

FINAL REGISTRATION REPORT

Part B

Section 5

Analytical Methods

Detailed summary of the risk assessment

Product code: SHA 105000 A

Product name(s): FERROCIOUS

Chemical active substance:

Ferric phosphate, 29.7 g/kg

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

Applicant: Sharda Cropchem España S.L.

Submission date: November 2020

Update date: March 2023

MS Finalisation date: July 2021 ; 10.2021; 05.2023

Version history

When	What
07.2021	RMS Assessment
10.2021	The Final Version of the RR
03.2023	Applicant update
05.2023	Assessment of Applicant's update (equivalence and RI determination and analytical methods validation) by ZRMS

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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 and relevant impurities.

Noticed data gaps:

no methods to show the determination of relevant impurities in the plant protection product have been provided.

Study is “on going”

- none

Ferric phosphate is listed in Annex IV of Regulation (EC) No 396/2005. Therefore, a residue definition and MRLs were not established.

Analytical methods for determination of residues are not required.

Commodity/crop	Supported/ Not supported
Fruit crops	Not required
Vegetable crops	Not required
Field crops	Not required
Grapevine	Not required
Ornamentals	Not required
Hop	Not required

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 Ferric phosphate in plant protection product is provided as follows:

Reference: KCP 5.1.1

Report Iron phosphate 2.9% GB: Analysis of active substances content and physicochemical properties of initial preparation and preparation after accelerated storage procedure (CIPAC MT 46.3). B. Krzysiak-Warzała, Report No. 20/2017/BA-AD, 2016

Guideline(s): No

Deviations: No

GLP: Yes

Acceptability: Yes

Materials and methods

The XRF analysis were performed according to the internal test procedure. In measurements energy dispersive X-ray fluorescence spectrometer (EDXRF) were used.

Tested material

Iron phosphate 2.9% GB
Active substance: Iron phosphate
Percentage of mixture components: 2.9%
CAS number: 10045-86-0
Batch number: SCL-58946
Manufacturing date: 15.02.2017
Expiry date: 14.02.2019
Producer: Sharda Cropchem Limited.

Blank formulation

Iron phosphate 2.9% GB
Batch number: SCL-14589
Manufacturing date: 16.02.2017

Equipment

Bruker Spectrometer EDXRF Ranger S2
Fusion Fluxana, Vulcan type
SCALTEC analytical balance

Reagents

Flux agent Lithium tetraborate, PD Instruments

Fluxing parameters

The sample (1 g) was mixed with the flux (approx. 8 g of lithium tetraborate) in platinum crucible. The mixture was heated in a fuser to give a borate alloy.

XRF measurement conditions

X-Ray tube voltage: 40 kV
X-Ray tube current: 250 μ A
Filter: AL 500 μ m
Time of scan: 100s
The measurements included the sum of the signals FeK $_{\alpha 1}$ and FeK $_{\beta 1}$, i.e. energy range: 6.710 \pm 0.621 keV.

Validation - Results and discussions

The validation of the analytical method for the determination of ferric in the test item Iron Phosphate 2.97% GB was performed and provided the following parameters:

Table 5.2-1: Methods suitable for the determination of Ferric phosphate in plant protection product Iron phosphate 2.97% GB

	Ferric phosphate
Author(s), year	B. Krzysiak-Warzała, 2016

	Ferric phosphate
Principle of method	XRF
Linearity (linear between mg/L / % range of the declared content) (correlation coefficient, expressed as r)	0.32 – 1.709% of Fe $Y = 0.0555x - 0.0075$ $R = 0.999473$
Precision – Repeatability Mean n = 3 (%RSD)	%RSD = 0.69 – 3.48%
Accuracy n = 5 (% Recovery)	%Recovery = 98.5 – 101.1%
Interference/ Specificity	No interference

Conclusion

The analytical method for determination of iron phosphate phosphate in the test item Iron Phosphate 2.97% GB was validated.

