

REGISTRATION REPORT

Part B

Section 5

Analytical Methods

Detailed summary of the risk assessment

Product code: 102000028562

Product name: Deltamethrin + Flupyradifurone EC 85 (10+75 g/L)

Chemical active substances:

Deltamethrin, 10 g/L

Flupyradifurone, 75 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: Bayer Crop Science Division

Submission date: 01/08/2019 (intended)

MS Finalisation date: June 2021 (initial assessment)

February 2022 (final Core Assessment)

Version history

When	What
August 2019	Original Bayer Crop Science Division submission
June 2021	Initial zRMS assessment. The report in the dRR format has been prepared by the Applicant, therefore all comments, additional evaluations and conclusions of the zRMS are presented in grey commenting boxes. Minor changes are introduced directly in the text and highlighted in grey . Not agreed or not relevant information are struck through and shaded for transparency .
February 2022	Final report (Core Assessment updated following the commenting period) Additional information/assessments included by the zRMS in the report in response to comments recieved from the cMS and the Applicant are highlighted in yellow . Information no longer relevant is struck through and shaded .

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5 Analytical methods

5.1 Conclusion and summary of assessment

General information:	Conclusions from the assessment were prepared using grey commenting boxes. Rewording changes or text amendments were done using grey highlights in the text. The parts of the text added by the zRMS evaluator are highlighted in grey, whereas the parts struck off are visibly marked with the grey font.
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zRMS conclusions:

Deltamethrin

Analytical methods for residues (Regulation (EU) N° 283/2013, Annex Part A, point 4.2 & point 7.4.2)

Residue definitions for monitoring purposes

Food of plant origin	Cis-deltamethrin
Food of animal origin	Cis-deltamethrin
Soil	Cis-deltamethrin
Sediment	Cis-deltamethrin
Water surface	Cis-deltamethrin
drinking/ground	Cis-deltamethrin
Air	Cis-deltamethrin
Body fluids and tissues	Cis-deltamethrin

Plant residue definition for monitoring (RD-Mo)	Cis - Deltamethrin
Plant residue definition for risk assessment (RD-RA)	Sum of cis - deltamethrin and its alpha-R isomer and trans-isomer
Animal residue definition for monitoring (RD-Mo)	Deltamethrin
Animal residue definition for risk assessment (RD-RA)	Sum of deltamethrin and its alpha-R isomer and trans-isomer

Excerpt from the EFSA Journal 2015;13(11):4309:

“Methods of analysis in plants

During the peer review under Directive 91/414/EEC, an analytical method using GC-ECD, was evaluated for the determination of deltamethrin in plant matrices with a limit of quantification (LOQ) of 0.02 mg/kg in high water content, high fat content, acidic and dry commodities. According to the current guideline, the method is not considered highly specific and a confirmatory method is still required. Independent laboratory validation (ILV) data are available for the determination of deltamethrin in high water content, high fat content and acidic commodities but not for dry commodities (Sweden, 2002; European Commission, 2002). Consequently, an analytical method fully validated and its ILV is still required for dry commodities. An analytical method for the determination of deltamethrin in complex matrices, such as spices and herbal infusions, is not available and it is still required.

Hence it is concluded that there are indications that deltamethrin can be monitored with an LOQ of 0.02 mg/kg in high water content, high fat content, acidic and dry commodities but full validation data are still required (confirmatory method for all the matrices and ILV for dry commodities). A fully validated analytical method for the determination of deltamethrin in spices and herbal infusion is not available and it is still required.”

Methods of analysis in livestock

During the peer review under Directive 91/414/EEC, an analytical method using GC-ECD and its ILV, was evaluated for the determination of deltamethrin in food of animal origin with an LOQ of 0.02 mg/kg in milk, meat, fat, liver, kidney and eggs (Sweden, 2002; European Commission, 2002). The method is not considered highly specific. Consequently, a confirmatory method is still required.

Hence, there are indications that deltamethrin can be monitored in animal tissues, in milk and eggs at the LOQ of 0.02 mg/kg but a confirmatory method is still required.”

The Applicant submitted a number of methods for analysis of residues of deltamethrin for the generation of pre-authorization data and methods for post-authorization control and monitoring purposes.

The details of the evaluation of new and additional studies are referred in Appendix 2.

Currently, some methods are evaluated in the AIR process for deltamethrin (DRAR, 2018). This process is not finalized at this time.

Flupyradifurone

According to the EFSA Journal 2015;13(2):4020:

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin	Two separate residue definitions: 1) Flupyradifurone 2) DFA, expressed as DFA
Food of animal origin	Two separate residue definitions: 1) Flupyradifurone 2) DFA, expressed as DFA
Soil	Flupyradifurone
Water surface	Flupyradifurone
drinking/ground	Flupyradifurone
Air	Flupyradifurone

Monitoring/ Enforcement methods

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	HPLC-MS/MS method 01330 with acetonitrile/water (4/1, v/v) with 2.2 mL/L formic acid extraction. LOQ 0.01 mg/kg for flupyradifurone for lettuce, wheat, orange, rape seed potato, and wheat. LOQ 0.05 mg/kg for hop. LOQ 0.02 mg/kg for DFA for lettuce, wheat, orange, rape seed potato, and wheat. LOQ 0.10 mg/kg for hop.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	HPLC-MS/MS acetonitrile/water (4/1, v/v), with the addition of heptane in the cases of fat and milk. LOQ 0.01 mg/kg for flupyradifurone and LOQ 0.02 mg/kg for DFA in fat, liver, kidney, muscle, egg and milk.
Soil (principle of method and LOQ)	HPLC-MS/MS after extraction with acetonitrile. LOQ of 5 µg/kg for flupyradifurone
Water (principle of method and LOQ)	HPLC-MS/MS LOQ for flupyradifurone is 0.05 µg/L in drinking and surface water.
Air (principle of method and LOQ)	HPLC/MS-MS after extraction with acetonitrile. LOQ for flupyradifurone 7 µg /m ³
Body fluids and tissues (principle of method and LOQ)	No methods required.

“Two separate residue definitions for monitoring were proposed in food of plant and animal origin: flupyradifurone and the second, its metabolite DFA expressed as DFA (see Section 3). Appropriate single HPLC-MS/MS methods exist for monitoring residues in food and feed of plant origin with LOQs of 0.01 mg/kg flupyradifurone and with LOQs of 0.02 mg/kg DFA respectively, in all commodities, except for hops, for which the respective LOQs were 0.05 mg/kg a.s. and 0.10 mg/kg DFA. Residues of flupyradifurone and DFA in food of animal origin can be monitored with single HPLC-MS/MS method with LOQs of 0.01 mg/kg a.s. and 0.02 mg/kg DFA respectively, in all matrices.

HPLC-MS/MS methods exist for monitoring flupyradifurone in the environmental matrices with LOQs of 5 µg/kg in soil, 0.05 µg/L in surface water and drinking water and 7 µg/m³ in the air, respectively. The active substance is not classified or proposed to be classified as toxic according to Regulation (EC) No 1272/2008 (CLP Regulation),6 therefore a method of analysis is not required for body fluids and tissues.”

Additionally in EFSA Journal 2020;18(6):6133 it is stated that:

“The availability of analytical enforcement methods for the determination of flupyradifurone and DFA in plant matrices was investigated in the framework of the EU pesticides peer review (EFSA, 2015). It was concluded that a method (method reference number 01330) using HPLC-MS/MS is sufficiently validated for the determination of flupyradifurone and DFA residues; LOQs achievable with the method were 0.01 and 0.007 mg/kg for flupyradifurone and DFA (expressed as DFA), respectively, in plant matrices with high water (lettuce), high starch (wheat, potato), high acid (oranges) and high oil content (rapeseed). In hops, the validated LOQ for the determination of flupyradifurone is 0.05 mg/kg and for DFA (expressed as DFA), it is 0.03 mg/kg. The validation data for high starch content crop matrix is sufficiently representative to cover high protein content plant matrix (OECD, 2007a–h).

EFSA concludes that a sufficiently validated analytical method is available for the enforcement of flupyradifurone and DFA residues in the crops under consideration.”

The Applicant submitted a number of methods for analysis of residues of flupyradifurone and DFA for the generation of pre-authorization data and methods for post-authorization control and monitoring purposes.

The details of the evaluation of new and additional studies are referred in Appendix 2.

The data are sufficient in order to cover this application. No further data are required.

Sufficiently sensitive and selective analytical methods are available for the active substances. The preparation Specification 102000028562 does not contain any relevant impurities.

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
Oilseed rape, mustard seeds	Supported

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

5.1.1 Analysis of the plant protection product (KCP 5.1.1)

5.1.1.1 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 deltamethrin and flupyradifurone in plant protection product is provided as follows:

Comments of zRMS:	The analytical method is sufficiently described and is fully validated in accordance with SANCO/3030/99 rev.4.
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Analytical method

Reference:	KCP 5.1.1/01
Title:	Determination of deltamethrin and flupyradifurone in formulations - Assay - HPLC, external standard
Report:	Michel, A.; 2014; AM023614MF1; M-485797-01-1
Authority registration No:	-
Guideline(s):	REGULATION (EC) No 1107/2009 , Comission Regulation 545/2011, 5.1 US EPA OCSPP 830.1800
Deviations:	--
GLP/GEP:	no
Acceptability:	yes
Duplication (if vertebrate study):	no

The same method of analysis (AM023614MF1) is used for both active substances deltamethrin and flupyradifurone. They are separated from formulation components on reversed phase column (XBridge Phenyl from Waters; 50 x 4.6 mm; 2.5 µm) using isocratic elution. After UV detection at 270 nm, the quantitative evaluation is carried out by comparing the peak areas with those of reference items, using an external standard.

Chromatographic conditions

Injection volume: 3 µL
Flow rate: 2 / 3 mL/min
Column temperature: 50 °C
Eluent : A) Phosphoric acid 0.01 mol/L (% v/v)
B) Acetonitrile (% v/v)

	time (min)*	% A	% B	flow rate (mL/min)
Separation	0	80	20	2
	2.0	80	20	2
	2.2	35	65	2
	5.0	35	65	2
Rinsing gradient	5.1	05	95	3
	5.9	05	95	3
	6.0	80	20	2
	7.0	80	20	2

*Adjust the equilibration time according to the pump- and injection system.

Running time: approx. 7 min
Total retention times : deltamethrin approx. 4.4 min
flupyradifurone approx. 1.6 min

Analytical method validation

Reference:	KCP 5.1.1/02
Title:	Validation of HPLC-method AM023614MF1 - Determination of deltamethrin and flupyradifurone in formulations - deltamethrin + flupyradifurone EC 85 (10+75 g/L)
Report:	Kienow, A.; Michel, A.; 2014; VB1-AM023614MF1; M-485798-01-1
Authority registration No:	-
Guideline(s):	REGULATION (EC) No 1107/2009 , Comission Regulation (EU) 284/2013, 5.1, SANCO/3030/99 rev. 4, US EPA OCSPP 830.1800
Deviations:	--
GLP/GEP:	no
Acceptability:	yes
Duplication (if vertebrate study):	no

Table 0-1 Method suitable for the determination of active substances deltamethrin and flupyradifurone in plant protection product DLT+FPF EC 85

Following parameters were checked		Results
Linearity	For each a.i.: 8 concentrations (single injections); Range: 50-150 % of expected concentration (confer Linearity).	deltamethrin: The function is linear in the operation range. Correlation coefficient r_k : 0.99995 Regression equation: $y = 0.3313x - 0.0007$ flupyradifurone: The function is linear in the operation range. Correlation coefficient r_k : 0.99999 Regression equation: $y = 0.3511x + 0.3801$
Precision	6 samples (single injection) from one batch; Assessment of repeatability (confer Precision).	The Relative Standard Deviation (RSD) of the analyte was determined to be: deltamethrin: RSD: 0.09 % flupyradifurone: RSD: 0.06 % The precision is found to be acceptable. No outliers have been detected.
Accuracy	For each a.i.: 6 samples of laboratory-prepared synthetic formulation containing known weight of analyte; Statistical assessment of the recovery results; Calculation of the confidence interval (confer Accuracy).	deltamethrin: Mean Recovery: 99.6 % Confidence interval of recovery: 99.59 ± 0.71 flupyradifurone: Mean recovery: 100.2 % Confidence interval of recovery: 100.16 ± 0.29 The method shows no constant systematic error. The method shows no proportional systematic error.
Specificity	Comparison of retention times and UV-spectra from reference items and sample (confer Specificity).	The UV-spectra of analyte in the sample and reference items show no spectral difference; The retention times of analyte and reference items are identical.
Interferences from other substances	Comparison of reference item, sample and blank chromatograms with regard to interferences (confer Interferences).	No interferences were found.

Conclusion

The analytical method **AM023614MF1** for the determination of deltamethrin and flupyradifurone in the formulation was found to be valid.

5.1.1.2 Description of analytical methods for the determination of relevant impurities (KCP

5.1.1)

The preparation Specification 102000028562 does not contain any relevant impurities.

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

With respect to toxicological, eco-toxicological or environmental aspects the product DLT+FPF EC 85 does not contain any relevant formulants. Therefore, a special analytical method and validation is not needed.

5.1.1.4 Applicability of existing CIPAC methods (KCP 5.1.1)

There is no CIPAC method available for the determination of deltamethrin + flupyradifurone in formulations.

5.1.2 Methods for the determination of residues (KCP 5.1.2)

Deltamethrin

An overview on the acceptable methods and possible data gaps for analysis of residues of deltamethrin 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](#).

For the crop matrices submitted in this Registration Report, additional validations were conducted with a limited dataset of recoveries during the conduct of the residue studies. For the detailed evaluation of these additional validation data (if not already evaluated at EU level), please refer to [Appendix 2](#).

Table 0-2: Validated methods for the generation of pre-authorization data

Component of residue definition: deltamethrin (cis-, alpha-R-, trans-)				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
Plants: strawberry (fruit), tomato (fruit), lambs lettuce, green peas, wheat (grain), wheat (straw), barley (whole plant) and oilseed rape (seed) Further validations: Residue studies: Oilseed rape	Primary Method 00855/M004	0.01 mg/kg 0.05 mg/kg for straw and whole plant/green material	LC-MS/MS	Lakaschus, S, Winter, O., 2009, M-356934-01-1 , Peer reviewed in 2016 by BEL authorities for the evaluation of DLT EW15 see Appendix 2 Further validations: Reported in residue reports: M-578527-02-1 (15-2132) M-641044-01-1 (16-2044) see Appendix 2
Storage stability study: Tomato fruit Wheat green material Dry peas	Primary / Confirmatory Method 01207	0.1 mg/kg	HPLC-MS/MS	Reported in storage stability study: M-480441-06-1 (S13-03307) see Appendix 2
Component of residue definition: cis-deltamethrin				
Animal products, food of animal origin,... (Residues)	Same as post-authorisation methods			Please refer to enforcement methods

Component of residue definition: deltamethrin (cis-, alpha-R-, trans-)				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
Component of residue definition: deltamethrin (cis-, trans-)				
Soil (Environmental fate)	Primary	0.002 µg/L (Deltamethrin (cis and trans))	GC-ECD	Method CA004 Grigor, A.; 1991; M-137727-01-1 EC Peer review Programme
	Primary	0.1 µg/kg	HPLC-MS/MS	Method 00877 Brumhard, B.; 2005; M-247896-01-1 Brumhard, B.; 2009; M-246580-02-1 (including amendment) <i>Currently under evaluation in the AIR process of deltamethrin.</i> see Appendix 2
	Primary (proposed as new enforcement method)	0.2 µg/kg (cis-Deltamethrin)	HPLC-MS/MS	Method 01358 Freitag, T.; 2013; M-451547-01-1 <i>Currently under evaluation in the AIR process of deltamethrin.</i> see Appendix 2
Water (Environmental fate)	Primary	0.05 µg/L	GC-ECD	Method EM F11/99-0 Martens, R.; 1999; M-192230-01-1 Deltamethrin, Addendum to Monograph Annex B
	Primary	0.003 µg/L	GC-ECD with MS-MS	Method 01-31949 Class, T.; 2001; M-240561-01-1 Deltamethrin, Addendum to Monograph Annex B
	Primary	0.005 µg/L (Deltamethrin (alpha-R, cis and trans))	HPLC-MS	Method 00886 Brumhard, B.; 2005; M-248040-01-1 Peer reviewed in 2016 by BEL authorities for the evaluation of DLT EW15 <i>Currently under evaluation in the AIR process of deltamethrin.</i> see Appendix 2
	Primary	0.002 µg/L	HPLC-MS	Method 00886/M001 Krebber, R.; Braune, M.; 2007; M-291746-01-1 <i>Currently under evaluation in the AIR process of deltamethrin.</i> see Appendix 2
	Primary	0.05 µg/L (cis-deltamethrin)	HPLC-MS/MS	Method 01383 Krebber, R.; Braune, M.; 2013; M-464818-01-1 <i>Currently under evaluation in the AIR process of deltamethrin.</i> see Appendix 2
	ILV	0.05 µg/L (cis-deltamethrin)	HPLC-MS/MS	ILV to method 01383 Stanislowski, T.; 2013; M-471762-01-1 <i>Currently under evaluation in the AIR process of deltamethrin.</i> see Appendix 2

Component of residue definition: deltamethrin (cis-, alpha-R-, trans-)				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
Soil, water,... (Efficacy)	Not Relevant			
Body fluids (Toxicology)	Primary	50 µg/L (cattle blood)	HPLC-MS/MS	Method 01127 Krebber, R.; 2009; M-348630-01-1 Peer reviewed in 2016 by BEL authorities for the evaluation of DLT EW15 <i>Currently under evaluation in the AIR process of deltamethrin.</i> see Appendix 2
Air (Exposure)	No relevant. No operator, worker, bystander exposure study performed with DLT EC 100			
Water (Ecotoxicology)	Primary	0.0123 µg/L (detection limit)	GC-ECD	██████ Bettencourt, M. J.; Mitchell, K. L.; 1990; M-166368-01-1 EC Review Report 6504/ VI/99-final (2002), 1-78
	Primary	0.0123 µg/L (detection limit)	GC-ECD	██████; 1990; M-135553-01-1 EC Review Report 6504/ VI/99-final (2002), 1-78
	Primary	0.51 mg/L	HPLC-UV	██████████████████; 2001; M-199816-01-1 see Appendix 2
	Primary	15.63 µg/L	HPLC-UV	Sowig, P.; Weller, O.; Gosch, H.; 2000; M-196047-01-1 see Appendix 2
	Primary	0.125 µg/L	HPLC-MS/MS	Method 01307 Braune, M.; 2011; M-410093-01-1 <i>Currently under evaluation in the AIR process of deltamethrin.</i> Appendix 2: Yes
	Primary	0.08 mg/L	HPLC-UV	██████████████████ 2001; M-199793-01-1 Appendix 2: Yes
	Primary	1.1 ng/L	GC-ECD	Sowig, P.; Gosch, H.; Weller, O.; 2000; M-194240-01-1 Appendix 2: Yes
	Primary	0.07 mg/L	HPLC-UV	Weller, O.; Gosch, H.; Sowig, P.; 2000; M-196114-01-1 Appendix 2: Yes
	Primary	0.005 µg/L (Deltamethrin (alpha-R, cis and trans))	HPLC-MS	Method 00886 Brumhard, B.; 2005; M-248040-01-1 Peer reviewed in 2016 by BEL authorities for the evaluation of DLT EW15 <i>Currently under evaluation in the AIR process of deltamethrin.</i> Appendix 2: Yes
	Primary	0.002 µg/L	HPLC-MS	Method 00886/M001 Krebber, R.; Braune, M.; 2007;

Component of residue definition: deltamethrin (cis-, alpha-R-, trans-)				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
				M-291746-01-1 Peer reviewed in 2016 by BEL authorities for the evaluation of DLT EW15 <i>Currently under evaluation in the AIR process of deltamethrin.</i> Appendix 2: Yes
	Primary	Minimal detectable concentration = 0.0123 µg/L (for a 1000 mL sample)	GC-ECD	Giddings, J. M.; Bayne, M. C. R.; Mitchell, K. L.; Shepherd, S. P.; 1990; M-131038-01-1 Appendix 2: Yes
Sediment (Ecotoxicology)	Primary	0.2 µg/kg	HPLC-MS/MS	Method 01306 Freitag, T.; Koch, V.; 2011; M-418179-01-1 <i>Currently under evaluation in the AIR process of deltamethrin.</i> Appendix 2: Yes
	Primary	0.1 µg/kg	HPLC-MS/MS	Method 00877 Brumhard, B.; 2005; M-247896-01-1 Peer reviewed in 2016 by BEL authorities for the evaluation of DLT EW15 <i>Currently under evaluation in the AIR process of deltamethrin.</i> Appendix 2: Yes
Avian feed (Ecotoxicology)	Primary	not reported	GC-ECD	Beavers, J. B.; Lattin, A.; Smith, G. J.; Jaber, M.; 1991; M-149397-01-1 EFSA Scientific Report 6504/VI/99- final (2002), 1-78
	Primary	not reported	GC-ECD	Beavers, J. B.; Lattin, A.; Smith, G. J.; Jaber, M.; 1991; M-149398-01-1 EFSA Scientific Report 6504/VI/99- final (2002), 1-78
Bees, flowers/ blossoms, green material, honey/ nectar, pollen and wax (Ecotoxicology)	Primary	10 µg/kg (all sample materials)	HPLC-MS/MS	Method 01347 Schoening, R.; Willmes, J.; 2013; M-444791-01-1 <i>Currently under evaluation in the AIR process of deltamethrin.</i> Appendix 2: Yes
Employed feeding solutions (Ecotoxicology)	Primary	10 µg/kg	HPLC-MS/MS	Method 01347 (modified) Schoening, R.; Willmes, J.; 2013; M-469484-01-1 <i>Currently under evaluation in the AIR process of deltamethrin.</i> Appendix 2: Yes
Water, buffer solutions,... (Properties)	Not relevant for an EC formulation			

Flupyradifurone

An overview on the acceptable methods for analysis of residues of flupyradifurone for the generation of pre-authorization data is given in the following table. For the detailed evaluation of new/additional studies please refer to [Appendix 2](#).

