-
Difficult (if required, depends on intended use)	Primary	1.0 mg/kg	LC-MS/MS	EU agreed (This method is specific, validated on two mass transitions, so confirmatory is not required)
	ILV	1.0 mg/kg	LC-MS/MS	EU agreed
	Confirmatory (if required)	-	-	-

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 Dithianon in animal matrices is given in the following tables (please refer to the EFSA Journal 2010; 8 (11): 1904).

Table 5.3-3: Validated methods for food and feed of animal origin (if appropriate)

Component of residue definition: Dithianon				
Matrix type	**Method type**	**Method LOQ**	**Principle of method (*i.e.* GC-MS or HPLC-UV)**	**Author(s), year / missing**
Milk	Primary	0.01 mg/kg	HPLC-ECD	EU agreed
		0.01 mg/kg	LC-MS/MS	EU agreed (This method is specific, validated on two mass transitions, so confirmatory is not required)
	ILV	0.01 mg/kg	HPLC-ECD	EU agreed
	Confirmatory (if required)	0.01 mg/kg	LC-MS	EU agreed
Eggs	Primary	0.01 mg/kg	HPLC-ECD	EU agreed
	ILV	0.01 mg/kg	HPLC-ECD	EU agreed
	Confirmatory (if required)	0.01 mg/kg	LC-MS	EU agreed
Muscle	Primary	0.01 mg/kg	HPLC-ECD	EU agreed
	ILV	0.01 mg/kg	HPLC-ECD	EU agreed
	Confirmatory (if required)	0.01 mg/kg	LC-MS	EU agreed
Fat	Primary	0.01 mg/kg	HPLC-ECD	EU agreed
		0.01 mg/kg	LC-MS/MS	EU agreed (This method is specific, validated on two mass transitions, so confirmatory is not required)
	ILV	0.01 mg/kg	HPLC-ECD	EU agreed
	Confirmatory (if required)	0.01 mg/kg	LC-MS	EU agreed
Kidney, liver	Primary	0.01 mg/kg	LC-MS/MS	EU agreed (This method is specific, validated on two mass transitions, so confirmatory is not required)
	ILV	-	-	-
	Confirmatory (if required)	-	-	-

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 Dithianon in soil is given in the following tables (please refer to the EFSA Journal 2010; 8 (11): 1904).

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

Component of residue definition: Dithianon			
Method type	**Method LOQ**	**Principle of method (*i.e.* GC-MS or HPLC-UV)**	**Author(s), year / missing**
Primary	0.01 mg/kg	LC-MS	EU agreed (The method is considered to be highly specific and therefore no confirmatory method is necessary)
	0.01 mg/kg	LC-MS/MS	EU agreed (This method is specific, validated on two mass transitions, so confirmatory is not required)
Confirmatory	-	-	-

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 Dithianon in surface and drinking water is given in the following tables (please refer to the EFSA Journal 2010; 8 (11): 1904).

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

Component of residue definition: Dithianon				
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	LC-MS/MS	EU agreed (This method is specific, validated on two mass transitions, so confirmatory is not required)
	ILV	-	-	Not provided during EU review ILV for drinking water is a data requirement according to Reg. (EU) no. 283/2013 and Reg. (EU) 284/2013.
	Confirmatory	-	-	-
Surface water	Primary	0.05 µg/L	LC-MS/MS	EU agreed (This method is specific, validated on two mass transitions, so confirmatory is not required)
	Confirmatory	-	-	-

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 Dithianon in air is given in the following tables (please refer to the EFSA Journal 2010; 8 (11): 1904).

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

Component of residue definition: Dithianon			
Method type	**Method LOQ**	**Principle of method (i.e. GC-MS or HPLC-UV)**	**Author(s), year / missing**
Primary	0.001 mg/m^3	HPLC-UV	EU agreed
Confirmatory	-	-	According to SANCO/825/00 rev. 8.1, confirmatory is not required (sufficient confirmatory methods are available for the determination in soil and water).

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 Dithianon in body fluids and tissues is given in the following table (please refer to the EFSA Journal 2010; 8 (11): 1904).

Table 5.3-7: Methods for body fluids and tissues (if appropriate)

Component of residue definition: Dithianon			
Method type	**Method LOQ**	**Principle of method (i.e. GC-MS or HPLC-UV)**	**Author(s), year / missing**
Primary	0.05 mg/L for human urine and blood	LC-MS/MS	EU agreed (This method is specific, validated on two mass transitions, so confirmatory is not required)
Confirmatory	-	-	-

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	Jose Angel Escudero	2016	Physico-Chemical Characterization of DITHIANON 70% WG Laboratorios Munuera Report No 15-4150-07 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**
KCP XX	Author	YYYY	Title Company Report N Source GLP/non GLP/GEP/non GEP Published/Unpublished	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**
KCP XX	Author	YYYY	Title Company Report N Source GLP/non GLP/GEP/non GEP Published/Unpublished	Y/N	Owner

Appendix 2 Detailed evaluation of submitted analytical methods

A 2.1 Analytical methods for Dithianon

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 2.1.2.1.1 Analytical method 1

A 2.1.2.1.1.1 Method validation

No new or additional studies have been submitted.

A 2.1.2.1.1.2 Independent laboratory validation

No new or additional studies have been submitted.

A 2.1.2.1.1.3 Confirmatory method

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