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 ferric phosphate, since the active substance has no relevant impurities.~~

No methods was submitted to show the determination of relevant impurities in the plant protection product. Study is “on going”

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:	The analytical method for determination of relevant impurities (Cd, Pb, Hg) is suitable for the determination of the content of each of the relevant impurity in the plant protection product Ferrocious in the presence of each other, active substances and other components. The proposed analytical method has been fully validated in terms of the interference, specificity, linearity, accuracy (recovery and repeatability) and LOQ values. Proposed method fulfils the requirements of SANCO/3030/99 rev. 5 guidance.
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Reference:

KCP 5.1.1-2

Report

Method validation and determination of relevant impurities Lead, Mercury and Cadmium in Iron Phosphate 2.9% GB. K. Vasu, 2023, Report No. 11256/2022

Guideline(s):

SANCO/3030/99 rev. 5

Deviations:

No

GLP:

Yes

Acceptability:

Yes

Materials and methods

The study was conducted to determine the relevant impurities content of cadmium, lead and mercury in Iron Phosphate 2.9% GB.

Material:

Test substance name: Iron Phosphate 2.9% GB

CAS No: 10045-86-0

Batch No: SCL-996001

Instrument conditions

Instrument name:	ICPMS
Make:	Thermo Fisher
Model:	iCAP RQ (quadruple)
Auto sampler model:	CETAC-ASX560
Detector:	MS Detector
Interface pressure:	1.94 – 1.98
Interface temperature:	31.35°C
Plasma cooling water flow:	0.91 lit/min
Exhaust flow:	0.309 – 0.359 mbar
Spray chamber temperature:	2.63°C
Nebulizer flow:	1.009 lit/min
Cool gas flow:	13 lit/min
Auxiliary flow:	0.798 lit/min
Measurement mode:	Standard
Sample run time:	60 seconds
Gas source:	Argon
Elements:	Hg, Cd, Pb

Specificity

Preparation of Standard Stock Solution

An aliquot of 5 mL ICP multi-element standard IV solution (purity 999 mg/L – Cadmium, 1001 mg/L – Lead) was taken into a 50 mL volumetric flask, diluted and made up to the mark with 2% nitric acid. The concentration was equivalent to 99.99 mg/L of cadmium and 100.1 mg/L of lead respectively.

This stock solution was used to prepare diluted standard solutions.

An aliquot of 5 mL Multi-element standard 2A – HG solution with purity 9.99 µg/mL (10.00 mg/L) was taken into a 50 mL volumetric flask, diluted and made up to the mark with 2% nitric acid. The concentration was equivalent to 1 mg/L of mercury.

This stock solution was used to prepare diluted standard solutions.

Preparation of blank formulation solution

An amount of 37.4654 g of blank formulation was weighed accurately into a pre-weighed silica crucible. Moistened the same with 3 mL of concentrated Nitric acid. The contents in the silica crucible was heated gently using a hot plate in a fuming cupboard, the heating process was continued until the sample was completely charred. After cooling the crucible content, the charred residue with mixed about 1 mL of concentrated Nitric acid and heated the content gently until white fumes were no longer evolved and ignited the crucible content at 600°C for one hour. The crucible and its contents were cooled in a desiccator and the content was dissolved completely in 100 mL 2% nitric acid in volumetric flask.

Preparation of sample stock solution

An amount of 37.5056 g of Iron Phosphate 2.9% GB was weighed accurately into a pre-weighed silica crucible. Moistened the sample with 3 mL of concentrated Nitric acid. The contents in the silica crucible was heated gently using a hot plate in a fuming cupboard, the heating process was continued until the sample was completely charred. After cooling the crucible content, the charred residues with mixed 1 mL of concentrated nitric acid and heated gently until white fumes were no longer evolved and ignited the

crucible content at 600°C for one hour. The crucible and its contents were cooled in a dessicator and the content was dissolved completely in 25 mL 2% nitric acid in volumetric flask.

Linearity

The linearity of the method was established by injecting six different concentrations of Multi element reference standard by IPC-MS and plotting their respective concentration against the respective peak intensity.