For the crop matrices submitted in this registration report, additional validations were conducted with a limited dataset of recoveries during the conduct of the residue studies. For the detailed evaluation of these additional validation data (if not already evaluated at EU level), please refer to [Appendix 2](#).

Table 0-3: Validated methods for the generation of pre-authorization data

Components of residue definition: Plant: Flupyradifurone (FPF), difluoroacetic acid (DFA)				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
Plant Dried bean seed Wheat forage Orange fruit Soybean seed Tomato fruit Wheat grain (Residues) Further validations: Residue studies: Oilseed rape Rotational crops studies: Potato Oilseed rape Barley Maize/corn Strawberry Brassica vegetables (cauliflower, broccoli)	Primary / Confirmatory Method 01304 , also known as RARVP013 to determine - FPF - DFA**	FPF: 0.01 mg/kg (dried bean seed, wheat forage, orange fruit, soybean seed, tomato fruit, wheat grain) DFA: 0.05 mg/kg* (dried bean seed, wheat forage, soybean seed, wheat grain) DFA: 0.02 mg/kg* (orange fruit, tomato fruit)	HPLC-MS/MS	Li, Y.; Schoening, R.; 2012; M-415504-02-2 , DAR, NL, 2015 ¹ , EFSA Journal 2015; 13(2):4020 EU agreed For method descriptions please refer also to: Li, Y.; 2010; M-401023-01-2 (RV-001-P10-02), Li, Y.; 2012; M-433355-01-1 (RV-001-P10-03) Further validations Reported in residue reports: M-641044-01-1 (16-2044) M-643446-01-1 (16-2131) M-645539-01-1 (16-2169) Reported in rotational crop studies: M-613149-01-1 (16-2510) M-617178-01-1 (16-2511) M-613466-01-1 (16-2521) M-612254-01-1 (16-2512) M-617943-01-1 (16-2524) M-617563-01-1 (16-2515) M-617941-01-1 (16-2516)
Processing studies: Soybean Cotton Potato Barley Wheat Corn				Reported in processing studies: M-428939-01-2 (RARVY029) M-433122-01-1 (RARVY033) M-430542-01-2 (RARVY038) M-546878-01-1 (13-3149) M-439853-01-1 (13-3410) M-440307-01-1 (10-3409) M-427047-01-2 (RARVY031) M-424774-01-1 (RARVY030) see Appendix 2

Components of residue definition: Plant: Flupyradifurone (FPF), difluoroacetic acid (DFA)				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
Plant Tomato fruit Grape bunch of grape Kidney bean dry seed Barley grain Summer rape seed (Residues) Further validations: Residue studies: Oilseed rape	Primary / Confirmatory Method 01212 to determine - FPF - DFA**	FPF: 0.01 mg/kg DFA: 0.02 mg/kg*	HPLC-MS/MS	Rosati, D.; 2012; M-428017-01-2 , DAR, NL, 2015 ¹ , EFSA Journal 2015; 13(2):4020 EU agreed Further validations Reported in residue reports: M-578527-02-1 (15-2132) see Appendix 2
Plant (Residues) Cocoa bean, green Coco bean, fermented Further validations: Oilseed rape straw Oilseed rape seed	Primary / Confirmatory Method 01304/M001** to determine - FPF - DFA	FPF: 0.01 mg/kg DFA: 0.02 mg/kg*	HPLC-MS/MS	Schoening, R.; Wilmes, J. (2014); M-476845-01-1 Reported in storage stability study: M-626405-01-1 (S17-05312) all in Appendix 2
Storage stability study: Tomato fruit Wheat green material Wheat grain Grape bunches Potato tuber Dry peas	Primary / Confirmatory Method 01207** to determine - FPF	FPF: 1 mg/kg	HPLC-MS/MS	Reported in storage stability study: M-480441-06-1 (S13-03307) see Appendix 2
Components of residue definition: Animal: Flupyradifurone (FPF), difluoroacetic acid (DFA)				
Animal Hen egg, egg white, egg yolk Hen fat Hen liver Hen muscle Hen fat Cattle milk Cattle cream Cattle skim milk Cattle fat, mesenteric Cattle fat, perirenal Cattle fat, subcutaneous Cattle, liver Cattle, kidney Cattle, muscle	Primary / Confirmatory Method RV-006-A17-01 to determine - DFA	DFA: 0.01 mg/kg***	HPLC-MS/MS	Kormos, T.; 2017; M-589558-01-1 Validations in: M-611007-01-1 (RARVN150) M-608471-01-1 (RARVN149) see Appendix 2
Components of residue definition: Flupyradifurone				
Soil, water, sediment,... (Environmental fate)				

Components of residue definition: Plant: Flupyradifurone (FPF), difluoroacetic acid (DFA)				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
Soil, water,... (Efficacy)	Not Relevant			
Feed, body fluids,... (Toxicology)				
Water (Ecotoxicology)	Primary 01182	0.05 µg/L	HPLC-MS/MS	Krebber, R., Sandau, C., 2010, M-363959-01-1 , Appendix 2
Nectar, pollen and blossoms (Ecotoxicology)	Primary 01206/M001		HPLC-MS/MS	Schöning, R., Köster, P., 2011, M-404877-01-1 , Appendix 2
Soil, water,... (Ecotoxicology)				
Water, buffer solutions,... (Properties)				

¹ Netherlands, 2015. Draft Assessment Report on the new active substance flupyradifurone prepared by the rapporteur Member State Netherlands in the framework of Regulation (EC) 1107/2009, February, 2015.

* LOQ expressed in flupyradifurone equivalents (corresponds to an LOQ of 0.0067 mg/kg when expressed in DFA equivalents (molecular weight of flupyradifurone = 288.68 g/mol; molecular weight of DFA = 96.03 g/mol)).

** These methods are also capable to determine BYI 02960-difluoroethylamino-furanone (DFEAF) and 6-chloronicotinic acid (6-CNA); however, as these compounds are not part of any residue definitions, they will not summarized further below.

*** LOQ of DFA in the DFA feeding study is expressed in DFA equivalents.

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

5.2.1 Analysis of the plant protection product (KCP 5.2)

The analytical method for the determination of the active substance in the plant protection product mentioned under point 5.2.1 can be used for post-authorization control and monitoring purposes.

5.2.2 Description of analytical methods for the determination of residues of Deltamethrin (KCP 5.2)

5.2.2.1 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 5.2-1: 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	cis-deltamethrin	0.01 mg/kg (LOQ)	SANTE/10024/2016 Reg. (EU) 2018/832
Plant, high acid content		0.01 mg/kg (LOQ)	SANTE/10024/2016 Reg. (EU) 2018/832
Plant, high protein/high starch content (dry)		0.01 mg/kg (LOQ) 0.02 mg/kg (LOQ)	SANTE/10024/2016 Reg. (EU) 2018/832

Matrix	Residue definition	MRL / limit	Reference for MRL/level Remarks
commodities)			
Plant, high oil content		0.01 mg/kg (LOQ)	SANTE/10024/2016 Reg. (EU) 2018/832
Plant, difficult matrices (hops, spices, tea)		Not available	SANTE/10024/2016 Reg. (EU) 2018/832
Muscle	cis-deltamethrin	0.01 mg/kg (LOQ) 0.02 mg/kg	SANTE/10024/2016 Reg. (EU) 2018/832
Milk		0.01 mg/kg (LOQ) 0.05 mg/kg	SANTE/10024/2016 Reg. (EU) 2018/832
Eggs		0.01 mg/kg (LOQ) 0.02 mg/kg	SANTE/10024/2016 Reg. (EU) 2018/832
Fat		0.01 mg/kg (LOQ) 0.1 mg/kg	SANTE/10024/2016 Reg. (EU) 2018/832
Liver, kidney		0.01 mg/kg (LOQ) 0.02 mg/kg	SANTE/10024/2016 Reg. (EU) 2018/832
Soil (Ecotoxicology)			
	Deltamethrin	0.2 µg/kg (LOQ)	European Commission, Peer review Programme, ECCO Meetings, Deltamethrin, Rapporteur Member State: Sweden, September 1998
		0.05 mg/kg	Common limit
Drinking water (Human toxicology)	Deltamethrin	0.05 µg/L (LOQ)	European Commission, Peer review Programme, ECCO Meetings, Deltamethrin, Rapporteur Member State: Sweden, September 1998
		0.1 µg/L	General limit for drinking water
Surface water (Ecotoxicology)	Deltamethrin	0.05 µg/L (LOQ)	European Commission, Peer review Programme, ECCO Meetings, Deltamethrin, Rapporteur Member State: Sweden, September 1998
Air	Deltamethrin	0.4 µg/m ³ (LOQ: GC-ECD) 0.27 µg/m ³ (LOQ: GC-ECD, GC-MSD)	Deltamethrin, Addendum to Monograph Annex B., Rev.2 July 2002
Tissue (meat or liver)	cis-deltamethrin	LOQ = 0.01 0.1 mg/kg	Common limit
Body fluids		LOQ = 50 µg/L (cattle blood)	SANCO/825/00 rev.8.1

5.2.2.2 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 deltamethrin in plant matrices is given in the following tables. For the detailed evaluation of new/additional studies it is referred to [Appendix 2](#).

Table 5.2-2: 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: cis-deltamethrin				
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	GC-MS (Three ions monitored)	Weber, H; 2009, M-356076-01-1 , report No 00086/M089 see Appendix 2 <i>Currently under evaluation in the AIR process of deltamethrin</i>
	ILV	0.01 mg/kg	GC-MS (Three ions monitored)	Merdian, H; 2009, M-356306-01-1 , report No P/B 1681 G see Appendix 2 <i>Currently under evaluation in the AIR process of deltamethrin</i>
	Confirmatory (if required)	Not required, due to the specificity of the MS detector		
High acid content	Primary	0.01 mg/kg	GC-MS (Three ions monitored)	Weber, H; 2009, M-356076-01-1 , report No 00086/M089 see Appendix 2 Peer reviewed in 2016 by BEL for the evaluation of DLT EW15 <i>Currently under evaluation in the AIR process of deltamethrin</i>
	ILV	0.01 mg/kg	GC-MS (Three ions monitored)	Merdian, H; 2009, M-356306-01-1 , report No P/B 1681 G see Appendix 2 Peer reviewed in 2016 by BEL for the evaluation of DLT EW15 <i>Currently under evaluation in the AIR process of deltamethrin</i>
	Confirmatory (if required)	Not required, due to the specificity of the MS detector		
High oil content	Primary	0.01 mg/kg	GC-MS (Three ions monitored)	Weber, H; 2009, M-356076-01-1 , report No 00086/M089 see Appendix 2 Peer reviewed in 2016 by BEL for the evaluation of DLT EW15 <i>Currently under evaluation in the AIR process of deltamethrin</i>
	ILV	0.01 mg/kg	GC-MS (Three ions monitored)	Merdian, H; 2009, M-356306-01-1 , report No P/B 1681 G see Appendix 2 Peer reviewed in 2016 by BEL for the evaluation of DLT EW15 <i>Currently under evaluation in the AIR process of deltamethrin</i>
	Confirmatory (if required)	Not required, due to the specificity of the MS detector		
High protein/high starch content (dry)	Primary	0.01 mg/kg	GC-MS (Three ions monitored)	Weber, H; 2009, M-356076-01-1 , report No 00086/M089 see Appendix 2 Peer reviewed in 2016 by BEL for the evaluation of DLT EW15 <i>Currently under evaluation in the AIR process of deltamethrin</i>
	ILV	0.01 mg/kg	GC-MS (Three ions monitored)	Merdian, H; 2009, M-356306-01-1 , report No P/B 1681 G

Component of residue definition: cis-deltamethrin				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
				see Appendix 2 Peer reviewed in 2016 by BEL for the evaluation of DLT EW15 <i>Currently under evaluation in the AIR process of deltamethrin</i>
	Confirmatory (if required)	Not required, due to the specificity of the MS detector		
Difficult (if required, depends on intended use)	Not available			

For any special comments or remarkable points concerning the analytical methods for the determination of residues in plant matrices, please refer to [Appendix 2](#).

Table 5.2-3: Statement on extraction efficiency

	Method for products of plant origin
Required, available from:	Cross validation of extraction methods for the determination of residues of deltamethrin in plant materials by HPLC-MS/MS. Schoening, R.; Willmes, J.; 2014; MR-14/012; M-481952-02-1
Not required, because:	-

For the detailed evaluation of (additional) studies on extraction efficiency, it is referred to [Appendix 2](#).

5.2.2.3 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 deltamethrin in animal matrices is given in the following tables. For the detailed evaluation of new/additional studies it is referred to [Appendix 2](#).

Table 5.2-4: Validated methods for food and feed of animal origin (if appropriate)

Component of residue definition: cis-deltamethrin				
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	GC-MS (Three ions monitored)	Weber, H; 2009, M-351080-01-1 , report No 00086/M090 see Appendix 2 Peer reviewed in 2016 by BEL authorities for the evaluation of DLT EW15
	ILV	0.01 mg/kg	GC-MS (Three ions monitored)	Merdian, M; 2009, M-356331-01-1 , report No P/B 1682 G see Appendix 2 Peer reviewed in 2016 by BEL authorities for the evaluation of DLT EW15
	Confirmatory (if required)	Not required, due to the specificity of the MS detector		
Eggs	Primary	0.01 mg/kg	GC-MS (Three ions monitored)	Weber, H; 2009, M-351080-01-1 , report No 00086/M090 see Appendix 2

Component of residue definition: cis-deltamethrin				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
				Peer reviewed in 2016 by BEL authorities for the evaluation of DLT EW15
	ILV	0.01 mg/kg	GC-MS (Three ions monitored)	Merdian, H; 2009, M-356331-01-1 , report No P/B 1682 G see Appendix 2 Peer reviewed in 2016 by BEL authorities for the evaluation of DLT EW15
	Confirmatory (if required)	Not required, due to the specificity of the MS detector		
Muscle	Primary	0.01 mg/kg	GC-MS (Three ions monitored)	Weber, H; 2009, M-351080-01-1 , report No 00086/M090 see Appendix 2 Peer reviewed in 2016 by BEL authorities for the evaluation of DLT EW15
	ILV	0.01 mg/kg	GC-MS (Three ions monitored)	Merdian, H; 2009, M-356331-01-1 , report No P/B 1682 G see Appendix 2 Peer reviewed in 2016 by BEL authorities for the evaluation of DLT EW15
	Confirmatory (if required)	Not required, due to the specificity of the MS detector		
Fat	Primary	0.01 mg/kg	GC-MS (Three ions monitored)	Weber, H; 2009, M-351080-01-1 , report No 00086/M090 see Appendix 2 Peer reviewed in 2016 by BEL authorities for the evaluation of DLT EW15
	ILV	0.01 mg/kg	GC-MS (Three ions monitored)	Merdian, H; 2009, M-356331-01-1 , report No P/B 1682 G see Appendix 2 Peer reviewed in 2016 by BEL authorities for the evaluation of DLT EW15
	Confirmatory (if required)	Not required, due to the specificity of the MS detector		
Kidney, liver	Primary	0.01 mg/kg	GC-MS (Three ions monitored)	Weber, H; 2009, M-351080-01-1 , report No 00086/M090 see Appendix 2 Peer reviewed in 2016 by BEL authorities for the evaluation of DLT EW15
	ILV	0.01 mg/kg	GC-MS (Three ions monitored)	Merdian, H; 2009, M-356331-01-1 , report No P/B 1682 G see Appendix 2 Peer reviewed in 2016 by BEL authorities for the evaluation of DLT EW15
	Confirmatory (if required)	Not required, due to the specificity of the MS detector		

For any special comments or remarkable points concerning the analytical methods for the determination of

residues in animal matrices, please refer to [Appendix 2](#).

Table 5.2-5: Statement on extraction efficiency

	Method for products of animal origin
Required, available from:	The extraction efficiency comparison between methods of metabolism studies and feeding studies was not conducted at the time of the studies, because it was not required. It is not possible to perform an alternative cross-validation study since no incurred animal tissue samples are available.
Not required, because:	

5.2.2.4 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 deltamethrin in body fluids and tissues is given in the following table. For the detailed evaluation of new/additional studies it is referred to [Appendix 2](#).

Table 5.2-6: Methods for body fluids and tissues (if appropriate)

Component of residue definition: deltamethrin			
Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Primary	0.020 mg/kg (human plasma)	GC-ECD	Tillier, C.; 1988; M-149542-01-1 Sweden, 1998 ¹
Primary	0.010 mg/kg (urine)	GC-ECD	Tillier, C.; Devaux, P.; 1981; M-149546-01-1 Sweden, 1998 ¹
Primary	0.010 mg/kg (urine faeces)	GC-ECD	Akhtar, M. H.; 1982; M-115658-01-1 Sweden, 1998 ¹
Primary Method 01127	50 µg/L (cattle blood)	HPLC-MS/MS	Krebber, R.; 2009; M-348630-01-1 Peer reviewed in 2016 by BEL for the evaluation of DLT EW15 <i>Currently under evaluation in the AIR process of deltamethrin.</i>

¹ Sweden, 1998. Draft assessment report on the active substance deltamethrin prepared by the rapporteur Member State Sweden in the framework of Council Directive 91/414/EEC, October 1998.

For any special comments or remarkable points concerning the analytical methods for body fluids and tissues please refer to [Appendix 2](#).

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

An overview on the acceptable methods and possible data gaps for analysis of deltamethrin in soil is given in the following tables. For the detailed evaluation of new/additional studies it is referred to [Appendix 2](#).

Table 5.2-7: Validated methods for soil (if appropriate):

Component of residue definition: deltamethrin			
Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Primary	0.002 µg/L (Deltamethrin (cis- and trans-))	GC-ECD	Grigor, A.; 1991; M-137727-01-1 EC Peer review Programme ¹

Component of residue definition: deltamethrin			
Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Primary	0.1 µg/kg	HPLC-MS/MS	Method 00877 Brumhard, B.; 2005; M-247896-01-1 Brumhard, B.; 2009; M-246580-02-1 (including amendment). Peer reviewed in 2016 by BEL for the evaluation of DLT EW15 <i>Currently under evaluation in the AIR process of deltamethrin</i> see Appendix 2
Primary (proposed as new enforcement method)	0.2 µg/kg (cis-Deltamethrin)	HPLC-MS/MS	Method 01358 Freitag, T.; 2013; M-451547-01-1 . <i>Currently under evaluation in the AIR process of deltamethrin.</i> see Appendix 2

¹ EC Peer review Programme, ECCO Meetings, Deltamethrin, Rapporteur Member State: Sweden, September 1998

For any special comments or remarkable points concerning the analytical methods for soil please refer to [Appendix 2](#).

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

An overview on the acceptable methods and possible data gaps for analysis of deltamethrin in surface and drinking water is given in the following tables. For the detailed valuation of new/additional studies it is referred to Appendix 2.

Table 5.2-8: Validated methods for water (if appropriate)

Component of residue definition: deltamethrin				
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	GC-ECD	EM F11/99-0 Martens, R.; 1999; M-192230-01-1 Deltamethrin, Addendum to Monograph Annex B ¹
	Primary (proposed as new enforcement method)	0.05 µg/L (cis-deltamethrin)	HPLC-MS/MS	Method 01383 Krebber, R.; Braune, M.; 2013; M-464818-01-1 <i>Currently under evaluation in the AIR process of deltamethrin.</i> see Appendix 2
	ILV	0.05 µg/L (cis-deltamethrin)	HPLC-MS/MS	ILV to method 01383 Stanislawski, T.; 2013; M-471762-01-1 <i>Currently under evaluation in the AIR process of deltamethrin.</i> see Appendix 2
Surface water	Primary	0.05 µg/L	GC-ECD	EM F11/99-0 Martens, R.; 1999; M-192230-01-1 Deltamethrin, Addendum to Monograph Annex B ¹
	Primary	0.003 µg/L	GC-ECD with MS-MS	Method 01-31949 Class, T.; 2001; M-240561-01-1 Deltamethrin, Addendum to Monograph Annex B ¹
	Primary	0.005 µg/L (Deltamethrin (alpha-R, cis and trans))	HPLC-MS	Method 00886 Brumhard, B.; 2005; M-248040-01-1 Peer reviewed in 2016 by BEL for the evaluation of DLT EW15 <i>Currently under evaluation in the AIR process of deltamethrin.</i> see Appendix 2
	Primary	0.002 µg/L	HPLC-MS	Method 00886/M001 Krebber, R.; Braune, M.; 2007; M-291746-01-1 Peer reviewed in 2016 by BEL for the evaluation of DLT EW15 <i>Currently under evaluation in the AIR process of deltamethrin.</i> see Appendix 2
	Primary (proposed as new enforcement method)	0.05 µg/L (cis-deltamethrin)	HPLC-MS/MS	Method 01383 Krebber, R.; Braune, M.; 2013; M-464818-01-1 <i>Currently under evaluation in the AIR process of deltamethrin.</i> see Appendix 2
	ILV	0.05 µg/L (cis-deltamethrin)	HPLC-MS/MS	ILV to method 01383 Stanislawski, T.; 2013; M-

Component of residue definition: deltamethrin				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
				471762-01-1 <i>Currently under evaluation in the AIR process of deltamethrin see Appendix 2.</i>

¹ Deltamethrin, Addendum to Monograph Annex B, Rev.2 July 2002

For any special comments or remarkable points concerning the analytical methods for water please refer to [Appendix 2](#).

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

An overview on the acceptable methods and possible data gaps for analysis of deltamethrin in air is given in the following tables. There are no new methods submitted with the present dossier.

Table 5.2-9: Validated methods for air (if appropriate)

Component of residue definition: deltamethrin			
Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Primary	0.4 µg/m ³	GC-ECD	Class, T.; 1994; M-203491-01-1 Deltamethrin, Addendum to Monograph Annex B ¹
Primary Method 01-31951	0.27 µg/m ³	GC-ECD GC-MSD	Class, T.; 2001; M-075131-01-1 Deltamethrin, Addendum to Monograph Annex B ¹

¹ Deltamethrin, Addendum to Monograph Annex B., Rev.2 July 2002

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

5.2.2.8 Other studies/ information

No other studies or information

5.2.3 Description of analytical methods for the determination of residues of Flupyradifurone (KCP 5.2)

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

Plant and animals:

The residue definitions proposed in the Draft Assessment Report and also supported in the EFSA Conclusion are identical with the current legal residue definitions.

Table 5.2-10: Relevant residue definitions for monitoring/enforcement and levels for which compliance is required

Matrix	Residue definition	MRL / limit Flupyradifurone	MRL / limit DFA*	Reference for MRL/level Remarks
Plant, high water content	Two separate residue definitions: - Parent compound flupyradifurone (FPF, expressed in FPF equivalents) - DFA (expressed in DFA equivalents)	0.03 mg/kg (lowest MRL, lettuces and salad plants, RC) 0.01 mg/kg (lowest MRL, e.g. Brassica Bulb vegetables) 0.01 mg/kg (LOQ)	0.04 mg/kg¹ (lowest MRL, lettuces and salad plants, RC) 0.02 mg/kg (lowest MRL, e.g. Brassica vegetables Stone fruits) 0.02 mg/kg (LOQ)**	SANTE/10757/2016; Commission Regulation (EU) 2016/1902 (in order to adapt several temporary MRLs, an MRL evaluation report was submitted in March 2018 (updated in July 2018); see remark for further details) Commission Regulation 2021/1842
Plant, high acid content		0.01 mg/kg (LOQ)	0.02 mg/kg (LOQ)**	
Plant, high protein/high starch content (dry commodities)		0.01 mg/kg (lowest MRL, root and tuber veg., RC e.g. oat rice, rye) 0.01 mg/kg (LOQ)	0.09 mg/kg¹ (lowest MRL, root and tuber veg., RC) 0.2 mg/kg (lowest MRL, potatoes) 0.02 mg/kg (LOQ)**	
Plant, high oil content		0.4 mg/kg (proposed MRL oilseeds, PC ²) 0.01 mg/kg (lowest MRL) 0.01 mg/kg (LOQ)	0.2 mg/kg (proposed MRL oilseeds, PC ²) 0.02 mg/kg (lowest MRL) 0.02 mg/kg (LOQ)**	
Plant, difficult matrices (e.g. hops, spices, tea)		0.05 mg/kg (LOQ)	0.1 mg/kg (LOQ)	
Muscle	Two separate residue definitions: - Parent compound FPF (expressed in FPF equivalents) - DFA (expressed in DFA equivalents)	0.03 0.01 mg/kg (lowest MRL, swine poultry) 0.01 mg/kg (LOQ)	0.05 0.15 mg/kg (lowest MRL, poultry) 0.02 mg/kg (LOQ)**	
Milk		0.015 0.01 mg/kg (lowest MRL, swine) 0.01 mg/kg (LOQ)	0.03 mg/kg (lowest MRL, ruminant) 0.02 mg/kg (LOQ)**	
Eggs		0.01 mg/kg (LOQ)	0.03 0.1 mg/kg (lowest MRL, poultry) 0.02 mg/kg (LOQ)**	
Fat		0.015 0.01 mg/kg (lowest MRL, swine poultry) 0.01 mg/kg (LOQ)	0.03 mg/kg (lowest MRL, poultry) 0.02 mg/kg (LOQ)**	
Liver		0.08 0.01 mg/kg (lowest MRL, swine poultry) 0.01 mg/kg (LOQ)	0.15 mg/kg (lowest MRL, poultry goat) 0.02 mg/kg (LOQ)**	
Kidney		0.10 0.01 mg/kg (lowest MRL, swine poultry) 0.01 mg/kg (LOQ)	0.15 0.02 mg/kg (lowest MRL, poultry) 0.02 mg/kg (LOQ)**	
Soil (Ecotoxicology)	flupyradifurone	5 µg/kg 0.05 mg/kg		common limit (SANCO/825/00 rev. 8.1)
Drinking water (Human toxicology)	flupyradifurone	0.05 µg/L 0.1 µg/L		general limit for drinking water (SANCO/825/00 rev. 8.1)
Surface water	flupyradifurone	0.05 µg/L		Lowest endpoint is

Matrix	Residue definition	MRL / limit Flupyradifurone	MRL / limit DFA*	Reference for MRL/level Remarks
(Ecotoxicology)				Chironomus riparius (NOEC, 28d, spiked water) = 6.81 µg/L
Air	flupyradifurone	7 µg/m ³ (LOQ)		Lowest endpoint is Rat LC50 inhalation > 4.7 mg/L air/4 h (nose only)
Tissue (meat or liver)	flupyradifurone	0.01 0.1 mg/kg (LOQ)	0.02 mg/kg (LOQ)**	SANCO/825/00 rev.8.1
Body fluids	flupyradifurone	0.05 mg/L (LOQ)	-	SANCO/825/00 rev.8.1

* DFA expressed in DFA equivalents

** LOQ expressed in flupyradifurone equivalents (corresponds to an LOQ of 0.007 mg/kg when expressed in DFA equivalents (molecular weight of flupyradifurone = 288.68 g/mol; molecular weight of DFA = 96.03 g/mol))

¹ temporary MRL according to Commission Regulation (EU) 2016/1902

² an evaluation report was submitted to the Netherlands as EMS in Q1 2019

RC rotational crop; PC = primary crop

Remark: Some of the MRLs given within this table refer to temporary MRLs as EFSA identified some information on rotational crops as unavailable. In order to overcome this data gap, Bayer submitted additional studies in form of an evaluation report (D-017378-01-1) which was evaluated by the NL (Ctgb) and is currently under evaluation by EFSA. New MRLs are proposed for some plant (based on rotational crop data) and animal matrices.

Evaluator comments:

In the meantime new MRLs were set for flupyradifurone and DFA in Commission Regulation 2021/1842 of 20 October 2021, applying from 10 November 2021 on. The relevant information has been updated in Table 5.3-10.

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

An overview on the acceptable methods for analysis of flupyradifurone in plant matrices for post-authorization control and monitoring purposes is given in the following tables. No additional studies for the determination of flupyradifurone have been submitted.

Table 5.2-11: Validated methods for food and feed of plant origin (required for all matrix types, “difficult” matrix only when indicated by intended GAP)

Components of residue definitions: Plant: Flupyradifurone (FPF), difluoroacetic acid (DFA) Animal: Flupyradifurone (FPF), difluoroacetic acid (DFA)				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year, Document No (report) / missing / EU agreed
High water content (lettuce head)	Primary /Confirmatory Method 01330 to determine - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	HPLC-MS/MS 2 transitions (MRM) 2 stationary phases	<u>Schulte, G.; Bauer, J.; 2012; M-425848-01-1</u> EU agreed: DAR, NL, 2015 ¹ , EFSA, 2015 ²
	ILV - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	HPLC-MS/MS 2 transitions (MRM) 2 stationary phases	<u>Konrad, S.; 2012; M-427133-01-1</u> EU agreed: DAR, NL, 2015 ¹ , EFSA, 2015 ²
High acid content (orange fruit)	Primary /Confirmatory Method 01330 to determine - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	HPLC-MS/MS 2 transitions (MRM) 2 stationary phases	<u>Schulte, G.; Bauer, J.; 2012; M-425848-01-1</u> EU agreed: DAR, NL, 2015 ¹ , EFSA, 2015 ²
	ILV - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	HPLC-MS/MS 2 transitions (MRM) 2 stationary phases	<u>Konrad, S.; 2012; M-427133-01-1</u> EU agreed: DAR, NL, 2015 ¹ , EFSA, 2015 ²
High oil content (Rape seed)	Primary /Confirmatory Method 01330/M001 to determine - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	HPLC-MS/MS 2 transitions (MRM) 2 stationary phases	<u>Schulte, G.; Teubner, L.; 2012; M-438310-01-1</u> EU agreed DAR, NL, 2015 ¹ , EFSA, 2015 ²
	ILV - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	HPLC-MS/MS 2 transitions (MRM) 2 stationary phases	<u>Konrad, S.; 2012; M-439855-01-1</u> EU agreed DAR, NL, 2015 ¹ , EFSA, 2015 ²

Components of residue definitions: Plant: Flupyradifurone (FPF), difluoroacetic acid (DFA) Animal: Flupyradifurone (FPF), difluoroacetic acid (DFA)				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year, Document No (report) / missing / EU agreed
High protein/high starch content (dry) (wheat grain)	Primary /Confirmatory Method 01330 to determine - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	HPLC-MS/MS 2 transitions (MRM) 2 stationary phases	<u>Schulte, G.; Bauer, J.; 2012;</u> <u>M-425848-01-1</u> EU agreed DAR, NL, 2015 ¹ , EFSA, 2015 ²
	ILV - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	HPLC-MS/MS 2 transitions (MRM) 2 stationary phases	<u>Konrad, S.; 2012;</u> <u>M-427133-01-1</u> EU agreed DAR, NL, 2015 ¹ , EFSA, 2015 ²
Difficult (hops cone)	Primary Method 01330 to determine - FPF - DFA	0.05 mg/kg 0.1 mg/kg*	HPLC-MS/MS 2 transitions (MRM) 2 stationary phases	<u>Schulte, G.; Bauer, J.; 2012;</u> <u>M-425848-01-1</u> EU agreed DAR, NL, 2015 ¹ , EFSA, 2015 ²
	ILV	not required, as the ILV has been performed in three other matrices (lettuce fruit, orange fruit and wheat grain) for this method		

¹ Netherlands, 2015. Draft Assessment Report on the new active substance flupyradifurone prepared by the rapporteur Member State Netherlands in the framework of Regulation (EC) 1107/2009, February, 2015

² EFSA (European Food Safety Authority), 2015. Conclusion on the peer review of the pesticide risk assessment of the active substance flupyradifurone, EFSA Journal 2015; 13(2):4020, 1-101

* LOQ expressed in flupyradifurone equivalents (i.e. an LOQ of 0.02 mg/kg corresponds to an LOQ of 0.007 mg/kg when expressed in DFA equivalents (molecular weight of flupyradifurone = 288.68 g/mol; molecular weight of DFA = 96.03 g/mol))

For any special comments or remarkable points concerning the analytical methods for the determination of residues in plant matrices, please refer to [Appendix 2](#).

Table 5.2-12: Statement on extraction efficiency

	Method for products of plant origin
Required, available from:	--
Not required, because:	same extraction procedure was used as in plant metabolism studies

The extraction efficiency of the residue method for the determination of the relevant residues of flupyradifurone in plant matrices, consisting of the parent compound and its metabolite DFA, was assured by choosing the same extraction procedures as used in the plant metabolism studies. Nevertheless, an extraction efficiency study was conducted for the data generation method 01304 (DAR, NL, 2015). As the extraction procedures for the monitoring method 01330 are the same as for the data generation method 01304, the results of the study prove also satisfactory extraction efficiency with method 01330 (DAR, NL, 2015).

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

An overview on the acceptable methods for analysis of flupyradifurone in animal matrices is given in the following tables. No additional studies have been submitted.

Table 5.2-13: Validated methods for food and feed of animal origin (if appropriate)

Component of residue definition: Flupyradifurone (FPF), difluoroacetic acid (DFA)				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
Milk	Primary / Confirmatory Method 01214 to determine - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	HPLC-MS/MS 2 transitions (MRM) 2 stationary phases	<u>Schulte, G.; Bauer, J.; 2012;</u> <u>M-425837-01-1</u> EU agreed DAR, NL, 2015 ¹ , EFSA, 2015 ²
	ILV - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	see above	<u>Konrad, S.; 2012;</u> <u>M-427160-01-1</u> EU agreed DAR, NL, 2015 ¹ , EFSA, 2015 ²
Eggs	Primary / Confirmatory Method 01214 to determine - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	HPLC-MS/MS 2 transitions (MRM) 2 stationary phases	<u>Schulte, G.; Bauer, J.; 2012;</u> <u>M-425837-01-1</u> EU agreed DAR, NL, 2015 ¹ , EFSA, 2015 ²
	ILV - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	see above	<u>Konrad, S.; 2012;</u> <u>M-427160-01-1</u> EU agreed DAR, NL, 2015 ¹ , EFSA, 2015 ²
Muscle	Primary / Confirmatory Method 01214 to determine - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	HPLC-MS/MS 2 transitions (MRM) 2 stationary phases	<u>Schulte, G.; Bauer, J.; 2012;</u> <u>M-425837-01-1</u> EU agreed DAR, NL, 2015 ¹ , EFSA, 2015 ²
	ILV - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	see above	<u>Konrad, S.; 2012;</u> <u>M-427160-01-1</u> EU agreed DAR, NL, 2015 ¹ , EFSA, 2015 ²

Component of residue definition: Flupyradifurone (FPF), difluoroacetic acid (DFA)				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
Fat	Primary / Confirmatory Method 01214 to determine - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	HPLC-MS/MS 2 transitions (MRM) 2 stationary phases	<u>Schulte, G.; Bauer, J.; 2012;</u> <u>M-425837-01-1</u> EU agreed DAR, NL, 2015 ¹ , EFSA, 2015 ²
	ILV - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	see above	<u>Konrad, S.; 2012;</u> <u>M-427160-01-1</u> EU agreed DAR, NL, 2015 ¹ , EFSA, 2015 ²
Kidney, liver	Primary/ Confirmatory Method 01214 to determine - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	HPLC-MS/MS 2 transitions (MRM) 2 stationary phases	<u>Schulte, G.; Bauer, J.; 2012;</u> <u>M-425837-01-1</u> EU agreed DAR, NL, 2015 ¹ , EFSA, 2015 ²
	ILV - FPF - DFA	0.01 mg/kg 0.02 mg/kg*	see above	<u>Konrad, S.; 2012;</u> <u>M-427160-01-1</u> EU agreed DAR, NL, 2015 ¹ , EFSA, 2015 ²

¹ Netherlands, 2015. Draft Assessment Report on the new active substance flupyradifurone prepared by the rapporteur Member State Netherlands in the framework of Regulation (EC) 1107/2009, February, 2015

² EFSA (European Food Safety Authority), 2015. Conclusion on the peer review of the pesticide risk assessment of the active substance flupyradifurone, EFSA Journal 2015; 13(2):4020, 1-101

* LOQ expressed in flupyradifurone equivalents (corresponds to an LOQ of 0.0067 mg/kg when expressed in DFA equivalents (molecular weight of flupyradifurone = 288.68 g/mol; molecular weight of DFA = 96.03 g/mol))

For any special comments or remarkable points concerning the analytical methods for the determination of residues in animal matrices, please refer to [Appendix 2](#).

Table 5.2-14: Statement on extraction efficiency

	Method for products of animal origin
Required, available from:	--
Not required, because:	same extraction procedure was used as in livestock metabolism studies

The extraction efficiency of the residue method for the determination of the relevant residues of flupyradifurone in livestock matrices, consisting of the parent compound and its metabolite DFA, was assured by choosing the same extraction procedures as used in the livestock metabolism studies.

5.2.3.4 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 flupyradifurone in body fluids and tissues is given in the following table. For the detailed evaluation of new studies it is referred to [Appendix 2](#).

Table 5.2-15: Methods for body fluids and tissues (if appropriate)

Component of residue definition: Plasma (body fluid): Flupyradifurone (FPF)			
Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Primary/ Confirmatory Method 01495 to determine - FPF	0.05 mg/L (plasma)	HPLC-MS/MS (2 MRM transitions)	Kaussmann, M.; 2016; M-570324-01-1 see Appendix 2
Component of residue definition: Tissues: Flupyradifurone (FPF)			
Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Primary / Confirmatory Method 01214 to determine - FPF - DFA	0.01 mg/kg (tissues) 0.02 mg/kg* (tissues)	HPLC-MS/MS 2 transitions (MRM) 2 stationary phases	Schulte, G.; Bauer, J.; 2012; M-425837-01-1 EU agreed DAR, NL, 2015 ¹ , EFSA Journal 2015; 13(2):4020

¹ Netherlands, 2015. Draft Assessment Report on the new active substance flupyradifurone prepared by the rapporteur Member State Netherlands in the framework of Regulation (EC) 1107/2009, February, 2015

² EFSA (European Food Safety Authority), 2015. Conclusion on the peer review of the pesticide risk assessment of the active substance flupyradifurone, EFSA Journal 2015; 13(2):4020, 1-101

For any special comments or remarkable points concerning the analytical methods for body fluids and tissues please refer to [Appendix 2](#).

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

An overview on the acceptable methods and possible data gaps for analysis of flupyradifurone in soil is given in the following table. For the detailed valuation of new studies it is referred to [Appendix 2](#).

The following method for the analysis of soil has already been evaluated and accepted at EU level and therefore, no additional studies for soil have been submitted.

Table 5.2-16: Validated methods for soil (if appropriate)

Component of residue definition: flupyradifurone			
Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Primary	5 µg/kg	HPLC-MS/MS	Brumhard, B., Reineke, A., 2009, DAR, Netherlands, 2015 EU agreed
Confirmatory			

For any special comments or remarkable points concerning the analytical methods for soil please refer to [Appendix 2](#).

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

An overview on the acceptable methods and possible data gaps for analysis of flupyradifurone in surface and drinking water is given in the following table. For the detailed valuation of new studies it is referred to [Appendix 2](#).

Table 5.2-17: Validated methods for water (if appropriate)

Component of residue definition: flupyradifurone				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Drinking water	Primary method 01213	0.05µg/L	HPLC-MS/MS	Fargeix, G., Rosati, D., 2012, DAR, NL, 2015 ¹ , EU agreed
	ILV			
	Confirmatory			
Surface water	Primary method 01213	0.05µg/L	HPLC-MS/MS	Fargeix, G., Rosati, D., 2012, DAR, NL, 2015 ¹ , EU agreed
	Confirmatory			

¹ Netherlands, 2015. Draft Assessment Report on the new active substance flupyradifurone prepared by the rapporteur Member State Netherlands in the framework of Regulation (EC) 1107/2009, February, 2015

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

An overview on the acceptable methods and possible data gaps for analysis of flupyradifurone in air is given in the following table. For the detailed evaluation of new studies please refer to [Appendix 2](#). The following method for the analysis of air has already been evaluated and accepted at EU level and therefore, no additional studies for air have been submitted.

Table 5.2-18: Validated methods for air (if appropriate)

Component of residue definition: flupyradifurone			
Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Primary	7 µg/m ³	HPLC-MS/MS	Heinz, N., 2011, DAR, Netherlands, 2015 EU agreed
Confirmatory			

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

Appendix 2.

5.2.3.8 Other studies/ information

No other studies/information.

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Vertebrate study Y/N	Owner
KCP 5.1.1 / 01	Michel, A.	2014	Determination of deltamethrin and flupyradifurone in formulations - Assay - HPLC, external standard Report No.: AM023614MF1, Edition Number: M-485797-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: No unpublished	No	Bayer
KCP 5.1.1 / 02	Kienow, A.; Michel, A.	2014	Validation of HPLC-method AM023614MF1 - Determination of deltamethrin and flupyradifurone in formulations - deltamethrin + flupyradifurone EC 85 (10+75 g/L) Report No.: VB1-AM023614MF1, Edition Number: M-485798-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: No unpublished	No	Bayer
KCP 5.1.2.1 / 01 ... also filed: KCP 5.2.4 / 01	Brumhard, B.	2005	Analytical method 00877 for the determination of total residues of deltamethrin (AE F032640) in / on soil and sediment by HPLC-MS/MS Report No.: C047210, Edition Number: M-247896-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.1 / 02 ... also filed: KCP 5.2.4 / 02	Brumhard, B.	2009	Analytical method 00877 for the determination of total residues of Deltamethrin (AE F032640) in/on soil and sediment by HPLC-MS/MS Report No.: 00877, Edition Number: M-246580-02-1 Method Report No.: MR-081/04 Bayer CropScience AG, Monheim, Germany ... amended: 2009-03-31 GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.1 / 03 ... also filed: KCP 5.2.4 / 03	Freitag, T.	2013	Analytical method 01358 for the determination of cis-deltamethrin in soil by HPLC-MS/MS Report No.: MR-13/002, Edition Number: M-451547-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.1 / 04 ... also filed: KCP 5.2.5 / 01	Krebber, R.; Braune, M.	2013	Analytical method 01383 for the determination of deltamethrin in drinking and surface water by HPLC-MS/MS Report No.: MR-13/053, Edition Number: M-464818-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Vertebrate study Y/N	Owner
KCP 5.1.2.1 / 05 ... also filed: KCP 5.2.5 / 02	Stanislawski, T.	2013	Independent laboratory validation of BCS analytical method no. 01383 for the determination of deltamethrin in surface water, using LC/MS/MS Report No.: P 3021 G, Edition Number: M-471762-01-1 PTRL Europe GmbH, Ulm, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.1 / 06 ... also filed: KCP 5.2.5 / 03	Brumhard, B.	2005	Analytical method 00886 for the determination of total residues of deltamethrin (AE F032640) in surface water by HPLC-MS/MS Report No.: C047388, Edition Number: M-248040-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.1 / 07 ... also filed: KCP 5.2.5 / 04	Krebber, R.; Braune, M.	2007	Modification M001 of analytical method 00886 for the determination of total residues of deltamethrin (AE F032640) in surface water by HPLC-MS/MS Report No.: 00886/M001, Edition Number: M-291746-01-1 Method Report No.: MR-07/296 Bayer CropScience AG, Monheim, Germany GLP/GEP: No unpublished	No	Bayer
KCP 5.1.2.5 / 01	Lakaschus, S.; Winter; O.	2009	Validation of BCS Method 00855/M004 for the Determination of cis-deltamethrin, trans-deltamethrin and alpha-R-deltamethrin in foodstuff of plant origin Report No.: 00855/M004, Edition Number: M-356934-01-1 Method Report No.: BAY-0904V Eurofins Analytik GmbH, Dr. Specht Laboratorien, Hamburg, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 02 ... also filed: KCA 6.3.1.1 / 01	Schulte, G.	2017	Amendment no. 1: Determination of the residues of BYI 02960 and deltamethrin in/on rape after spray application of deltamethrin & flupyradifurone EC 085 in France (North), Germany and Belgium Report No.: 15-2132, Edition Number: M-578527-02-1 Bayer AG, Crop Science Division, Monheim, Germany ... amended: 2017-05-03 GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 03 ... also filed: KCA 6.3.1.1 / 02	Kaussmann, M.; Kerkering, S.	2018	Determination of the residues of BYI 02960 and deltamethrin in/on rape after spray application of deltamethrin & flupyradifurone EC 085 in Germany, Belgium and northern France Report No.: 16-2044, Edition Number: M-641044-01-1 Bayer AG, Crop Science Division, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer



Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Vertebrate study Y/N	Owner
KCP 5.1.2.5 / 04	Schoening, R.; Willmes, J.	2014	Cross validation of extraction methods for the determination of residues of deltamethrin in plant materials by HPLC-MS/MS Report No.: MR-14/012, Edition Number: M-481952-02-1 Bayer CropScience AG, Monheim, Germany ... amended: 2014-04-11 GLP/GEP: No unpublished	No	Bayer
KCP 5.1.2.5 / 05 ... also filed: KCA 6.1 / 02	Lakaschus, S.; Gizler, A.	2017	Amendment no. 3 to final report - 7 days freezer storage stability study with different combinations of a total of 61 analytes (parent and metabolite molecules) and five matrix types (high water / acidic / starch / protein / oil) Report No.: S13-03307, Edition Number: M-480441-06-1 Eurofins Agrosience Services Chem GmbH (EAS Chem), Hamburg, Germany ... amended: 2017-08-16 GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 06 ... also filed: KCP 5.2.3 / 01	Krebber, R.	2009	Analytical method 01127 for the determination of cyfluthrin and deltamethrin in blood by HPLC-MS/MS Report No.: MR-08/176, Edition Number: M-348630-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 07 ... also filed: KCA 6.3.1.1 / 04	Miara, C.; Nayyar, B.; Kowalski, N.	2018	Determination of the residues of BYI 02960 and deltamethrin in/on rape after spray application of deltamethrin & flupyradifurone EC 085 in Spain and Portugal Report No.: 16-2169, Edition Number: M-645539-01-1 Bayer AG, Crop Science Division, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 08 ... also filed: KCA 6.3.1.1 / 03	Miara, C.; Nayyar, B.; Kowalski, N.	2018	Determination of the residues of BYI 02960 and deltamethrin in/on rape after spray application of deltamethrin & flupyradifurone EC 085 in Spain, Portugal, southern France and Italy Report No.: 16-2131, Edition Number: M-643446-01-1 Bayer AG, Crop Science Division, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 09 ... also filed: KCA 6.6.2 / 01	Freitag, T.	2018	Determination of the residues of BYI 02960 in/on potato and soil after spraying of BYI 02960 SL 200 in the field in Germany, the Netherlands, Italy and Spain Report No.: 16-2510, Edition Number: M-613149-01-1 Bayer AG, Crop Science Division, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Vertebrate study Y/N	Owner
KCP 5.1.2.5 / 10 ... also filed: KCA 6.6.2 / 02	Freitag, T.; Effertz, C.	2018	Determination of the residues of BYI 02960 in/on the field rotational crop rape and soil after spray application of BYI 02960 SL 200 to bare soil in the field in Belgium and the Netherlands - Final report Report No.: 16-2511, Edition Number: M-617178-02-1 Bayer AG, Crop Science Division, Monheim, Germany ... amended: 2018-12-19 GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 11 ... also filed: KCA 6.6.2 / 03	Kaussmann, M.; van Berkum, S.	2018	Determination of the residues of BYI 02960 in/on the field rotational crop rape and soil after spray application of BYI 02960 SL 200 to bare soil in the field in Italy and Portugal Report No.: 16-2521, Edition Number: M-613466-02-1 Bayer AG, Crop Science Division, Monheim, Germany ... amended: 2018-12-19 GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 12 ... also filed: KCA 6.6.2 / 04	Freitag, T.; Kaussmann, M.	2018	Determination of the residues of BYI 02960 in/on the field rotational crop barley and soil after spray application of BYI 02960 SL 200 to bare soil in the field in United Kingdom and the Netherlands Report No.: 16-2512, Edition Number: M-612254-01-1 Bayer AG, Crop Science Division, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 13 ... also filed: KCA 6.6.2 / 07	Freitag, T.; van Berkum, S.	2018	Determination of the residues of BYI 02960 in/on the field rotational crop maize/corn and soil after spray application of BYI 02960 SL 200 to bare soil in the field in France (South) and Portugal - Final report Report No.: 16-2524, Edition Number: M-617943-01-1 Bayer AG, Crop Science Division, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 14 ... also filed: KCA 6.6.2 / 08	Freitag, T.; Hoffmeister, R.	2018	Determination of the residues of BYI 02960 in/on the field rotational crop strawberry and soil after spray application of BYI 02960 SL 200 to bare soil in the field in Belgium and the Netherlands Report No.: 16-2515, Edition Number: M-617563-01-1 Bayer AG, Crop Science Division, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 15 ... also filed: KCA 6.6.2 / 10	Freitag, T.; Effertz, C.	2018	Determination of the residues of BYI 02960 in/on the field rotational crop cauliflower, broccoli and soil after spray application of BYI 02960 SL 200 to bare soil in the field in Belgium, the Netherlands, Italy and Spain Report No.: 16-2516, Edition Number: M-617941-02-1 Bayer AG, Crop Science Division, Monheim, Germany ... amended: 2018-09-19 GLP/GEP: Yes unpublished	No	Bayer

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Vertebrate study Y/N	Owner
KCP 5.1.2.5 / 16 ... also filed: KCA 6.5.3 / 01	Lenz, C.	2012	BYI 02960 200 SL - Magnitude of the residue in/on soybean processed commodities Report No.: RARVY029, Edition Number: M-428939-01-2 Bayer CropScience LP, Stilwell, KS, USA GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 17 ... also filed: KCA 6.5.3 / 02	Lenz, C.; Beedle, E.	2012	BYI 02960 200 SL - Magnitude of the residue in cotton processed commodities (crop subgroup 20C) Report No.: RARVY033, Edition Number: M-433122-01-1 Bayer Corporation, Stilwell, KS, USA GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 18 ... also filed: KCA 6.5.3 / 03	Lenz, C.	2012	BYI 02960 200 SL - Magnitude of the residue in/on potato processed commodities Report No.: RARVY038, Edition Number: M-430542-01-2 Bayer CropScience LP, Stilwell, KS, USA GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 19 ... also filed: KCA 6.5.3 / 04	Freitag, T.; Hoffmeister, R.	2016	Determination of the residues of BYI 02960 in/on potato and the processed fractions (tuber, washed; peel washed; tuber, peeled; tuber, cooked; tuber with peel, cooked; fibre; pulp, dry; starch; waste; waste, dried; flakes; and crisps (Am.: chips)) after spray application of BYI 02960 SL 200 in the field in Germany and the Netherlands Report No.: 13-3149, Edition Number: M-546878-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 20 ... also filed: KCA 6.5.3 / 05	Schulte, G.; Ruhl, S.	2012	Processing study - Determination of the residues of BYI 02960 in/on spring barley and the processed fractions (malt sprouts; brewer's malt; brewer's grain, hops draff; brewer's yeast; beer; pearl barley; pearl barley rub off) after spraying of BYI 02960 SL 200 in the field in Germany Report No.: 10-3410, Edition Number: M-439853-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 21 ... also filed: KCA 6.5.3 / 06	Schulte, G.; Bauer, J.	2012	Processing study - Determination of the residues of BYI 02960 in/on wheat and the processed fractions (semolina; semolina bran; whiteflour bran; white flour; white bread; whole meal; wholemeal bread and wheat germ) after spraying of BYI 02960 SL 200 in the field in Germany Report No.: 10-3409, Edition Number: M-440307-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Vertebrate study Y/N	Owner
KCP 5.1.2.5 / 22 ... also filed: KCA 6.5.3 / 07	Lenz, C.; Fischer, D. R.	2012	BYI 02960 200 SL - Magnitude of the residue in/on wheat processed commodities Report No.: RARVY031, Edition Number: M-427047-01-2 Bayer CropScience LP, Stilwell, KS, USA GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 23 ... also filed: KCA 6.5.3 / 08	Lenz, C.	2012	BYI 02960 200 SL - Magnitude of the residue in/on field corn processed commodities Report No.: RARVY030, Edition Number: M-424774-01-1 Bayer CropScience LP, Stilwell, KS, USA GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 24	Schoening, R.; Willmes, J.	2014	Modification M001 of the analytical method 01304 for the determination of residues of BYI 02960 and its metabolites in plant materials by HPLC-MS/MS Report No.: 01304/M001, Edition Number: M-476845-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 25	Block, H.	2016	Final report amendment no. 2 to study 15-2109 / S15-01020 - Determination of the residues of flupyradifurone (BYI 02960) in/on spring oilseed rape after seed dressing with BYI 02960 FS 480 in Poland, Denmark and Germany Report No.: 15-2109, Edition Number: M-546226-03-1 Eurofins Agroscience Services GmbH, Stade, Germany ... amended: 2016-04-22 GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 26 ... also filed: KCA 6.1 / 03	Winter, O.; Amann, S.; Giesler, W.	2018	Storage stability of deltamethrin and flupyradifurone in oilseed rape (seed and straw) Report No.: S17-05312, Edition Number: M-626405-01-1 Eurofins Agroscience Services Chem GmbH, Hamburg, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.5 / 27	Kormos, T.	2017	An analytical method for the determination of residues of difluoroacetic acid in animal matrices using LC/MS/MS Report No.: RV-006-A17-01, Edition Number: M-589558-01-1 Bayer CropScience LP, RTP, NC, USA GLP/GEP: No unpublished	No	Bayer

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Vertebrate study Y/N	Owner
KCP 5.1.2.5 / 28 ... also filed: KCA 6.1 / 04 KCA 6.4.1 / 01	[REDACTED]	2017	Difluoroacetic acid - Magnitude of the residue in laying hens Report No.: RARVN150, Edition Number: M-611007-01-1 [REDACTED] GLP/GEP: Yes unpublished	Yes	Bayer
KCP 5.1.2.5 / 29 ... also filed: KCA 6.4.2 / 01	[REDACTED]	2017	Difluoroacetic acid - Magnitude of the residue in dairy cows Report No.: RARVN149, Edition Number: M-608471-01-1 [REDACTED] GLP/GEP: Yes unpublished	Yes	Bayer
KCP 5.1.2.6 / 01 ... also filed: KCP 10.2.1 / 01	[REDACTED]	2001	Acute toxicity to Oncorhynchus mykiss (rainbow trout) AE F108565 (metabolite of deltamethrin) substance, pure Code: AE F108565 00 1B99 0001 Report No.: C010902, Edition Number: M-199816-01-1 [REDACTED] GLP/GEP: Yes unpublished	Yes	Bayer
KCP 5.1.2.6 / 02	[REDACTED]	2000	Static-renewal acute toxicity to Oncorhynchus mykiss (rainbow trout) Deltamethrin emulsifiable concentrate 100 g/L Code: AE F032640 00 EC11 A308 Report No.: C007498, Edition Number: M-196047-01-1 [REDACTED] GLP/GEP: Yes unpublished	Yes	Bayer
KCP 5.1.2.6 / 03	Freitag, T.; Koch, V.	2011	Analytical method 01306 for the determination of deltamethrin and the metabolites a-R-deltamethrin and trans-deltamethrin in sediment by HPLC-MS/MS Report No.: MR-10/154, Edition Number: M-418179-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: No unpublished	No	Bayer
KCP 5.1.2.6 / 04	Bruns, E.	2012	Chironomus riparius 28-day chronic toxicity test with deltamethrin (tech.) in a water-sediment system using spiked sediment Report No.: EBDAL036, Edition Number: M-425202-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Vertebrate study Y/N	Owner
KCP 5.1.2.6 / 05	Braune, M.	2011	Method 01307 for the determination of deltamethrin, α -R-isomer of deltamethrin and trans-isomer of deltamethrin in test water from aquatic toxicity tests by HPLC-MS/MS Report No.: 01307, Edition Number: M-410093-01-1 Method Report No.: MR-10/162 Bayer CropScience AG, Monheim, Germany GLP/GEP: No unpublished	No	Bayer
KCP 5.1.2.6 / 06 ... also filed: KCP 10.2.1 / 02	Sowig, P.; Gosch, H.	2001	Acute toxicity to Daphnia magna (Waterflea) AE F108565 (Metabolite of deltamethrin) substance, pure Code: AE F108565 00 1B99 0001 Report No.: C010889, Edition Number: M-199793-01-1 Aventis CropScience GmbH, Frankfurt am Main, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.6 / 07	Sowig, P.; Gosch, H.; Weller, O.	2000	Acute toxicity to Daphnia magna (waterflea) Deltamethrin emulsifiable concentrate 100 g/L Code: AE F032640 00 EC11 A308 Report No.: C006590, Edition Number: M-194240-01-1 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.6 / 08	Weller, O.; Gosch, H.; Sowig, P.	2000	Algal growth inhibition - Pseudokirchneriella subcapitata Deltamethrin emulsifiable concentrate 100 g/L Code: AE F032640 00 EC11 A308 Report No.: C007531, Edition Number: M-196114-01-1 Aventis CropScience GmbH, Frankfurt am Main, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.6 / 09 ... also filed: KCP 10.2.3 / 02		2005	Biological effects and fate of deltamethrin EW 015 in outdoor mesocosm ponds Report No.: HBF/BT 07, Edition Number: M-246137-01-2  GLP/GEP: Yes unpublished	Yes	Bayer
KCP 5.1.2.6 / 10	Brumhard, B.; Loehrwald, K.H.	2007	Analysis of deltamethrin concentrations in sediment samples of ECT study no. P1MA Report No.: MR-07/297, Edition Number: M-291818-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Vertebrate study Y/N	Owner
KCP 5.1.2.6 / 11	Krebber, R.; Braune, M.	2007	Analysis of deltamethrin concentrations in water samples of ECT study no. PIMA Report No.: MR-07/295, Edition Number: M-291848-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.6 / 12	Schoening, R.; Willmes, J.	2013	Residue analytical method 01347 for the determination of residues of deltamethrin by HPLC with electrospray and MS/MS - detection Report No.: MR-012/067, Edition Number: M-444791-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: No unpublished	No	Bayer
KCP 5.1.2.6 / 13	Schoening, R.; Willmes, J.	2013	Determination of deltamethrin in feeding solutions from a 10d continuous honeybee feeding study (Study Number: S13-00151; Eurofins) Report No.: MR-13/135, Edition Number: M-469484-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.6 / 14	Giddings, J. M.; Bayne, M. C. R.; Mitchell, K. L.; Shepherd, S. P.	1990	LX165-08 (deltamethrin technical) - Toxicity to the freshwater green alga, Selenastrum capricornutum Report No.: A47090, Edition Number: M-131038-01-1 Springborn Laboratories, Inc. (SLS), USA GLP/GEP: Yes unpublished	No	Bayer
KCP 5.1.2.6 / 15	Krebber, R.; Sandau, C.	2010	Method 01182 for the determination of BYI 02960 in test water from aquatic toxicity tests by HPLC-MS/MS Report No.: 01182, Edition Number: M-363959-01-1 Method Report No.: MR-10/002 Bayer CropScience AG, Monheim, Germany GLP/GEP: No unpublished	No	Bayer
KCP 5.1.2.6 / 16	Schoening, R.; Koester, P.	2011	Modification M001 of the analytical method 01206 for the determination of residues of BYI 02960 and Difluoroethylaminofuranone by HPLC with electrospray and MS/MS - detection Report No.: 01206/M001, Edition Number: M-404877-01-1 Method Report No.: MR-10/137 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Vertebrate study Y/N	Owner
KCP 5.2.1 / 01	Weber, H.	2009	Validation of enforcement method DFG S19 (L 00.00-34) (BCS method ID 00086/M089) for the determination of cis-deltamethrin (AE F032640) in/on foodstuff of plant origin Report No.: S09-00553, Edition Number: M-351076-01-1 Eurofins Analytik GmbH, Dr. Specht Laboratorien, Hamburg, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.2.1 / 02	Merdian, H.	2009	Independent laboratory validation of the DFG method S19 (BCS method 00086/M089) for the determination of residues of cis-deltamethrin (AE F032640) in plant materials, using GC/MS Report No.: P/B 1681 G, Edition Number: M-356306-01-1 PTRL Europe GmbH, Ulm, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.2.2 / 01	Weber, H.	2009	Validation of enforcement method DFG S19 (L 00.00-34) (BCS method ID 00086/M090) for the determination of residues cis-deltamethrin (AE F032640) in/on foodstuff of animal origin Report No.: S09-00551, Edition Number: M-351080-01-1 Eurofins Analytik GmbH, Dr. Specht Laboratorien, Hamburg, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.2.2 / 02	Merdian, H.	2009	Independent laboratory validation of the DFG method S19 (BCS method 00086/M089) for the determination of residues of cis-deltamethrin (AE F032640) in foodstuffs of animal origin, using GC/MS Report No.: P/B 1682 G, Edition Number: M-356331-01-1 PTRL Europe GmbH, Ulm, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.2.3 / 01 ... also filed: KCP 5.1.2.5 / 06	Krebber, R.	2009	Analytical method 01127 for the determination of cyfluthrin and deltamethrin in blood by HPLC-MS/MS Report No.: MR-08/176, Edition Number: M-348630-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.2.3 / 02	Kaussmann, M.	2016	Analytical method 01495 for the determination of various pesticides and selected pesticide metabolites in blood plasma by HPLC-MS/MS Report No.: 01495, Edition Number: M-570324-01-1 Method Report No.: P683166506 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Vertebrate study Y/N	Owner
KCP 5.2.4 / 01 ... also filed: KCP 5.1.2.1 / 01	Brumhard, B.	2005	Analytical method 00877 for the determination of total residues of deltamethrin (AE F032640) in / on soil and sediment by HPLC-MS/MS Report No.: C047210, Edition Number: M-247896-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.2.4 / 02 ... also filed: KCP 5.1.2.1 / 02	Brumhard, B.	2009	Analytical method 00877 for the determination of total residues of Deltamethrin (AE F032640) in/on soil and sediment by HPLC-MS/MS Report No.: 00877, Edition Number: M-246580-02-1 Method Report No.: MR-081/04 Bayer CropScience AG, Monheim, Germany ... amended: 2009-03-31 GLP/GEP: Yes unpublished	No	Bayer
KCP 5.2.4 / 03 ... also filed: KCP 5.1.2.1 / 03	Freitag, T.	2013	Analytical method 01358 for the determination of cis-deltamethrin in soil by HPLC-MS/MS Report No.: MR-13/002, Edition Number: M-451547-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.2.5 / 01 ... also filed: KCP 5.1.2.1 / 04	Krebber, R.; Braune, M.	2013	Analytical method 01383 for the determination of deltamethrin in drinking and surface water by HPLC-MS/MS Report No.: MR-13/053, Edition Number: M-464818-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.2.5 / 02 ... also filed: KCP 5.1.2.1 / 05	Stanislawski, T.	2013	Independent laboratory validation of BCS analytical method no. 01383 for the determination of deltamethrin in surface water, using LC/MS/MS Report No.: P 3021 G, Edition Number: M-471762-01-1 PTRL Europe GmbH, Ulm, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 5.2.5 / 03 ... also filed: KCP 5.1.2.1 / 06	Brumhard, B.	2005	Analytical method 00886 for the determination of total residues of deltamethrin (AE F032640) in surface water by HPLC-MS/MS Report No.: C047388, Edition Number: M-248040-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Vertebrate study Y/N	Owner
KCP 5.2.5 / 04 ... also filed: KCP 5.1.2.1 / 07	Krebber, R.; Braune, M.	2007	Modification M001 of analytical method 00886 for the determination of total residues of deltamethrin (AE F032640) in surface water by HPLC-MS/MS Report No.: 00886/M001, Edition Number: M-291746-01-1 Method Report No.: MR-07/296 Bayer CropScience AG, Monheim, Germany GLP/GEP: No unpublished	No	Bayer

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

Please note that all data mentioned as part of DAR, RAR, or EFSA journals are considered as relied on.