Precision

Preparation of sample solution. An amount of 37.5731 g, 37.5494 g, 37.5855, 37.5212 and 37.5489 g of Iron Phosphate 2.9% GB was weighed accurately into a pre weighed silica crucible. Moistened the sample with 3 mL of concentrated nitric acid. The contents in the silica crucible was heated gently using a hot plate in a fuming cupboard, the heating processes were continued until the sample was completely charred. After cooling the crucible content the charred residue with mixed with about 1 mL of concentrated nitric acid and heated the content gently until white fumes were no longer evolved and ignited the crucible content at 600°C for one hour. The crucible and its contents were cooled in a desicator and the content was dissolved completely in 25 mL 2% nitric acid in volumetric flask. The bracketing injection of the standard and single injection of five sample preparations were analyzed under ICP-MS to determine the relative standard deviation as per Horwitz equation.

LOQ and LOD

The linearity standard solutions (0.007 mg/L of Cadmium, 0.007 mg/L of lead and 0.0002 mg/L of mercury) was used for the determination of LOD and LOQ.

Accuracy

The analytical method was validated in terms of recovery of the standard at three fortification levels: 0.001 mg/L of cadmium, 0.001 mg/L Lead, 0.00002 mg/L Mercury, 0.003 mg/L of Cadmium, 0.003 mg/L of lead and 0.0001 mg/L of mercury, 0.0035 mg/L of cadmium, 0.0035 mg/L of lead and 0.0002 mg/L of mercury.

Validation - Results and discussions

Table 5.2-2: Methods suitable for the determination of the relevant impurities in plant protection product (PPP) SHA 105000A/FERROCIOUS

	Cadmium	Lead	Mercury
Author(s), year	K. Vasu, 2023		
Principle of method	ICP-MS	ICP-MS	ICP-MS
Linearity (linear between mg/L) (correlation coefficient, expressed as r)	6 points 0.001 mg/L – 0.01 mg/L $y=17014301.4x+10886.575$ $R^2=0.9908$	6 points 0.001 mg/L – 0.01 mg/L $y=103513608.22x+101811.452$ $R^2=0.9935$	6 points 0.00003 mg/L – 0.00035 mg/L $y=103513608.22x+101811.452$ $y=58209531.3x+322.62$ $R^2=0.9935$ 0.9966
Precision – Repeatability Mean n = 5 (%RSD)	RSD = 2.7127% RSD _R =9.4017% RSD _r =6.2991% Hr=0.4307	RSD = 2.7713% RSD _R =9.3455% RSD _r =6.2615% Hr=0.4426	RSD = 5.5684% RSD _R =16.0487 RSD _r =10.7526% Hr=0.5179
Accuracy n = 3 x 3 concentrations (% Recovery)	Marginal recovery 0.001 mg/kg: 98.00% 0.0030 mg/kg: 98.98% 0.0035 mg/kg: 100.18%	Marginal recovery 0.001 mg/kg: 97.10% 0.0030 mg/kg: 92.15% 0.0035 mg/kg: 90.31%	Marginal recovery 0.00002 mg/kg: 95.75% 0.0001 mg/kg: 96.96% 0.0002 mg/kg: 83.97%
Interference/ Speci-	No interference. The	No interference. The method is	No interference. The method is

	Cadmium	Lead	Mercury
ficity	method is specific.	specific.	specific.
LOQ	0.001 mg/kg	0.001 mg/kg	0.00002 mg/kg
Comments	<ul style="list-style-type: none">- In Table 1 (p. 17) it appears to be a mistake in the row with STD-3. The aliquot taken should be 1.25 mL instead of 1 mL to give the final concentration of 0.00 mg/L used in linearity.- In point 9.2.5 Recovery, the author of the report states that a blank sample solution was fortified and used for recovery determination but the data in Table 20 indicate that it was the sample solution that was fortified and used in the determinations. However, the results of recovery are acceptable.		

Conclusion

According to SANCO/3030/99 rev. 5, the method has been accurately validated and is suitable for the determination of relevant impurities lead, cadmium and mercury in the product FERROCIOUS/SHA 105000 A.

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

5.2.1.4 Applicability of existing CIPAC methods (KCP 5.1.1)

A CIPAC method No. 629 is available for Ferric phosphate.