Deltamethrin

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
KCA 4.1.1 / 01	Giudicelli, J. C.	1990	Deltamethrin: Analytical method to verify certified limits. AgrEvo UK Crop Protection Ltd., Chesterford Park, United Kingdom Bayer Report No.: A70743 Edition Number: M-149238-01-1 Date: 1990-06-30 GLP/GEP: No, unpublished confidential	No	Bayer
KCA 4.1.1 / 02	Budgen, P.	2000	Analytical method deltamethrin Determination of AE F108564 and AE 0034609 in technical grade and pure active ingredient by HPLC Deltamethrin technical grade active ingredient Code: AE F032640 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer Report No.: C010359 Edition Number: M-198876-01-1 Date: 2000-10-18 GLP/GEP: No, unpublished confidential	No	Bayer
KCA 4.1.1 / 03	Hanks, A. R.	1990	Liquide chromatographic method for determination of technical deltamethrin and deltamethrin in pesticide formulations : CIPAC collaborative study. Association of Official Analytical Chemists -public data- Report No.: A70978 Edition Number: M-149460-01-1 Date: 1990-01-01 GLP/GEP: No, unpublished	No	-public data-
KCA 4.1.1 / 04	Martijn, A.; Dobrat, W.	1988	CIPAC - Analysis of technical and formulated pesticides (Deltamethrin). CIPAC; -public data- Report No.: A71086 Edition Number: M-149559-01-1 Date: 1988-01-01 GLP/GEP: No, unpublished	No	-public data-

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
KCA 4.1.1 / 05	Budgen, P.; Andel, M.	2000	Validation of the analytical method AL026/00-0 for the determination of AE F108564 and AE 0034609 in AE F032640 Deltamethrin technical grade active ingredient Code: AE F032640 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer Report No.: C010360 Edition Number: M-198878-01-1 Date: 2000-10-18 GLP/GEP: Yes, unpublished confidential	No	Bayer
KCA 4.1.1 / 06	Budgen, P.; Patzke, D.	2000	Validation of the analytical method AL027/00-0 for the determination of AE F108569 and AE 0437894 in AE F032640 Deltamethrin technical grade active ingredient Code: AE F032640 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer Report No.: C010358 Edition Number: M-198874-01-1 Date: 2000-10-18 GLP/GEP: Yes, unpublished confidential	No	Bayer
KCA 4.1.1 / 07	Budgen, P.; Guebert, C.	2000	Validation of the analytical method AL025/00-0 for the determination of AE F108565 and AE F108566 in AE F032640 Deltamethrin technical grade active ingredient Code: AE F032640 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer Report No.: C010356 Edition Number: M-198870-01-1 Date: 2000-10-18 GLP/GEP: Yes, unpublished confidential	No	Bayer
KCA 4.1.1 / 08	Feucht, G.; Michel, A.	2003	Analytical method Quantification of AE F032640 (deltamethrin) in formulations (DP, EC, EG, EW, SC, TB, WDG, WP) and technical grade active ingredient by high performance liquid chromatography (HPLC) Bayer Report No.: AL003/99-3 Edition Number: M-232849-01-1 Date: 2003-07-17 GLP/GEP: No, unpublished	No	Bayer

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
KCA 4.1.1 / 09	Feucht, G.	2010	Validation of the analytical method AL003/99-2 for the determination of AE F032640 (active ingredient) in technical AE F032640 - Amendment 1 of report PA02/074 Bayer Report No.: PA02/074 A1 Edition Number: M-231645-02-2 Method Report No.: AL003/99-2 Date: 2003-03-24 ... amended: 2010-03-31 GLP/GEP: No, unpublished confidential	No	Bayer
KCA 4.1.1 / 10	Anon.	2004	CIPAC Analytical method for Deltamethrin in TC, WG, WP, EC, SC, DP, WT, EG, EW & UL Bayer Report No.: M-274505-01-1 Date: 2004-12-31 GLP/GEP: No, unpublished	No	Bayer
KCA 4.1.1 / 11	Doerner-Rieping, S.; Junker, H.	2013	Determination of the enantiomeric purity of AE F032640 in technical grade and pure deltamethrin by high performance liquid chromatography (HPLC) Bayer Report No.: AM038013FP1 Edition Number: M-472746-01-1 Date: 2013-12-04 GLP/GEP: No, unpublished confidential	No	Bayer
KCA 4.1.1 / 12	Cichy, M.; Junker, H.	2010	Validation of the analytical method AM028810FP2 determination of the enantiomeric purity in technical grade and pure deltamethrin (AE F032640) by high performance liquid chromatography (HPLC) Bayer Report No.: PA10/079 Edition Number: M-398212-01-1 Date: 2010-12-21 GLP/GEP: Yes, unpublished confidential	No	Bayer

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
KCA 4.1.1 / 13	Doerner-Rieping, S.; Junker, H.	2013	Validation of analytical HPLC method AM038013FP1 - Determination of the enantiomeric purity of AE F032640 in technical grade and pure deltamethrin by high performance liquid chromatography (HPLC) - Deltamethrin (AE F032640) Bayer Report No.: PA13/107 Edition Number: M-472718-01-1 Date: 2013-11-26 GLP/GEP: No, unpublished confidential	No	Bayer
KCA 4.1.1 / 14	Doerner-Rieping, S.; Perez-Diaz, C.	2014	Determination of by-products of deltamethrin (AE F032640) in technical grade and pure active substance by high performance liquid chromatography (HPLC) Bayer Report No.: AM034912FP1 Edition Number: M-469685-02-1 Date: 2013-11-15 ... amended: 2014-02-24 GLP/GEP: No, unpublished confidential	No	Bayer
KCA 4.1.1 / 15	Doerner-Rieping, S.; Perez-Diaz, C.	2014	Amendment no1 to validation of analytical HPLC method AM034912FP1 - Determination of by-products of deltamethrin (AE F032640) in technical grade and pure active substance by high performance liquid chromatography (HPLC) Bayer Report No.: PA13/112 Edition Number: M-469686-02-1 Date: 2013-11-13 ... amended: 2014-02-24 GLP/GEP: Yes, unpublished confidential	No	Bayer
KCA 4.1.1 / 16	Cichy, M.	2002	Determination of 1,2-dichloroethane (AE C504722) and 2-propanol (AE 0171363) in technical deltamethrin (AE F032640) by GC (analytical method) Code: AE F032640 (Deltamethrin) Bayer Report No.: C025631 Edition Number: M-209701-01-1 Date: 2002-08-02 GLP/GEP: No, unpublished confidential	No	Bayer

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
KCA 4.1.1 / 17	Doerner-Rieping, S.	2016	Amendment no 1 to validation of the analytical method AL025/02-0 for the determination of 1,2-dichloroethane (AE C504722) and 2-propanol (AE 0171363) in technical deltamethrin (AE F032640) by GC Bayer Report No.: PA02/016 Edition Number: M-209703-01-1 Edition Number: M-209703-02-1 Date: 2002-09-10 ... amended: 2016-05-19 GLP/GEP: Yes, unpublished confidential	No	Bayer
KCA 4.1.1 / 18	Doerner-Rieping, S.; Perez-Diaz, C.	2014	Determination of triethylamine (AE 0171388) in technical grade and pure deltamethrin (AE F032640) by gas chromatography (GC) Bayer Report No.: M-474272-01-1 Method Report No.: AM038413FP1 Date: 2014-01-14 GLP/GEP: No, unpublished confidential	No	Bayer
KCA 4.1.1 / 19	Doerner-Rieping, S.; Perez-Diaz, C.	2014	Validation of analytical method AM038413FP1 determination of triethylamine (AE 0171388) in technical grade and pure deltamethrin (AE F032640) by gas chromatography (GC) Bayer Report No.: PA13/136 Edition Number: M-474279-01-1 Date: 2014-01-14 GLP/GEP: Yes, unpublished confidential	No	Bayer
KCA 4.1.2 / 01	Taylor, N. W.; Snowdon, P. J.	1996	Deltamethrin; analytical grade; active ingredient; Code: Hoe 032640 - Validation of analytical method; peaches; gas chromatography AgrEvo UK Crop Protection Ltd., Chesterford Park, United Kingdom Bayer Report No.: A56355 Report includes Trial Nos.: 203/07/001 Edition Number: M-140178-01-1 Date: 1996-05-03 GLP/GEP: Yes, unpublished	No	Bayer

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
KCA 4.1.2 / 02	Czarnecki, J. J.; McKinney, F. R.; Clayton, F. B.; Crotts, D. G.	1991	Validation of the analytical methodology for determination of combined residues of deltamethrin & trans-deltamethrin in cottonseed & cottonseed processed fractions. EN-CAS Analytical Laboratories, Winston-Salem, NC, USA Bayer Report No.: A71067 Edition Number: M-149543-02-1 Date: 1990-07-05 ... amended: 1991-08-08 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 03	Mestres, R.; Espinoza, C.; Chevallier, C.; Marti, G.	1979	Decamethrin residues analysis. Journal: Travaux de la Societe de Pharmacie de Montpellier Volume: 39 Issue: 4 Pages: 329;336 Year: 1979 Report No.: A71066 Edition Number: M-152254-01-2 GLP/GEP: n.a., published	No	published
KCA 4.1.2 / 04	Martens, R.	1998	Analytical method and validation for the determination of residues of endosulfan and deltamethrin by GC Deltamethrin, endosulfan Code: AE F032640 and AE F002671 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer Report No.: C000413 Report includes Trial Nos.: CR97/028 Edition Number: M-180617-02-1 Date: 1998-08-24 ... amended: 1998-11-30 GLP/GEP: No, unpublished	No	Bayer
KCA 4.1.2 / 05	Martens, R.	1998	Validation of analytical method DGM F01/97-0 for residues of endosulfan and deltamethrin in cucumber, orange, melon and tomato Deltamethrin, endosulfan Code: AE F032640, AE F002671 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer Report No.: C001152 Edition Number: M-181877-01-1 Date: 1998-11-18 GLP/GEP: Yes, unpublished	No	Bayer

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
KCA 4.1.2 / 06	Martens, R.	2000	Validation of analytical method DGM F01/97-0 for dry crops (grain) Deltamethrin Endosulfan Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer Report No.: C006935 Edition Number: M-194895-01-1 Date: 2000-04-03 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 07	Thier, W. G.	1979	Analytical method for the determination of Hoe 32640 OI (deltamethrin) in biological materials Hoechst AG, Frankfurt am Main, Germany Bayer Report No.: A38979 Edition Number: M-251195-01-2 Date: 1979-09-20 GLP/GEP: No, unpublished	No	Bayer
KCA 4.1.2 / 08	Akhtar, M. H.	1982	Gas chromatographic determination of Deltamethrin in biological samples Journal: Journal of Chromatography Issue: 246 Pages: 81-87 Year: 1982 Report No.: A34911 Edition Number: M-115658-01-1 GLP/GEP: n.a., published	No	published
KCA 4.1.2 / 09	Baldi, B. G.; McKinney, F. R.	1994	Analytical method for the G.C. determination of cis-deltamethrin, trans-deltamethrin and alpha-R-deltamethrin in selected processed grain fractions, grain dusts and whole grain from corn, wheat, sorghum and rice. EN-CAS Analytical Laboratories, Winston-Salem, NC, USA Bayer Report No.: A71069 Edition Number: M-149544-01-1 Date: 1994-01-01 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 10	Supatto, F.	1995	RU 22974 - Assay procedure in oily crops (method and validation) Roussel Uclaf, Romainville, France Bayer Report No.: C016898 Edition Number: M-203267-01-1 Date: 1995-12-14 GLP/GEP: No, unpublished	No	Bayer

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
KCA 4.1.2 / 11	Maffezzoni, M.	2001	Analytical method for the determination of deltamethrin in crop ADME Bioanalyses S.A., Vergeze, France Bayer Report No.: C017436 Edition Number: M-204274-01-1 Date: 2001-11-27 GLP/GEP: No, unpublished	No	Bayer
KCA 4.1.2 / 12	Martens, R.	2000	Data generation and enforcement method for residues on plant material by GC Deltamethrin, Endosulfan Code: AE F032640, AE F002671 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer Report No.: C007949 Edition Number: M-240943-01-1 Date: 2000-03-28 GLP/GEP: No, unpublished	No	Bayer
KCA 4.1.2 / 13	Martens, R.	2000	Validation of analytical method DGM F01/97-1 for foodstuff of animal origin (milk, eggs, meat, fat, liver, kidney) Deltamethrin Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer Report No.: C009558 Edition Number: M-198798-01-1 Date: 2000-09-06 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 14	Haines, B.; Tauber, R.	2001	Independent Laboratory Validation for the Determination of Residues of Deltamethrin in Lettuce, Oranges, Milk and Fat and Endosulfan in Lettuce and Oranges Using Method DGM F01/97-1 Xenos Laboratories, Inc., Ottawa, ON, Canada Bayer Report No.: B003259 Edition Number: M-238899-01-1 Date: 2001-03-29 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 15	Benwell, L.	1992	Deltamethrin: The validation of the analytical method for the determination of residues in field beans and soil. Hazleton Lab., United Kingdom Bayer Report No.: A49410 Edition Number: M-138460-01-1 Date: 1992-10-01 GLP/GEP: Yes, unpublished	No	Bayer

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
KCA 4.1.2 / 16	Bixler, T. A.	1990	The GLC determination of the combined residues of deltamethrin and trans-deltamethrin in Mexican cherry tomatoes. Hoechst Roussel Agri-Vet Company, Somerville, NJ, USA Bayer Report No.: A71089 Edition Number: M-149562-01-1 Date: 1990-01-05 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 17	Grigor, A.	1991	Analytical method for the determination of deltamethrin, trans-deltamethrin and degradates in soil by gas chromatography. Chemalysis, Inc., USA Bayer Report No.: A48622 Edition Number: M-137727-01-1 Date: 1991-07-26 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 18	Mestres, R.; Chevallier, C.; Espinoza, C.	1978	Dosage des residus de decamethrine dans l'eau. University of Montpellier, Faculte de Pharmacie, Montpellier, France Bayer Report No.: A74147 Edition Number: M-152399-01-1 Date: 1978-07-08 GLP/GEP: No, unpublished	No	Bayer
KCA 4.1.2 / 19	Class, T.	2001	Analytical Method for the Determination of Deltamethrin in Surface Water PTRL Europe GmbH, Ulm, Germany Bayer Report No.: B003535 Report includes Trial Nos.: 01 G 31949 Edition Number: M-240561-01-1 Date: 2001-10-31 GLP/GEP: No, unpublished	No	Bayer

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
KCA 4.1.2 / 20	Martens, R.	1999	Enforcement method and validation for water by GC Deltamethrin, endosulfan Code: AE F032640, AE F002671 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer Report No.: C005528 Report includes Trial Nos.: CR99/023 Edition Number: M-192230-01-1 Date: 1999-10-05 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 21	Mestres, R.; Chevallier, C.; Espinoza, C.	1978	Analytical method for decamethrine residue analysis in water. University of Montpellier, Faculte de Pharmacie, Montpellier, France -public data- Report No.: A20239 Edition Number: M-093408-01-1 Date: 1978-07-08 GLP/GEP: No, unpublished	No	-public data-
KCA 4.1.2 / 22	Idstein, H.; Merz, H. D.; Klug, R.	1993	Bestimmung von Deltamethrin (Hoe 032640) in Luft mittels GC. Hoechst AG, Frankfurt am Main, Germany Bayer Report No.: A50771 Edition Number: M-131778-01-1 Date: 1993-06-02 GLP/GEP: No, unpublished	No	Bayer
KCA 4.1.2 / 23	Class, T.	1994	Determination of deltamethrin (Hoe 032640) in air by GC validation of the analytical method No.: AL005/93-0 provided by the sponsor. PTRL Europe GmbH, Ulm, Germany Bayer Report No.: A52594 Edition Number: M-133404-01-1 Date: 1994-03-31 GLP/GEP: Yes, unpublished	No	Bayer

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
KCA 4.1.2 / 24	Class, T.	1994	Validation of an analytical method for the determination of deltamethrin in air (Method and validation) PTRL Europe GmbH, Ulm, Germany Bayer Report No.: C012850 Report includes Trial Nos.: P138G Edition Number: M-203491-01-1 Date: 1994-03-01 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 25	Class, T.	2001	Validation of an Analytical Method for the Determinatin of Deltamethrin in Air PTRL Europe GmbH, Ulm, Germany Bayer Report No.: B003367 Report includes Trial Nos.: 01 G 31951 P 482 G Edition Number: M-240404-01-1 Date: 2001-06-29 GLP/GEP: No, unpublished	No	Bayer
KCA 4.1.2 / 26	Huff, D. K.; McKinney, F. R.	1994	Method development and validation for the determination of deltamethrin (alpha-R-, cis- and trans-) and tralomethrin in dairy cow tissues (with poultry matrices added by amendment). EN-CAS Analytical Laboratories, Winston-Salem, NC, USA Bayer Report No.: A71076 Edition Number: M-149550-01-1 Date: 1994-07-29 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 27	Brumhard, B.	2005	Analytical method 00877 for the determination of total residues of deltamethrin (AE F032640) in / on soil and sediment by HPLC-MS/MS Bayer Report No.: C047210 Report includes Trial Nos.: 00877 Edition Number: M-247896-01-1 Date: 2005-03-04 GLP/GEP: Yes, unpublished	No	Bayer

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
KCA 4.1.2 / 28	Brumhard, B.	2010	Analytical method 00877 for the determination of total residues of Deltamethrin (AE F032640) in/on soil and sediment by HPLC-MS/MS Bayer Report No.: 00877 Edition Number: M-246580-02-2 Method Report No.: MR-081/04 Date: 2005-03-04 ... amended: 2009-03-31 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 29	Brumhard, B.	2005	Analytical method 00886 for the determination of total residues of deltamethrin (AE F032640) in surface water by HPLC-MS/MS Bayer Report No.: C047388 Report includes Trial Nos.: 00886 Edition Number: M-248040-01-1 Date: 2005-03-04 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 30	Krebber, R.; Braune, M.	2007	Modification M001 of analytical method 00886 for the determination of total residues of deltamethrin (AE F032640) in surface water by HPLC-MS/MS Bayer Report No.: 00886/M001 Edition Number: M-291746-01-1 Method Report No.: MR-07/296 Date: 2007-08-21 GLP/GEP: No, unpublished	No	Bayer
KCA 4.1.2 / 31	Krebber, R.	2009	Analytical method 01127 for the determination of cyfluthrin and deltamethrin in blood by HPLC-MS/MS Bayer Report No.: MR-08/176 Edition Number: M-348630-01-1 Date: 2009-06-03 GLP/GEP: Yes, unpublished	No	Bayer

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
KCA 4.1.2 / 32	Diot, R.	2004	Modification M001 to the analytical method 00855 for the determination of residues of deltamethrin (AE F032640) in/on apple, kiwi and plum by GC/MSD Bayer Report No.: C040164 Report includes Trial Nos.: 04-03 Edition Number: M-228400-01-1 Date: 2004-05-25 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 33	Diot, R.	2004	Supplement E001 to the analytical method 00855/M001 for the determination of residues of deltamethrin (AE F032640) in/on pear, cherry, tomato, peach, and processed fractions of apple, pear and peach by GC/MSD Bayer Report No.: C042013 Report includes Trial Nos.: 04-05 Edition Number: M-231816-01-1 Date: 2004-05-28 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 34	Diot, R.	2004	Supplement E002 to the analytical method 00855/M001 for the determination of residues of deltamethrin (AE F032640) in/on melon, zucchini, artichoke, pepper, sugar beet, field pea and lettuce by GC/MSD Bayer Report No.: C043675 Report includes Trial Nos.: 00855/M001/E002 04-08 Edition Number: M-234987-01-1 Date: 2004-09-07 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 35	Zimmer, D.; Philipowski, C.	2004	Residue analytical method 00855/M002 for the determination of residues of cis-deltamethrin (AE F032640) in/on pepper (fruit), zucchini (fruit), tomato (fruit), olive (fruit), melon (fruit, pulp), sugarbeet (body, leaf with root collar), cob Bayer Report No.: 00855/M002 Report includes Trial Nos.: P602045501 Edition Number: M-236022-01-1 Date: 2004-10-05 GLP/GEP: Yes, unpublished	No	Bayer

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
KCA 4.1.2 / 37	Lakaschus, S.; Winter, O.	2009	Validation of BCS Method 00855/M004 for the Determination of cis-deltamethrin, trans-deltamethrin and alpha-R-deltamethrin in foodstuff of plant origin Eurofins Analytik GmbH, Dr. Specht Laboratorien, Hamburg, Germany Bayer Report No.: 00855/M004 Report includes Trial Nos.: EASSM/S09-02191 Edition Number: M-356934-01-1 Method Report No.: BAY-0904V Date: 2009-09-17 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 38	[REDACTED]	2000	Acute toxicity to Oncorhynchus mykiss (rainbow trout) in a static-renewal system Deltamethrin oil in water emulsion 15 g/L Code: AE F032640 00 EW01 B103 [REDACTED] Bayer Report No.: C008365 Edition Number: M-197428-01-1 Date: 2000-07-18 GLP/GEP: Yes, unpublished	Yes	Bayer
KCA 4.1.2 / 39	Sowig, P.; Gosch, H.; Weller, O.	2000	Acute toxicity to Daphnia magna (waterflea) Deltamethrin oil in water emulsion 15 g/L Code: AE F032640 00 EW01 B103 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer Report No.: C008334 Edition Number: M-197398-01-1 Date: 2000-07-05 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 40	Sowig, P.; Gosch, H.; Weller, O.	2000	Algal growth inhibition - Pseudokirchneriella subcapitata Deltamethrin oil in water emulsion 15 g/L Code: AE F032640 00 EW01 B103 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer Report No.: C008323 Edition Number: M-197387-01-1 Date: 2000-07-05 GLP/GEP: Yes, unpublished	No	Bayer

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
KCA 4.1.2 / 41	Braune, M.	2011	Method 01307 for the determination of deltamethrin, á-R-isomer of deltamethrin and trans-isomer of deltamethrin in test water from aquatic toxicity tests by HPLC-MS/MS Bayer Report No.: 01307 Edition Number: M-410093-01-1 Method Report No.: MR-10/162 Date: 2011-06-15 GLP/GEP: No, unpublished	No	Bayer
KCA 4.1.2 / 42	[REDACTED]	2005	Fate and effects of Thiacloprid & Deltamethrin OD 100 + 10 in outdoor mesocosm ponds [REDACTED] Report No.: BAY-018/4-52 Edition Number: M-259938-01-2 Date: 2005-11-03 GLP/GEP: Yes, unpublished	Yes	Bayer
KCA 4.1.2 / 43	Krebber, R.; Braune, M.	2007	Analysis of deltamethrin concentrations in water samples of ECT study no. P1MA Bayer Report No.: MR-07/295 Edition Number: M-291848-01-1 Date: 2007-08-24 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 44	Schoening, R.; Willmes, J.	2013	Residue analytical method 01347 for the determination of residues of deltamethrin by HPLC with electrospray and MS/MS - detection Bayer Report No.: MR-012/067 Edition Number: M-444791-01-1 Date: 2013-01-14 GLP/GEP: No, unpublished	No	Bayer
KCA 4.1.2 / 45	[REDACTED]	1990	(LX 165-08, deltamethrin technical) - Acute (28-Day) toxicity to rainbow trout (Oncorhynchus mykiss) under flow-through conditions. [REDACTED] Bayer Report No.: A47111 Edition Number: M-135553-01-1 Date: 1990-04-11 GLP/GEP: Yes, unpublished ... also filed: KCA 8.2.1 / 03 KCA 8.2.2.1 / 01	Yes	Bayer

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
KCA 4.1.2 / 46	Freitag, T.; Koch, V.	2011	Analytical method 01306 for the determination of deltamethrin and the metabolites a-R-deltamethrin and trans-deltamethrin in sediment by HPLC-MS/MS Bayer Report No.: MR-10/154 Edition Number: M-418179-01-1 Date: 2011-11-18 GLP/GEP: No, unpublished	No	Bayer
KCA 4.1.2 / 47	Braune, M.	2013	Method 01369 for the determination of BCS-BY84407 in test water by HPLC-MS/MS Bayer Report No.: MR-13/038 Edition Number: M-451312-01-1 Date: 2013-04-12 GLP/GEP: No, unpublished	No	Bayer
KCA 4.1.2 / 48	Braune, M.	2013	Analytical method 01371 for the determination of BCS-CW57835 in test water from aquatic toxicity tests by HPLC-UV Bayer Report No.: MR-13/043 Edition Number: M-451531-01-1 Date: 2013-04-17 GLP/GEP: No, unpublished	No	Bayer
KCA 4.1.2 / 49	Schoening, R.; Willmes, J.	2013	Determination of deltamethrin in feeding solutions from a 10d continuous honeybee feeding study (Study Number: S13-00151; Eurofins) Bayer Report No.: MR-13/135 Edition Number: M-469484-01-1 Date: 2013-11-13 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 50	Dix, M. E.	2013	Method validation for seven pyrethroids in formulated sediment by gas chromatography using mass selective detection with negative chemical ionization Smithers Viscient, Wareham, MA, USA Pyrethroid Working Group Report No.: 13656.6124 Edition Number: M-554274-01-1 Date: 2013-10-03 GLP/GEP: No, unpublished	No	Pyrethroid Working Group

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
KCA 4.1.2 / 51	Dix, M. E.	2015	Method validation for seven pyrethroids in freshwater by gas chromatography using selective detection with negative chemical ionization Smithers Viscient, Wareham, MA, USA Pyrethroid Working Group Report No.: 13656.6125 Edition Number: M-536985-01-1 Date: 2015-10-03 GLP/GEP: No, unpublished	No	Pyrethroid Working Group
KCA 4.1.2 / 52	Dix, M. E.	2013	Method extension for eight pyrethroids in freshwater by gas chromatography using mass selective detection with negative chemical ionization and liquid chromatography with mass spectrometry Smithers Viscient, Wareham, MA, USA Pyrethroid Working Group Report No.: 13656.6174 Edition Number: M-554282-01-1 Date: 2013-10-03 GLP/GEP: No, unpublished	No	Pyrethroid Working Group
KCA 4.1.2 / 53	Brumhard, B.; Loehrwald, K.H.	2007	Analysis of deltamethrin concentrations in sediment samples of ECT study no. P1MA Bayer Report No.: MR-07/297 Edition Number: M-291818-01-1 Date: 2007-08-22 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 54	Schoening, R.; Diehl, P.	2013	Analytical phase report - Assessment of side effects on the honeybee (<i>Apis mellifera</i> L.), exposed to <i>Phacelia tanacetifolia</i> , sprayed sequentially with deltamethrin during flowering in a long-term field study in North Alsace, France Eurofins Agrosience Services GmbH, Niefern-Oeschelbronn, Germany Bayer Report No.: S10-03820 Edition Number: M-451145-01-1 Date: 2013-04-15 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 55	Schoening, R.; Diehl, P.	2013	Analytical phase report - Assessment of side effects on the honeybee (<i>Apis mellifera</i> L.), exposed to <i>Phacelia tanacetifolia</i> , sprayed sequentially with deltamethrin during flowering in a long-term field study in Mid Alsace, France Bayer Report No.: S10-03824 Edition Number: M-451154-01-1 Date: 2013-04-15 GLP/GEP: Yes, unpublished	No	Bayer

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
KCA 4.1.2 / 56	Desmaris, F.; Diot, R.; Mousques, A.	2017	Deltamethrin - Questions by the RMS CRD on the analytical methods/validation relating to chemical active in the frame of AIR process Bayer Report No.: M-588243-01-1 Date: 2017-05-20 GLP/GEP: n.a., unpublished ... also filed: KCA 4.2 / 17	No	Bayer
KCA 4.1.2 / 36	Diot, R.	2004	Modification M003 to the analytical method 00855 for the determination of residues of deltamethrin (AE F032640) in/on olive and rape by GC/MSD and in/on Brussels sprout, rape and sugar beet by GC-MS/MS Bayer Report No.: C043677 Report includes Trial Nos.: 00855/M003 04-10 Edition Number: M-234990-01-1 Date: 2004-09-07 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.1.2 / 57	Desmaris, F.	2018	Additional chromatograms of study reports: RA-2409/03 (sugar beet) - RA-2410/03 (sugar beet) - RA-2436/03 (sugar beet) - 08-2215 (barley post-harvest) - 08-2214 (wheat post-harvest) Bayer Report No.: M-641700-01-1 Date: 2018-11-09 GLP/GEP: No, unpublished	No	Bayer
KCA 4.1.2 / 58	Sadler, T.	2019	Linearity data for method HRAV-10 and method DGM F01/97-0 Bayer Report No.: M-646787-01-1 Date: 2019-01-18 GLP/GEP: n.a., unpublished ... also filed: KCA 6.1 / 06	No	Bayer
KCA 4.1.2 / 59	Sadler, T.	2019	Validation data for method used in study report 2010/0064/01 Bayer Report No.: M-646878-01-1 Date: 2019-01-18 GLP/GEP: n.a., unpublished ... also filed: KCA 8.2.4.1 / 11	No	Bayer

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
KCA 4.2 / 01	Tillier, C.; Devaux, P.	1981	Quantitative determination of deltamethrin in urine. Roussel Uclaf, Romainville, France Bayer Report No.: A71071 Edition Number: M-149546-01-1 Date: 1981-09-24 GLP/GEP: No, unpublished	No	Bayer
KCA 4.2 / 02	Tillier, C.	1989	RU 22974: Assay procedure in plasma. Roussel Uclaf, Romainville, France Bayer Report No.: A70887 Edition Number: M-149371-01-1 Date: 1989-12-21 GLP/GEP: No, unpublished	No	Bayer
KCA 4.2 / 03	Tillier, C.	1988	Assay procedure for the analysis of deltamethrin residues in human plasma. Roussel Uclaf, Romainville, France Bayer Report No.: A71065 Edition Number: M-149542-01-1 Date: 1988-05-20 GLP/GEP: No, unpublished	No	Bayer
KCA 4.2 / 04	Weber, H.	2009	Validation of enforcement method DFG S19 (L 00.00-34) (BCS method ID 00086/M089) for the determination of cis-deltamethrin (AE F032640) in/on foodstuff of plant origin Eurofins Analytik GmbH, Dr. Specht Laboratorien, Hamburg, Germany Bayer Report No.: S09-00553 Edition Number: M-351076-01-1 Date: 2009-07-07 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.2 / 05	Merdian, H.	2009	Independent laboratory validation of the DFG method S19 (BCS method 00086/M089) for the determination of residues of cis-deltamethrin (AE F032640) in plant materials, using GC/MS PTL Europe GmbH, Ulm, Germany Bayer Report No.: P/B 1681 G Edition Number: M-356306-01-1 Date: 2009-09-23 GLP/GEP: Yes, unpublished	No	Bayer

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
KCA 4.2 / 06	Weber, H.	2009	Validation of enforcement method DFG S19 (L 00.00-34) (BCS method ID 00086/M090) for the determination of residues cis-deltamethrin (AE F032640) in/on foodstuff of animal origin Eurofins Analytik GmbH, Dr. Specht Laboratorien, Hamburg, Germany Bayer Report No.: S09-00551 Edition Number: M-351080-01-1 Date: 2009-07-07 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.2 / 07	Merdian, H.	2009	Independent laboratory validation of the DFG method S19 (BCS method 00086/M089) for the determination of residues of cis-deltamethrin (AE F032640) in foodstuffs of animal origin, using GC/MS PTSL Europe GmbH, Ulm, Germany Bayer Report No.: P/B 1682 G Edition Number: M-356331-01-1 Date: 2009-09-23 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.2 / 08	Justus, K.	2014	Extraction efficiency testing of the residue analytical method 00855/M002 for the determination of residues of cis-deltamethrin (AE F032640) in crops using aged radioactive residues - Surrogate - Bayer Report No.: EnSa-14-0317 Edition Number: M-481954-02-1 Date: 2014-04-01 ... amended: 2014-04-02 GLP/GEP: No, unpublished	No	Bayer
KCA 4.2 / 09	Schoening, R.; Willmes, J.	2014	Cross validation of extraction methods for the determination of residues of deltamethrin in plant materials by HPLC-MS/MS Bayer Report No.: MR-14/012 Edition Number: M-481952-02-1 Date: 2014-04-01 ... amended: 2014-04-11 GLP/GEP: No, unpublished	No	Bayer
KCA 4.2 / 10	Freitag, T.	2013	Analytical method 01358 for the determination of cis-deltamethrin in soil by HPLC-MS/MS Bayer Report No.: MR-13/002 Edition Number: M-451547-01-1 Date: 2013-04-17 GLP/GEP: Yes, unpublished	No	Bayer

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
KCA 4.2 / 11	Krebber, R.; Braune, M.	2013	Analytical method 01383 for the determination of deltamethrin in drinking and surface water by HPLC-MS/MS Bayer Report No.: MR-13/053 Edition Number: M-464818-01-1 Date: 2013-09-02 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.2 / 12	Stanislawski, T.	2013	Independent laboratory validation of BCS analytical method no. 01383 for the determination of deltamethrin in surface water, using LC/MS/MS PTRL Europe GmbH, Ulm, Germany Bayer Report No.: P 3021 G Edition Number: M-471762-01-1 Date: 2013-11-18 GLP/GEP: Yes, unpublished	No	Bayer
KCA 4.2 / 13	Schoening, R.; Snowdon, P.	2015	Review of analytical methods for the determination of deltamethrin residues in products of plant and animal origin Bayer Report No.: M-537967-01-1 Date: 2015-11-03 GLP/GEP: n.a., unpublished	No	Bayer
KCA 4.2 / 14	Specht, W.; Thier, H. P.	1987	Organochlorine, organophosphorus, nitrogen-containing and other pesticides - Gas-chromatographic determination after cleanup by gel permeation chromatography and silica gel minicolumn chromatography Publisher: Deutsche Forschungsgemeinschaft / VCH Location: Weinheim Journal: Manual of Pesticide Residue Analysis Volume: I Pages: 383 - 400 Year: 1987 Report No.: 00086 Edition Number: M-006227-01-1 GLP/GEP: No, published	No	published

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
KCA 4.2 / 15	Anon.	1996	Analytical methods for pesticide residues in foodstuffs Multi-residue method 1 Pesticides amenable to gas chromatography Journal: Ministry of Public Health, Welfare and Sport, NLD Volume: June Issue: Part I Pages: 1;22 Year: 1996 Report No.: C048287 Edition Number: M-249648-01-1 Date: 1996-01-01 GLP/GEP: No, published	No	published
KCA 4.2 / 16	Radix, P.	2016	Deltamethrin - Answer to CRD question Volume 3CA Part B 5: Analytical methods/validation relating to the active Bayer Report No.: M-555924-01-1 Date: 2016-06-01 GLP/GEP: n.a., unpublished	No	Bayer
KCA 4.2 / 17	Desmaris, F.; Diot, R.; Mousques, A.	2017	Deltamethrin - Questions by the RMS CRD on the analytical methods/validation relating to chemical active in the frame of AIR process Bayer Report No.: M-588243-01-1 Date: 2017-05-20 GLP/GEP: n.a., unpublished ... also filed: KCA 4.1.2 / 56	No	Bayer
KCA 4.2 / 18	Mousquès, A., Sadler, T.	2019	Method validation data in support of the determination of deltamethrin in other crop fractions not assigned to a specific group Bayer Report No.: M-647563-01-1 Date: 2019-01-25 GLP/GEP: n.a., unpublished	No	Bayer
KCA 4.2 / 19	Mousquès, A., Sadler, T.	2019	Method validation data in support of the determination of deltamethrin in high starch commodities Bayer Report No.: M-647564-01-1 Date: 2019-01-25 GLP/GEP: n.a., unpublished	No	Bayer

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
KCA 4.2 / 20	Mousquès, A., Sadler, T.	2019	Method validation data in support of the determination of deltamethrin in high oil plant commodities Bayer Report No.: M-647565-01-1 Date: 2019-01-25 GLP/GEP: n.a., unpublished	No	Bayer
KCA 4.2 / 21	Sadler, T.; Mousquès, A.	2019	Method validation data in support of the determination of deltamethrin high acid content plant commodities Bayer Report No.: M-647566-01-1 Date: 2019-01-25 GLP/GEP: n.a., unpublished	No	Bayer
KCA 4.2 / 22	Mousquès, A.; Sadler, T.	2019	Method validation data in support of the determination of deltamethrin in high water commodities Bayer Report No.: M-647640-01-1 Date: 2019-01-25 GLP/GEP: n.a., unpublished	No	Bayer

Flupyradifurone

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KIIA 4.2.1 /02	Wagner, S.	2011	Validation of AM008809MP1 - Flupyradifurone (BYI 02960) - Determination of technical grade active substance HPLC - ISTD Bayer CropScience, Report No.: VB1-AM008809MP1, Edition Number: M-409002-01-1 Date: 2011-06-06 GLP/GEP: no, unpublished	N	Bayer
KIIA 4.3 /01	Schulte, G.; Bauer, J.	2012	Analytical method 01330 for the determination of residues of BYI 02960 and its metabolite difluoroacetic acid in/on plant matrix by HPLC-MS/MS - Enforcement method plant Bayer CropScience, Report No.: 01330, Edition Number: M-425848-01-1 Method Report No.: 01330 Date: 2012-02-22 GLP/GEP: yes, unpublished	N	Bayer
KIIA 4.3 /02	Konrad, S.	2012	Independent lab validation of BCS method 01330 for the determination of residues of BYI 02960 and its metabolite difluoroacetic acid in/on plant matrices by HPLC-MS/MS Currenta GmbH & Co. OHG, Leverkusen, Germany Bayer CropScience, Report No.: 2011/0134/01, Edition Number: M-427133-01-1 Method Report No.: 2011/0134/01 EPA MRID No.: 48843818 Date: 2012-02-28 GLP/GEP: yes, unpublished	N	Bayer
KIIA 4.3 /03	Li, Y.; Schoening, R.	2011	Amendment No. 1 - Validation of Bayer CropScience method RV-001-P10-02 - An analytical method for the determination of residues of BYI 02960, 6-chloronicotinic acid, difluoroacetic acid, and difluoroethyl-amino-furanone in plant matrices using LC/MS/MS Bayer CropScience LP, Stilwell, KS, USA Bayer CropScience, Report No.: RARVP013, Edition Number: M-415504-02-1 Method Report No US: RARVP013 Date: 2011-10-12 ...Amended: 2012-01-11 GLP/GEP: yes, unpublished	N	Bayer

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KIIA 4.3 /04	Justus, K.	2011	Extraction efficiency testing of the residue analytical method RV-001-P10-02 for the determination of BYI 02960, 6-chloronicotinic acid, difluoroacetic acid and difluoroethyl-amino-furanone in plant matrices using aged radioactive residues Bayer CropScience, Report No.: MEF-11/793, Edition Number: M-419323-01-1 EPA MRID No.: 48843821 Date: 2011-12-01 GLP/GEP: yes, unpublished	N	Bayer
KIIA 4.3 /05	Rosati, D.	2012	Analytical method no 01212 for the determination of residues of BYI 02960 and its metabolites BCS-AA56716 (DFA), AE F161089 (6CNA) and BCS-CC98193 (furanone) in/on plant material by HPLC-MS/MS Bayer S.A.S., Bayer CropScience, Lyon, France Bayer CropScience, Report No.: 01212, Edition Number: M-428017-01-1 Method Report No.: MR-10/174 Date: 2012-03-27 GLP/GEP: yes, unpublished	N	Bayer
KIIA 4.3 /06	Schulte, G.; Bauer, J.	2012	Analytical method 01214 for the determination of residues of BYI 02960 and its metabolite difluoroacetic acid in/on animal matrices by HPLC-MS/MS - Enforcement method animal Bayer CropScience, Report No.: 01214, Edition Number: M-425837-01-1 Method Report No.: 01214 EPA MRID No.: 48843825 Date: 2012-02-22 GLP/GEP: yes, unpublished	N	Bayer
KIIA 4.3 /07	Konrad, S.	2012	Independent lab validation of BCS method 01214 for the determination of residues of BYI 02960 and its metabolite difluoroacetic acid in/on animal matrices by HPLC-MS/MS Currenta GmbH & Co. OHG, Leverkusen, Germany Bayer CropScience, Report No.: 2011/0164/01, Edition Number: M-427160-01-1 Method Report No.: 2011/0164/01 EPA MRID No.: 48843826 Date: 2012-02-28 GLP/GEP: yes, unpublished	N	Bayer

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KIIA 4.3 /08	[REDACTED]	2012	BYI 02960 - Magnitude of the residue in dairy cows - Amended report [REDACTED] Bayer CropScience, Report No.: RARVP050-1, Edition Number: M-428416-02-1 EPA MRID No.: 48843842 Date: 2012-04-03 ...Amended: 2012-05-31 GLP/GEP: yes, unpublished ...also filed: KIIA 6.1.1 /02 ...also filed: KIIA 6.4.2 /01	Y	Bayer
KIIA 4.3 /09	[REDACTED]	2012	BYI 02960 - Magnitude of the residue in laying hens [REDACTED] Bayer CropScience, Report No.: RARVP041, Edition Number: M-428933-01-1 Date: 2012-04-05 GLP/GEP: yes, unpublished ...also filed: KIIA 6.4.1 /01	Y	Bayer
KIIA 4.3 /10	Schulte, G.; Teubner, L.	2012	Modification M001 of the analytical method 01330 for the determination of residues of BYI 02960 and its metabolite difluoroacetic acid in/on plant matrix by HPLC-MS/MS- Enforcement method plant Bayer CropScience, Report No.: MR-12/054, Edition Number: M-438310-01-1 Date: 2012-09-10 GLP/GEP: yes, unpublished	N	Bayer
KIIA 4.3 /11	Konrad, S.	2012	Independent lab validation of BCS method 01330/M001 for the determination of residues of BYI 02960 and its metabolite difluoroacetic acid in/on plant matrices by HPLC-MS/MS Currenta GmbH & Co. OHG, Leverkusen, Germany Bayer CropScience, Report No.: 01330/M001, Edition Number: M-439855-01-1 Date: 2012-10-15 GLP/GEP: yes, unpublished	N	Bayer

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KIIA 4.4 /01	Brumhard, B.: Reineke, A.	2009	Analytical method 01074 for the determination of BYI 02960 in soil using LC/MS/MS Bayer CropScience, Report No.: 01074, Edition Number: M-337752-01-1 Method Report No.: MR-07/337 Date: 2009-02-24 GLP/GEP: yes, unpublished	N	Bayer
KIIA 4.5 /01	Fargeix, G.; Rosati, D.	2012	Analytical method no 01213 for the determination of residues of BYI 02960 in drinking and surface water by HPLC-MS/MS Bayer S.A.S., Bayer CropScience, Lyon, France Bayer CropScience, Report No.: 01213, Edition Number: M-428019-01-1 Method Report No.: MR-12/022 Date: 2012-03-29 GLP/GEP: yes, unpublished	N	Bayer
KIIA 4.7 /01	Heinz, N.	2011	BYI 02960: Analytical method for determination in air PTRL Europe GmbH, Ulm, Germany Bayer CropScience, Report No.: P 2419 G, Edition Number: M-420657-01-1 EPA MRID No.: 48843838 Date: 2011-12-14 GLP/GEP: yes, unpublished	N	Bayer

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 Deltamethrin

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

A 2.1.1.1 Description of analytical methods for the determination of residues in plant matrices (KCP 5.1)

A 2.1.1.1.1 Analytical method 1 (00855/M004)

A 2.1.1.1.1.1 Method validation

Comments of zRMS:	<p>The method 00855/M004 was successfully validated for the determination of residues of <i>cis</i>-deltamethrin, <i>trans</i>-deltamethrin and α-R-deltamethrin in foodstuff of plant origin (strawberry (fruit), tomato (fruit), lambs lettuce, green peas, wheat (grain), wheat (straw), barley (whole plant) and oilseed rape (seed)).</p> <p>The limit of quantification (LOQ) for <i>cis</i>-, <i>trans</i>- and α-(R)-deltamethrin was 0.01 mg/kg for strawberry (fruit), tomato (fruit), lambs lettuce, green peas, wheat (grain) and oilseed rape (seed) and 0.05 mg/kg for wheat (straw) and barley (whole plant).</p> <p>For all matrices mean recovery values obtained by LC-MS/MS for <i>trans</i>-, <i>cis</i>- and α-(R)-deltamethrin for both fortification levels (LOQ and the ten times LOQ level) comply with the standard acceptance criteria of SANCO/825/00, which requires that the mean recovery at each fortification level should be in the range of 70-110%). Furthermore, as required by the standard acceptance criteria, the overall relative standard deviation as well as the relative standard deviation for each fortification level were <20%.</p> <p>Two MRM transitions were monitored for each analyte. Therefore, the LC-MS/MS method is highly specific and an additional confirmatory method is not necessary.</p> <p>This method meets all guideline criteria according to SANCO/3029/99 rev. 4 and SANCO/825/00 rev. 8.1.</p> <p>The study is acceptable.</p>
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Reference:	KCP 5.1.2.5/01
Title:	Validation of BCS Method 00855/M004 for the Determination of <i>cis</i> -deltamethrin, <i>trans</i> -deltamethrin and α -R-deltamethrin in foodstuff of plant origin
Report:	Lakaschus, S.; Winter, O.; 2009; 00855/M004; M-356934-01-1
Authority registration No:	
Guideline(s):	91/414/EEC, 96/46/EC 4.2.1 SANCO/3029/99 rev. 4 of 1/07/2000 SANCO 7(825/00 rev.7 of 17/03/2004 OECD (ENV7JM7MONO (2007)
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

In order to validate the method for the determination of *trans*-, *cis*- and α -(R)-deltamethrin in foodstuff of plant origin a series of recovery experiments was performed by fortifying control (untreated) specimens of strawberry (fruit), tomato (fruit), lambs lettuce, green peas, wheat (grain), wheat (straw), barley (whole plant) and oilseed rape (seed).

The BCS Method 00855/M002 for the determination of *cis*-deltamethrin was used as a basis and extended for the analysis of *trans*-deltamethrin and α -(R)-deltamethrin. The extended method is referred to as BCS Method 00855/M004. The conventional extraction of olive from the precursor method 00855/M002 was used for oilseed rape (seed). Additionally ^{13}C -labelled isomers of deltamethrin were used as internal standards for each corresponding unlabelled deltamethrin isomer. In cases where matrix effects were nearly identical the internal standards of *cis*- ^{13}C -deltamethrin and *trans*- ^{13}C -deltamethrin were used for the determination of α -(R)-deltamethrin since these standards had a higher purity than α -(R)- ^{13}C -deltamethrin.