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 of Ferric phosphate (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	According to Commission Regulation (EC) No 2015/1166 amending Reg. (EC) 540/2011, The Commission further considers that ferric phosphate is a low-risk active substance pursuant to Article 22 of Regulation (EC) No 1107/2009. Ferric phosphate is not a substance of concern and fulfils the conditions set in point 5 of Annex II to Regulation (EC) No 1107/2009. Ferric phosphate consists of compounds that are ubiquitous in the environment and that are essential for animal and plant functions. Additionally, ferric phosphate is a natural constituent of the human diet.		COMMISSION IMPLEMENTING REGULATION (EU) 2015/1166
Plant, high acid content			
Plant, high protein/high starch content (dry commodities)			
Plant, high oil content			
Plant, difficult matrices (hops, spices, tea)			
Muscle			
Milk			
Eggs			
Fat			
Liver, kidney			
Soil (Ecotoxicology)			
Drinking water (Human toxicology)			
Surface water (Ecotoxicology)			
Air			
Tissue (meat or liver)			
Body fluids			

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

According to Commission Regulation (EC) No 2015/1166 amending Reg. (EC) 540/2011, The Commission further considers that ferric phosphate is a low-risk active substance pursuant to Article 22 of Regulation (EC) No 1107/2009. Ferric phosphate is not a substance of concern and fulfils the conditions set in point 5 of Annex II to Regulation (EC) No 1107/2009. Ferric phosphate consists of compounds that are ubiquitous in the environment and that are essential for animal and plant functions. Additionally, ferric phosphate is a natural constituent of the human diet.

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

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

According to Commission Regulation (EC) No 2015/1166 amending Reg. (EC) 540/2011, The Commission further considers that ferric phosphate is a low-risk active substance pursuant to Article 22 of Regulation (EC) No 1107/2009. Ferric phosphate is not a substance of concern and fulfils the conditions set in

point 5 of Annex II to Regulation (EC) No 1107/2009. Ferric phosphate consists of compounds that are ubiquitous in the environment and that are essential for animal and plant functions. Additionally, ferric phosphate is a natural constituent of the human diet.

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

According to Commission Regulation (EC) No 2015/1166 amending Reg. (EC) 540/2011, The Commission further considers that ferric phosphate is a low-risk active substance pursuant to Article 22 of Regulation (EC) No 1107/2009. Ferric phosphate is not a substance of concern and fulfils the conditions set in point 5 of Annex II to Regulation (EC) No 1107/2009. Ferric phosphate consists of compounds that are ubiquitous in the environment and that are essential for animal and plant functions. Additionally, ferric phosphate is a natural constituent of the human diet.

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

According to Commission Regulation (EC) No 2015/1166 amending Reg. (EC) 540/2011, The Commission further considers that ferric phosphate is a low-risk active substance pursuant to Article 22 of Regulation (EC) No 1107/2009. Ferric phosphate is not a substance of concern and fulfils the conditions set in point 5 of Annex II to Regulation (EC) No 1107/2009. Ferric phosphate consists of compounds that are ubiquitous in the environment and that are essential for animal and plant functions. Additionally, ferric phosphate is a natural constituent of the human diet.

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

According to Commission Regulation (EC) No 2015/1166 amending Reg. (EC) 540/2011, The Commission further considers that ferric phosphate is a low-risk active substance pursuant to Article 22 of Regulation (EC) No 1107/2009. Ferric phosphate is not a substance of concern and fulfils the conditions set in point 5 of Annex II to Regulation (EC) No 1107/2009. Ferric phosphate consists of compounds that are ubiquitous in the environment and that are essential for animal and plant functions. Additionally, ferric phosphate is a natural constituent of the human diet.

5.3.2.8 Other studies/ information

Not required

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	B. Krzysiak-Warzała	2016	Iron phosphate 2.9% GB: Analysis of active substances content and physicochemical properties of initial preparation and preparation after accelerated storage procedure (CIPAC MT 46.3). Report No. 20/2017/BA-AD GLP, unpublished	N	Sharda Cropchem Limited
KCP 5.1.1-2	K. Vasu	2023	Method validation and determination of relevant impurities lead, mercury and cadmium in Iron Phosphate 2.9% GB. Bioscience Research Foundation Report No. 11256/2022 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 Ferric phosphate

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 2.1.3 Other Studies/ Information

No new or additional studies have been submitted