The specimen weights taken for analysis were 10 g for strawberry (fruit), tomato (fruit), lambs lettuce, green peas, wheat (grain) and 5 g for wheat (straw), barley (whole plant) and oilseed rape (seed).

Extraction of residues was achieved by homogenisation with acetone/dichlormethan/n-hexane (1/1/1, v/v/v). Depending on the nature of the sample material, the obtained raw extracts were diluted and directly analyzed by LC-MS/MS without further clean up, or cleaned up by solid phase extraction on a SCX-cartridge, or by gel permeation chromatography (GPC), respectively. The HPLC column was a C18 Ascentis Express. The final extracts were analysed for trans-, cis- and α -(R)-deltamethrin using a Hewlett-Packard Series 1200 HPLC (Agilent Technologies) coupled to a PE-Sciex API 4000 tandem mass spectrometer with IonSpray[®] interface. Two MRM transitions were monitored for all the isomers m/z 523 \rightarrow 281 as 1st MRM (quantification) and m/z 525 \rightarrow 283 as 2nd MRM (confirmation).

For all eight matrices, the control specimens were analysed in duplicate, and fortified specimens were analysed in quintuplicate for each fortification level, limits of quantification (LOQ) and at ten times LOQ. Two characteristic mass transitions are monitored for each deltamethrin isomer.

Results and discussions

In order to ensure unambiguous identification two mass transitions were monitored and evaluated for all isomers (MRM 523 \rightarrow 281 and MRM 525 \rightarrow 283). No significant interferences from the specimen matrices were detected at the retention time corresponding to the deltamethrin isomers in any of the control specimens.

Analytical grade reference materials of trans-deltamethrin (94.0 %), cis-deltamethrin (99.6 %) and α -(R)-deltamethrin (94.3 %) were used for preparing all required solutions. trans-¹³C-deltamethrin (99.0 %), cis-¹³C-deltamethrin (>99 %) and α -(R)-¹³C-deltamethrin (91 %) were used as internal standards.

The tests for strawberry (fruit), tomato (fruit), green peas (seed) and wheat straw showed matrix effects for α -(R)-deltamethrin analogue to cis-deltamethrin as well as to trans-deltamethrin in oilseed rape seed.

The purity of α -(R)-¹³C-deltamethrin was less than trans-¹³C- and cis-¹³C-deltamethrin. Therefore residues of α -(R)-deltamethrin were determined using cis-¹³C-deltamethrin for strawberry (fruit), tomato (fruit), green peas (seed) and wheat (straw) and trans-¹³C-deltamethrin for oilseed rape (seed) as the internal standards.

The ratio of the analyte peak area to the internal standard peak area was determined in each sample. During method calibration a curve with variable analyte concentrations of 1.25 to 100 ng/mL and a constant amount of the internal standard (100 ng/mL) was recorded and used for the calculation of an average response factor. The detector showed linear response for solvent standards of all three deltamethrin isomers ranging from 1.25 ng/mL to 100 ng/mL. The correlation coefficients were found to be 0.9995 and 0.9990 for trans-deltamethrin, 0.9996 and 0.9992 for cis-deltamethrin and ranged between 0.9987 to 0.9999 for α -(R)-deltamethrin.

For all matrices, analysis of control specimens by LC-MS/MS indicated that residues of the test substance were below 30% of the LOQ.

The limit of quantification (LOQ) for cis-, trans- and α -(R)-deltamethrin was 0.01 mg/kg for edible matrices like strawberry (fruit), tomato (fruit), lambs lettuce, green peas, wheat (grain) and oilseed rape (seed) and the limit of detection (LOD) was 0.003 mg/kg. For not edible matrices like wheat (straw) and barley (whole plant) the limit of quantification (LOQ) was 0.05 mg/kg and the limit of detection (LOD) was 0.01 mg/kg. A stability check was performed by fortifying control extracts of each matrix in toluene (or acetonitrile for OSR) at 50 ng/mL with trans-, cis-, α -(R)-deltamethrin. The test indicated no significant decline of the recoveries during a storage period of at least seven days in toluene and acetonitrile for all matrices under cool and dark conditions (+4°C).

The accuracy (analytical recovery) of the method was determined by comparing the measured and nominal concentrations from the recovery experiments.

For all eight matrices, mean recovery values obtained by LC-MS/MS for both fortification levels (LOQ and the ten times LOQ level) for trans-, cis- and α -(R)-deltamethrin, comply with the standard acceptance criteria of SANCO Guideline 825/00, which requires that the mean recovery at each fortification level should be in the range of 70 - 110 %. Furthermore, the overall relative standard deviation and the relative standard deviation for each fortification level was \leq 20 %.

Table A 1: Recovery results from method validation of cis-deltamethrin and isomers using the analytical method in different plant matrices

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
<i>cis-deltamethrin</i>					
strawberry (fruit)	0.01	5	103	1.3	m/z 523→281 (quantification)
	0.10	5	103	0.8	
	0.01	5	103	2.5	m/z 525→283 (confirmation)
	0.10	5	104	0.8	
tomato (fruit)	0.01	5	100	1.5	m/z 523→281 (quantification)
	0.10	5	102	3.3	
	0.01	5	100	1.6	m/z 525→283 (confirmation)
	0.10	5	102	2.2	
lambs lettuce	0.01	5	99	2.3	m/z 523→281 (quantification)
	0.10	5	104	3.0	
	0.01	5	100	4.6	m/z 525→283 (confirmation)
	0.10	5	102	3.7	
green peas	0.01	5	89	2.1	m/z 523→281 (quantification)
	0.10	5	91	2.6	
	0.01	5	91	1.8	m/z 525→283 (confirmation)
	0.10	5	90	4.3	
wheat (straw)	0.05	5	80	5.3	m/z 523→281 (quantification)
	0.50	5	73	6.3	
	0.05	5	81	3.5	m/z 525→283 (confirmation)
	0.50	5	72	5.0	
wheat (grain)	0.01	5	100	3.3	m/z 523→281 (quantification)
	0.10	5	97	2.7	
	0.01	5	100	4.4	m/z 525→283 (confirmation)
	0.10	5	95	3.1	
barley (whole plant)	0.05	5	96	2.3	m/z 523→281 (quantification)
	0.50	5	96	1.1	
	0.05	5	96	1.9	m/z 525→283 (confirmation)
	0.50	5	96	2.1	
oilseed rape (seeds)	0.01	5	98	1.9	m/z 523→281 (quantification)
	0.10	5	101	2.9	
	0.01	5	98	3.0	m/z 525→283 (confirmation)
	0.10	5	98	1.5	

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
<i>α-(R)-deltamethrin</i>					
strawberry (fruit)	0.01	5	84	7.3	m/z 523→281 (quantification)
	0.10	5	94	5.2	
	0.01	5	83	5.2	m/z 525→283 (confirmation)
	0.10	5	93	2.9	
tomato (fruit)	0.01	5	91	3.2	m/z 523→281 (quantification)
	0.10	5	100	2.5	
	0.01	5	91	2.7	m/z 525→283 (confirmation)
	0.10	5	99	2.3	
lambs lettuce	0.01	5	98	6.0	m/z 523→281 (quantification)
	0.10	5	90	15	
	0.01	5	97	5.6	m/z 525→283 (confirmation)
	0.10	5	88	16	
green peas	0.01	5	79	8.7	m/z 523→281 (quantification)
	0.10	5	88	1.7	
	0.01	5	79	6.7	m/z 525→283 (confirmation)
	0.10	5	87	2.3	
wheat (straw)	0.05	5	80	5.4	m/z 523→281 (quantification)
	0.50	5	71	6.9	
	0.05	5	80	6.5	m/z 525→283 (confirmation)
	0.50	5	70	6.7	
wheat (grain)	0.01	5	91	3.2	m/z 523→281 (quantification)
	0.10	5	94	0.9	
	0.01	5	93	4.0	m/z 525→283 (confirmation)
	0.10	5	94	1.6	
barley (whole plant)	0.05	5	90	2.8	m/z 523→281 (quantification)
	0.50	5	88	3.4	
	0.05	5	91	3.5	m/z 525→283 (confirmation)
	0.50	5	90	2.6	
oilseed rape (seeds)	0.01	5	80	11	m/z 523→281 (quantification)
	0.10	5	87	2.0	
	0.01	5	83	6.7	m/z 525→283 (confirmation)
	0.10	5	86	2.0	

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
<i>trans-deltamethrin</i>					
strawberry (fruit)	0.01	5	102	2.9	m/z 523→281 (quantification)
	0.10	5	102	2.5	
	0.01	5	102	2.1	m/z 525→283 (confirmation)
	0.10	5	103	2.5	
tomato (fruit)	0.01	5	98	3.9	m/z 523→281 (quantification)
	0.10	5	101	2.3	
	0.01	5	101	3.6	m/z 525→283 (confirmation)
	0.10	5	101	2.4	
lambs lettuce	0.01	5	99	3.6	m/z 523→281 (quantification)
	0.10	5	104	3.2	
	0.01	5	100	5.2	m/z 525→283 (confirmation)
	0.10	5	103	2.6	
green peas	0.01	5	90	2.8	m/z 523→281 (quantification)
	0.10	5	90	3.0	
	0.01	5	90	3.3	m/z 525→283 (confirmation)
	0.10	5	89	2.7	
wheat (straw)	0.05	5	80	6.0	m/z 523→281 (quantification)
	0.50	5	71	5.9	
	0.05	5	80	7.0	m/z 525→283 (confirmation)
	0.50	5	71	8.0	
wheat (grain)	0.01	5	100	3.7	m/z 523→281 (quantification)
	0.10	5	98	3.0	
	0.01	5	102	4.7	m/z 525→283 (confirmation)
	0.10	5	96	4.3	
barley (whole plant)	0.05	5	97	4.4	m/z 523→281 (quantification)
	0.50	5	96	0.9	
	0.05	5	98	6.1	m/z 525→283 (confirmation)
	0.50	5	96	2.0	
oilseed rape (seeds)	0.01	5	103	2.8	m/z 523→281 (quantification)
	0.10	5	104	2.2	
	0.01	5	107	3.5	m/z 525→283 (confirmation)
	0.10	5	104	3.4	

Table A 2: Characteristics for the analytical method used for validation of cis-deltamethrin and its isomers trans- and α -(R)- residues in different plant matrices

	<i>cis</i> -Deltamethrin	<i>trans</i> -deltamethrin	α -(R)-deltamethrin
Specificity	mass spectrum is provided in Appendix 4 of the method report blank value < 30 % LOQ)	mass spectrum is provided in Appendix 4 of the method report blank value < 30 % LOQ)	mass spectrum is provided in Appendix 4 of the method report blank value < 30 % LOQ)
Calibration (type, number of data points)	individual calibration data presented in Appendix 1 calibration line equation presented for each MRM number of data points>5 (6) MRM 523→281: R = 0.9996 MRM 525→283: R = 0.9992	individual calibration data presented in Appendix 1 calibration line equation presented for each MRM number of data points>5 (6) MRM 523→281: R = 0.9995 MRM 525→283: R = 0.9990	individual calibration data presented in Appendix 1 calibration line equation presented for each MRM number of data points>5 (6) MRM 523→281: R = 0.9987; 0.9997; 0.9999 with the three internal standards MRM 525→283: R = 0.9987; 0.9990; 0.9999 with the three internal standards
Calibration range	Internal Standard Linearity with one point calibration of the Peak Area Ratio of <i>cis</i> -Deltamethrin (MRM 523→281 and MRM 525→283) and <i>cis</i> - ¹³ C-Deltamethrin (MRM 529→281) in the Concentration Range 1.25-100 ng/mL in HPLC Solvent	Internal Standard Linearity with one point calibration of the Peak Area Ratio of <i>trans</i> -Deltamethrin (MRM 523→281 and MRM 525→283) and <i>cis</i> - ¹³ C-Deltamethrin (MRM 529→281) in the Concentration Range 1.25-100 ng/mL in HPLC Solvent	Internal Standard Linearity with one point calibration of the Peak Area Ratio of <i>a</i> -(R)-Deltamethrin (MRM 523→281 and MRM 525→283) and <i>cis</i> - ¹³ C-Deltamethrin (MRM 529→281) or <i>trans</i> - ¹³ C-Deltamethrin (MRM 529→281) or <i>a</i> -(R)- ¹³ C-Deltamethrin (MRM 529→281) in the Concentration Range 1.25-100 ng/mL in HPLC Solvent
Assessment of matrix effects is presented	yes	yes	yes
Limit of determination/quantification	LOQ = 0.01 mg/kg except in wheat (straw) and barley (whole plant) where LOQ=0.05 mg/kg	LOQ = 0.01 mg/kg except in wheat (straw) and barley (whole plant) where LOQ=0.05 mg/kg	LOQ = 0.01 mg/kg except in wheat (straw) and barley (whole plant) where LOQ=0.05 mg/kg

Conclusion

The data presented demonstrate that the validated method permits the determination of residues of trans-, cis-, α -(R)- deltamethrin in strawberry (fruit), tomato (fruit), lambs lettuce, green peas, wheat (grain), wheat (straw), barley (whole plant) and oilseed rape (seed) with acceptable accuracy, precision and repeatability being fully compliant with current regulatory requirements.

The analytical method was successfully validated. The demands of SANCO guideline 825/00 rev. 7 (17/03/04) and SANCO 3029/99 rev. 4 (11/07/00) were fulfilled.

A 2.1.1.1.2 Method validation in study reports 15-2132, 16-2044

Comments of zRMS:	Full validation data is documented with the method 00855/M004 itself for matrices representing 5 major crop groups, including strawberry (fruit), tomato (fruit), lambs lettuce, green peas, wheat (grain), wheat (straw), barley (whole plant) and oilseed rape (seed). For rape (green material and straw), a full validation (2 controls and 5 repetitions each at two fortification levels) of additional recoveries was done within the course of the study 15-2132. For rape (seed) a full validation (2 controls and 5 repetitions each at two fortification levels) of additional validation recoveries was analyzed within the course of the study 16-
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	<p>2044, because some adaptations to the method 00855/M004 were implemented. The limits of quantitation (LOQ) for deltamethrin and its isomers AE F108569 and AE 0035073 are 0.05 mg/kg for rape (green material) and rape (straw) and 0.01 mg/kg for rape (seed).</p> <p>The individual and average recoveries at each fortification level and overall per matrix were within the range of 70 – 110% for all analytes. The RSD values were below 20%.</p> <p>All method validation data complies with the current guideline requirements for data collection methods. The validation of method 00855/M004 can therefore be considered successful for the additional tested matrices.</p>
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Primary crops:

Reference:	KCP 5.1.2.5/02
Title:	Amendment no. 1: Determination of the residues of BYI 02960 and deltamethrin in/on rape after spray application of deltamethrin & flupyradifurone EC 085 in France (North), Germany and Belgium
Report:	Schulte, G.; 2017; 15-2132; M-578527-02-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations:	yes, see report
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/03
Title:	Determination of the residues of BYI 02960 and deltamethrin in/on rape after spray application of deltamethrin & flupyradifurone EC 085 in Germany, Belgium and northern France
Report:	Kaussmann, M.; Kerkerling, S.; 2018; 16-2044; M-641044-01-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP 860.1500, Crop Field Trial
Deviations:	None
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Full validation data for deltamethrin and its isomers, alpha-*R*-deltamethrin and trans-deltamethrin were documented with the method 00855/M004 itself for matrices representing five major crop groups, including strawberry (fruit), tomato (fruit), lambs lettuce, green peas, wheat (grain), wheat (straw), barley (whole plant) and oilseed rape (seed). In addition, further validation sets (two control samples, 5 repetitions each at two fortification levels) on oilseed rape green material, seed and straw were conducted within the course of the following studies:

Results and discussions

Apparent residues in control samples were below 30% of the LOQ. Mean recoveries per fortification level for both analytes were in a range of 70 – 110 % with RSD < 20%.

Table A 3: Recovery results from method validation for deltamethrin residues using the analytical method 00855/M004

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
cis-deltamethrin					
oilseed rape (seeds)	0.01	5	92	9.7	m/z 523 → 281 (16-2044)
	0.10	5	90	13.2	
oilseed rape (green material)	0.05	5	98	0.9	m/z 523 → 281 (15-2132)
	0.50	5	101	1.0	
	0.05	5	103	2.3	m/z 525 → 283 (15-2132)
	0.50	5	99	3.1	
oilseed rape (straw)	0.05	5	99	2.4	m/z 523 → 281 (15-2132)
	0.50	5	101	1.3	
	0.05	5	101	4.1	m/z 525 → 283 (15-2132)
	0.50	5	102	1.3	
alpha-R-deltamethrin					
oilseed rape (seeds)	0.01	5	89	11.6	m/z 523 → 281 (16-2044)
	0.10	5	86	13.3	
oilseed rape (green material)	0.05	5	96	2.2	m/z 523 → 281 (15-2132)
	0.50	5	97	1.9	
	0.05	5	97	2.6	m/z 525 → 283 (15-2132)
	0.50	5	99	2.7	
oilseed rape (straw)	0.05	5	97	5.2	m/z 523 → 281 (15-2132)
	0.50	5	98	1.6	
	0.05	5	97	6.6	m/z 525 → 283 (15-2132)
	0.50	5	100	2.9	

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
<i>trans-deltamethrin</i>					
oilseed rape (seeds)	0.01	5	89	12.4	m/z 523 → 281 (16-2044)
	0.10	5	93	13.3	
oilseed rape (green material)	0.05	5	95	2.6	m/z 523 → 281 (15-2132)
	0.50	5	101	1.8	
	0.05	5	98	3.7	m/z 525 → 283 (15-2132)
	0.50	5	100	1.3	
oilseed rape (straw)	0.05	5	98	2.2	m/z 523 → 281 (15-2132)
	0.50	5	98	1.3	
	0.05	5	104	5.7	m/z 525 → 283 (15-2132)
	0.50	5	99	1.7	

Conclusion

The method referenced as 00855/M004 was sufficiently validated for the determination of residues of deltamethrin and its isomers, alpha-*R*-deltamethrin and trans-deltamethrin in oilseed rape commodities (seeds, green plant material, straw) with a limit of quantification of 0.05 mg/kg in green material and straw and 0.01 mg/kg in seeds for each analyte.

A 2.1.1.1.3 Extraction efficiency - Cross validation of extraction methods

Comments of zRMS:	Both methods, 00855/M004 and 00086/M089, meet all necessary criteria to sufficiently extract and determine the residues of deltamethrin, <i>cis</i> -deltamethrin, <i>trans</i> -isomer and α - <i>R</i> -isomer of deltamethrin in plant matrices (barley grain, lettuce head, orange fruit and olive fruit). The study is acceptable.
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Reference:	KCP 5.1.2.5/04
Title:	Cross validation of extraction methods for the determination of residues of deltamethrin in plant materials by HPLC-MS/MS
Report:	Schoening, R.; Willmes, J.; 2014; MR-14/012; M-481952-02-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC European Commission Guidance Document for Generating and Reporting Methods of Analysis in Support of Pre-registration data Requirements for Annex II (part A, Section 4) and Annex III (part A, section 5) of directive 91/414, SANCO/3029/99 rev. 4, 11/07/00 Guidance document on residue analytical methods, SANCO/825/00/rev. 8.1, European Commission, Directorate General Health and Consumer Protection 16/11/2010 US EPA Residue Chemistry Test Guideline OCSPP 860.1340: Residue Analytical Method
Deviations:	not specified
GLP/GEP:	no
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The analytical method 00855/M004 ([M-356934-01-1](#)) was developed to determine the residues of parent *cis*-deltamethrin, *trans*-isomer and α -R-isomer of deltamethrin and the multi-residue method 00086/M089 ([M-351076-01-1](#)) derived from DFG S19 was developed to determine the residues of parent *cis*-deltamethrin in plant matrices. The objective of this study was to investigate the extraction efficiency of these two methods in comparison to the methods used in the metabolism studies.

For comparison of the extraction efficiency:

- Incurred residues of deltamethrin from barley grain, lettuce head, orange fruit and olive fruit samples from residue trials conducted in 2010 and 2011 were extracted according to the methods 00855/M004 and 00086/M089, as well as according to the procedure used during the metabolism studies 305W-1 ([M-149515-01-1](#)), 89-0090 & HLA 6187-110 ([M-149567-01-1](#)) and 306W-1 ([M-149571-01-1](#)). All thus obtained extracts were measured using the same approach as in the method 00855/M004.

Comparison of the residue levels of *cis*-deltamethrin, *trans*-isomer of deltamethrin and α -R-isomer of deltamethrin determined after extraction according to the methods 00855/M004 and 00086/M089 with the residue levels of *cis*-deltamethrin, *trans*-isomer and α -R-isomer of deltamethrin determined after extraction according to the metabolism study 305W-1 ([M-149515-01-1](#)), 89-0090 & HLA 6187-110 ([M-149567-01-1](#)) and 306W-1 ([M-149571-01-1](#)) provided the extraction efficiency of the methods 00855/M004 and 00086/M089.

Extraction

Barley, lettuce, orange and olive samples were extracted according to the methods 00855/M004 ([M-356934-01-1](#)) and 00086/M089 ([M-351076-01-1](#)), as well as according to the procedure used during the metabolism studies 305W-1 ([M-149515-01-1](#)), 89-0090 & HLA 6187-110 ([M-149567-01-1](#)) and 306W-1 ([M-149571-01-1](#)). All thus obtained extracts were measured using the same approach as in method 00855/M004.

- The lettuce head and orange fruit samples were extracted once with methanol/water (1/1, v/v) and twice with methanol as described in the metabolism study 305W-1 ([M-149515-01-1](#)).
- The olive fruit samples were extracted three times with hexane, three times with CHCl₃/methanol (1/3, v/v) and three times with methanol/water (8/3, v/v) as described in the metabolism study 89-0090 & HLA 6187-110 ([M-149567-01-1](#)).

- The barley grain samples were extracted three times with methanol, twice with methanol/water (1/2, v/v) and twice with water as described in the metabolism study 306W-1 ([M-149571-01-1](#)).
 - In method 00855/M004 the samples of barley grain, lettuce head and orange fruit were extracted with a mixture of acetone/dichloromethane/n-hexane (1/1/1, v/v/v). Olive fruit samples were extracted with acetone/dichloromethane/n-hexane (1/1/1, v/v/v), evaporated to dryness, re-dissolved in acetonitrile and afterwards stirred against hexane.
 - In method 00086/M089 ([M-351076-01-1](#)) the extraction was carried out with acetone/water (2/1, v/v) followed by stirring with ethyl acetate/cyclohexane (1/1, v/v).
- The extracts obtained using each of the four procedures were measured using the same approach as in method 00855/M004.

Results and discussions

During the analysis of the samples coming out of the residue trials concurrent recoveries were performed. All results of the concurrent recoveries were acceptable for the purpose of the current study.

Each sample was analysed three times using each extraction procedure.

For each analyte, the extraction efficiency of the methods 00855/M004 and 00086/M89 is calculated as the ratio (expressed as percentage) between the average residues measured after extracting the samples according to these procedures and the average residues measured using the corresponding procedure of the metabolism studies. Either studies 305W-1 ([M-149515-01-1](#)) for lettuce and orange samples, or 89-0090 & HLA 6187-110 ([M-149567-01-1](#)) for olive samples and or 306W-1 ([M-149571-01-1](#)) for barley grain.

It was noticed that for barley grain samples, the extracts resulting of the metabolism procedures presented content **in trans-isomer**. For lettuce head samples and olive fruit samples, the extracts resulting of the metabolism procedures presented content **in α -R-isomer**. It is very unlikely that the metabolism extraction procedures are able to extract these isomers and not the residue extraction procedure. It seems more probably that due to the length and complexity of the metabolism extraction procedure isomerization of the cis-deltamethrin into trans-isomer and α -R-isomer has occurred in some extent.

Based on this hypothesis a second extraction efficiency calculation was performed, using the sum of cis-deltamethrin and trans-isomer or cis-deltamethrin and α -R-isomer observed after extraction according to the metabolism conditions. This second calculation is mentioned at the bottom of Table 1, Table 3 and Table 4 provided in document [M-481952-02-1](#).

No residues above the LOQ were found in the control samples.

For the all samples results were not corrected for concurrent recoveries.

Table A 4: Residue Levels and Extraction Efficiency for cis-deltamethrin and its isomers α -R-deltamethrin and trans-deltamethrin in Barley Grain

Analyte	Sample 10-2032-04	Mean residue levels [mg/kg] Extraction Efficiency [%]		
		Metabolism conditions (306W-1)	Method 00855/M004	Method 00086/M089
cis-deltamethrin	0011E	0.086 mg/kg 100%	0.085 mg/kg 99%	0.069 mg/kg 80%
trans-isomer		0.015 mg/kg 100%	-- mg/kg -- %	-- mg/kg -- %
α -R-isomer		-- mg/kg -- %	-- mg/kg -- %	-- mg/kg -- %
cis-deltamethrin + trans-isomer		0.101 mg/kg 100%	0.085 mg/kg 84%	0.069 mg/kg 68%

Note : The extraction efficiency of the methods 00855/M004 and 00086/M089 is calculated as the ratio (expressed as percentage) between the average residues measured using these extraction procedures and the average residues measured using the extraction procedure of the metabolism study 306W-1 ([M-149571-01-1](#)).

Table A 5: Residue Levels and Extraction Efficiency for cis-deltamethrin and its isomers α -R-deltamethrin and trans-deltamethrin in Orange Fruit

Analyte	Sample 10-2302	Mean residue levels [mg/kg] Extraction Efficiency [%]		
		Metabolism conditions (305W-1)	Method 00855/M004	Method 00086/M089
cis-deltamethrin	110024893	0.028 mg/kg 100%	0.027 mg/kg 95%	0.030 mg/kg 106%
	100215479	0.029 mg/kg 100%	0.026 mg/kg 89%	0.030 mg/kg 104%
trans-isomer	110024893	-- mg/kg -- %	-- mg/kg -- %	-- mg/kg -- %
	100215479	-- mg/kg -- %	-- mg/kg -- %	-- mg/kg -- %
α phs-R-isomer	110024893	-- mg/kg -- %	-- mg/kg -- %	-- mg/kg -- %
	100215479	-- mg/kg -- %	-- mg/kg -- %	-- mg/kg -- %

Note : The extraction efficiency of the methods 00855/M004 and 00086/M089 is calculated as the ratio (expressed as percentage) between the average residues measured using these extraction procedures and the average residues measured using the extraction procedure of the metabolism study 305W-1 ([M-149515-01-1](#)).

Table A 6: Residue Levels and Extraction Efficiency for cis-deltamethrin and its isomers α -R-deltamethrin and trans-deltamethrin in Olive Fruit.

Analyte	Sample S10-00015	Mean residue levels [mg/kg] Extraction Efficiency [%]		
		Metabolism conditions (89-0090 & HLA 6187-110)	Method 00855/M004	Method 00086/M089
cis-deltamethrin	03-002A	0.410 mg/kg 100%	0.466 mg/kg 114%	0.520 mg/kg 126%
	04-002A	0.414 mg/kg 100%	0.540 mg/kg 131%	0.612 mg/kg 149%
trans-isomer	03-002A	-- mg/kg -- %	-- mg/kg -- %	-- mg/kg -- %
	04-002A	-- mg/kg -- %	-- mg/kg -- %	-- mg/kg -- %
α phs-R-isomer	03-002A	-- mg/kg -- %	-- mg/kg -- %	-- mg/kg -- %
	04-002A	0.017 mg/kg 100%	-- mg/kg -- %	-- mg/kg -- %
cis-deltamethrin + α phs-R-isomer	03-002A	0.410 mg/kg 100%	0.466 mg/kg 114%	0.520 mg/kg 126%
	04-002A	0.431 mg/kg 100%	0.540 mg/kg 126%	0.612 mg/kg 143%

Note : The extraction efficiency of the methods 00855/M004 and 00086/M089 is calculated as the ratio (expressed as percentage) between the average residues measured using these extraction procedures and the average residues measured using the extraction procedure of the metabolism study 89-0090 & HLA 6187-110 ([M-149567-01-1](#)).

Table A 7: Residue Levels and Extraction Efficiency for *cis*-deltamethrin and its isomers α -*R*-deltamethrin and *trans*-deltamethrin in Lettuce Head.

Analyte	Sample 11-2052	Mean residue levels [mg/kg] Extraction Efficiency [%]		
		Metabolism conditions (305W-1)	Method 00855/M004	Method 00086/M089
<i>cis</i> -deltamethrin	01-0016E	0.275 mg/kg 100%	0.316 mg/kg 122%	0.328 mg/kg 124%
	02-0010E	0.426 mg/kg 100%	0.528 mg/kg 127%	0.594 mg/kg 143%
<i>trans</i> -isomer	01-0015E	-- mg/kg -- %	-- mg/kg -- %	-- mg/kg -- %
	02-0010E	-- mg/kg -- %	-- mg/kg -- %	-- mg/kg -- %
α - <i>R</i> -isomer	01-0015E	0.054 mg/kg 100%	-- mg/kg -- %	-- mg/kg -- %
	02-0010E	0.083 mg/kg 100%	-- mg/kg -- %	-- mg/kg -- %
<i>cis</i> -deltamethrin + α - <i>R</i> -isomer	01-0016E	0.329 mg/kg 100%	0.316 mg/kg 103%	0.328 mg/kg 105%
	02-0010E	0.509 mg/kg 100%	0.528 mg/kg 106%	0.594 mg/kg 120%

Note : The extraction efficiency of the methods 00855/M004 and 00086/M089 is calculated as the ratio (expressed as percentage) between the average residues measured using these extraction procedures and the average residues measured using the extraction procedure of the metabolism study 305W-1 ([M-149515-01-1](#)).

Conclusion

The methods 00855/M004 and 00086/M089 meet all necessary criteria to sufficiently extract and determine the residues of *cis*-deltamethrin, *trans*-isomer and α -*R*-isomer of deltamethrin in plant matrices.

A 2.1.1.1.2 Analytical method method 2 (01207)

A 2.1.1.1.2.1 Method validation (tomato fruit, wheat green material and dry peas)

Comments of zRMS:	<p>The analytical method BCS 01207 was successfully validated for the determination of residues of deltamethrin and its isomers, α-<i>R</i>-deltamethrin and <i>trans</i>-deltamethrin in tomato fruit, wheat green material and dry peas with a limit of quantification of 0.1 mg/kg.</p> <p>Amendment No. 3 is written to provide additional information for the validation of flupyradifurone</p> <ol style="list-style-type: none"> 1. On request of the sponsor a full scan spectrum and the product ion spectra of flupyradifurone are added to the report. 2. On request of the sponsor the linearity ranges for flupyradifurone are expressed as mass fractions of the original sample in mg/kg and the percentage of the fortification level at the lower and upper level is calculated for the used linearity curves of flupyradifurone. 3. Starting 2017-01-01 the name of the sponsor changed. <p>Accepted.</p>
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Reference:	KCP 5.1.2.5/05
Title:	Amendment no. 3 to final report - 7 days freezer storage stability study with different combinations of a total of 61 analytes (parent and metabolite molecules) and five matrix types (high water / acidic / starch / protein / oil)
Report:	Lakaschus, S.; Gizler, A.; 2017; S13-03307; M-480441-06-1
Authority registration No:	
Guideline(s):	Commission Regulation (EU) No 544/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for active substances US EPA Residue Chemistry Test Guideline OPPTS 860.1380: Storage Stability Data OECD Test Guideline 506, adopted 16 October 2007
Deviations:	see report
GLP/GEP:	yes

Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The data generation method 01207 was validated for the determination of residues of deltamethrin and its isomers, alpha-*R*-deltamethrin and trans-deltamethrin in tomato fruit, wheat green material and dry peas within the storage stability study S13-03307 ([Lakaschus, S.; Gizler, A.; 2017; M-480441-06-1](#)). A full set of validation data was conducted in the different matrices at the spiking level relevant for the storage stability study (0.1 mg/kg).

For the analysis of deltamethrin, the water content of different sample materials was adjusted to 5 g followed by the addition of acetonitrile, leading to a acetonitrile/water ratio of (4/1, v/v) followed by shaking. Thereafter the samples were left to soak under solvent for 15 minutes. After shaking a salt mixture (Mg₂SO₄/NaCl/Na₃ citrate 2 H₂O/Na₂H citrate 6 H₂O) (4/1/1/0.5,w/w/w/w) was added followed by shaking again and centrifugation. A defined aliquot of 1.0 mL of the acetonitrile phase was transferred into a test tube and blown down to dryness in a gentle stream of nitrogen at 40°C. The remainder was dissolved in 1.0 mL of the internal standard in acetonitrile / 10mM ammoniumformate (9/1, v/v). This solution was used for the LC-MS/MS detection.

The MS/MS instrument was operated in the Multiple Reaction Monitoring mode (MRM). One MRM transition was monitored for quantification, m/z 523 → 281, a second one for confirmation, m/z 529 → 283, for all analytes.

Results and discussions

The validation described within the storage stability study S13-03307 using method 01207 was performed on tomato, fruit, wheat, green material, and peas, dried. Mean recoveries were within the 70 - 110% range. The RSD values were well below 20%. The results are summarized in the table below.

Table A 8: Recovery results from method validation of deltamethrin residues using the analytical method 01207

Matrix	Fortification level (mg/kg)	Single recoveries (%)	n	Mean recovery (%)	RSD (%)	Comments
<i>cis-deltamethrin</i>						
Tomato, fruit	0.1	93; 93; 96; 95; 93	5	94	1.5	m/z 523 → 281
	0.1	94; 90; 93; 91; 94	5	92	2.0	m/z 529 → 283
Wheat, green material	0.1	84; 80; 85; 89; 92	5	86	5.4	m/z 523 → 281
	0.1	85; 80; 85; 88; 87	5	85	3.6	m/z 525 → 283
Peas, dried	0.04	85; 87; 85; 77; 83	5	83	4.6	m/z 523 → 281
	0.04	87; 85; 83; 77; 81	5	83	4.7	m/z 529 → 283
<i>alpha-R-deltamethrin</i>						
Tomato, fruit	0.1	97; 93; 94; 94; 95	5	95	1.6	m/z 523 → 281
	0.1	96; 96; 97; 98; 91	5	96	2.8	m/z 529 → 283
Wheat, green material	0.1	84; 86; 90; 92; 93	5	89	4.4	m/z 523 → 281
	0.1	84; 86; 89; 91; 89	5	88	3.2	m/z 525 → 283
Peas, dried	0.04	85; 83; 85; 79; 84	5	83	3.0	m/z 523 → 281
	0.04	87; 85; 83; 78; 83	5	83	4.0	m/z 529 → 283
<i>trans-deltamethrin</i>						
Tomato, fruit	0.1	91; 99; 99; 99; 91	5	96	4.6	m/z 523 → 281
	0.1	94; 103; 98; 99; 94	5	98	3.9	m/z 529 → 283
Wheat, green material	0.1	85; 84; 89; 90; 94	5	88	4.6	m/z 523 → 281
	0.1	83; 86; 89; 91; 96	5	89	5.6	m/z 525 → 283
Peas, dried	0.04	85; 85; 88; 78; 85	5	84	4.4	m/z 523 → 281
	0.04	84; 81; 81; 76; 86	5	82	4.6	m/z 529 → 283

Table A 9: Characteristics for the analytical method used for validation of residues in different plant commodities

	Deltamethrin	alpha-R-deltamethrin	trans-deltamethrin
Specificity	blank value < 30% of fortification level of 0.1 mg/kg mass spectra are presented within the report S13-03307		
Calibration (type, number of data points)	1/x weighted linear regression individual calibration data and calibration line equation presented; number of data points ≥ 5 ; $r \geq 0.99$		
Calibration range	Accepted calibration range in concentration units : Tomato fruit, wheat green material: 2.5-100µg/L corresponding calibration range in mass ratio units for the sample: 0.01-0.4 mg/kg Dry peas: 1.0-20 µg/L corresponding calibration range in mass ratio units for the sample: 0.004-0.08 mg/kg	Accepted calibration range in concentration units : Tomato fruit, wheat green material: 2.5-100µg/L corresponding calibration range in mass ratio units for the sample: 0.01-0.4 mg/kg Dry peas: 1.0-20 µg/L corresponding calibration range in mass ratio units for the sample: 0.004-0.08 mg/kg	Accepted calibration range in concentration units : Tomato fruit, wheat green material: 2.5-100µg/L corresponding calibration range in mass ratio units for the sample: 0.01-0.4 mg/kg Dry peas: 1.0-20 µg/L corresponding calibration range in mass ratio units for the sample: 0.004-0.08 mg/kg
Assessment of matrix effects is presented	Matrix effects are compensated by using matrix-matched standards		
Limit of quantification	LOQ: 0.1 mg/kg	LOQ: 0.1 mg/kg	LOQ: 0.1 mg/kg

Conclusion

The data collection method 01207 (based on QuEChERS) meets all necessary performance requirements to determine residues of deltamethrin and its isomers alpha-R-deltamethrin and trans-deltamethrin in tomato fruit, wheat, green material and dry peas (pulses) with a limit of quantification of 0.1 mg/kg (spiking level of the study).

A 2.1.1.2 Description of analytical methods for the determination of residues in animal matrices (KCP 5.1)

A 2.1.1.2.1 Analytical method 01127 for the determination of deltamethrin in blood

A 2.1.1.2.1.1 Method validation

Comments of zRMS:	See point A 2.1.2.3.
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Reference:	KCP 5.1.2.5/06
Title:	Analytical method 01127 for the determination of cyfluthrin and deltamethrin in blood by HPLC-MS/MS
Report:	Krebber, R.; 2009; MR-08/176; M-348630-01-1
Authority registration No:	
Guideline(s):	SANCO/825/00 rev. 7 of March 17, 2004; BBA Guideline: Residue Analytical Methods for Post-Registration Control Purposes of July 21, 1998; EU: 96/46/EC amending Council Directive 91/414/EEC of 16 July 1996
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Please refer to section A 2.1.2.3.1 for the respective summary of this method as this method was used in

support of pre- as well as post-authorization method.

A 2.1.1.3 Description of analytical methods for the determination of residues in support to environmental fate studies (KCP 5.1)

A 2.1.1.3.1 Analytical method 00877 (including amendment) for the determination of deltamethrin (cis-deltamethrin) and its isomers alpha-R-deltamethrin and trans-deltamethrin in soil and sediment

A 2.1.1.3.1.1 Method validation

Comments of zRMS:	See point 2.1.2.4.1
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Please refer to section A 2.1.2.4.1 for the respective summary of this method as this method was used in support of pre- as well as post-authorization method.

Reference:	KCP 5.1.2.1/01
Title:	Analytical method 00877 for the determination of total residues of deltamethrin (AE F032640) in / on soil and sediment by HPLC-MS/MS
Report:	Brumhard, B.: 2005; C047210; M-247896-01-1
Authority registration No:	
Guideline(s):	--
Deviations:	--
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.1/02
Title:	Analytical method 00877 for the determination of total residues of Deltamethrin (AE F032640) in/on soil and sediment by HPLC-MS/MS
Report:	Brumhard, B.: 2009; 00877; M-246580-02-1
Authority registration No:	
Guideline(s):	EC Guidance Document on Residue Analytical Methods, SANCO/825/00 rev.7 of March 17,2004 BBA Guideline: Residue Analytical Methods for Post-Registration Control Purposes of July 21, 1998 Commission Directive 96/46/EC amending Council Directive 91/414/EEC of 16 July 1996 US EPA OPPTS 835.6100, 835.6200
Deviations:	With the exception of recognised differences that exist between the GLP principles/standards of OECD and those FIFRA and JMAFF (for instance, authority granted agency inspectors).
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

A 2.1.1.3.2 Analytical method 01358 for the determination of cis-deltamethrin residues in/on soil/sediment

A 2.1.1.3.2.1 Method validation

Comments of zRMS:	See point A 2.1.2.4.2
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Reference:	KCP 5.1.2.1/03
Title:	Analytical method 01358 for the determination of cis-deltamethrin in soil by HPLC-MS/MS
Report:	Freitag, T.; 2013; MR-13/002; M-451547-01-1
Authority registration No:	
Guideline(s):	<p>Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC</p> <p>European Commission Guidance Document for Generating and Reporting Methods of Analysis in Support of Pre-Registration data Requirements for Annex II (part A, Section 4) and Annex III (part A, section 5) of directive 91/414, SANCO/3029/99 rev. 4, 11/07/00</p> <p>Guidance document on residue analytical methods, SANCO/825/00/rev. 8.1, European Commission, Directorate General Health and Consumer Protection 16/11/2010</p> <p>US EPA Residue Chemistry Test Guideline OCSPP 860.1340: Residue Analytical Method</p>
Deviations:	not applicable
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Please refer to section [A 2.1.2.4.2](#) for the respective summary of this method as this method was used in support of pre- as well as post-authorization method.

A 2.1.1.3.3 Analytical method 01383 for the determination of cis-deltamethrin residues in drinking and surface water and ILV

A 2.1.1.3.3.1 Method validation

Comments of zRMS:	See point A 2.1.2.5.1.
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Reference:	KCP 5.1.2.1/04
Title:	Analytical method 01383 for the determination of deltamethrin in drinking and surface water by HPLC-MS/MS
Report:	Krebber, R.; Braune, M.; 2013; MR-13/053; M-464818-01-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC • EC Guidance Document on Residue Analytical Methods, SANCO/825/00 rev. 8.1 of November 16, 2010 • European Commission Guidance Document for Generating and Reporting Methods of Analysis in Support of Pre-Registration data Requirements for Annex II (part A, Section 4) and Annex III (part A, section 5) of directive 91/414, SANCO/3029/99 rev. 4, July 11, 2000
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.1/05
Title:	Independent laboratory validation of BCS analytical method no. 01383 for the determination of deltamethrin in surface water, using LC/MS/MS
Report:	Stanislawski, T.; 2013; P 3021 G; M-471762-01-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC European Commission Guidance Document for Generating and Reporting Methods of Analysis in Support of Pre-Registration data Requirements for Annex II (part A, Section 4) and Annex III (part A, section 5) of directive 91/414, SANCO/3029/99 rev. 4, 11/07/00 Guidance document on Pesticide Residue Analytical Methods, SANCO/825/00/rev. 8.1, European Commission, Directorate General Health and Consumer Protection 16/11/2010 Commission Regulation (EU) No. 283/2013 of 1 March 2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market.
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Please refer to section [A 2.1.2.5.1](#) for the respective summary of this method as this method was used in support of pre- as well as post-authorization method.

A 2.1.1.3.4 Analytical method 00886 for the determination of deltamethrin (cis-deltamethrin) and its isomers alpha-R-deltamethrin and trans-deltamethrin in surface water

A 2.1.1.3.4.1 Method validation

Comments of zRMS:	See comments in point A 2.1.2.5.2
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Reference:	KCP 5.1.2.1/06
Title:	Analytical method 00886 for the determination of total residues of deltamethrin (AE F032640) in surface water by HPLC-MS/MS
Report:	Brumhard, B.; 2005; C047388; M-248040-01-1
Authority registration No:	
Guideline(s):	--
Deviations:	--
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Please refer to section [A 2.1.2.5.2](#) A 2.1.2.5.1 for the respective summary of this method as this method was used in support of pre- as well as post-authorization method.

A 2.1.1.3.5 Analytical method 00886/M001 for the determination of deltamethrin residues in surface water

A 2.1.1.3.5.1 Method validation

Comments of zRMS:	See point A 2.1.2.5.3
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Reference:	KCP 5.1.2.1/07
Title:	Modification M001 of analytical method 00886 for the determination of total residues of deltamethrin (AE F032640) in surface water by HPLC-MS/MS
Report:	Krebber, R.; Braune, M.; 2007; 00886/M001; M-291746-01-1
Authority registration No:	
Guideline(s):	US EPA OPPTS 835.6100, 835.6200
Deviations:	not specified
GLP/GEP:	no
Acceptability:	
Duplication (if vertebrate study):	

Please refer to section [A 2.1.2.5.3](#) A 2.1.2.5.1 for the respective summary of this method as this method was used in support of pre- as well as post-authorization method.

A 2.1.1.4 Description of analytical methods for the determination of residues in support to toxicological studies (KCP 5.1)

No analytical methods have been submitted in support to toxicological studies.

A 2.1.1.5 Description of analytical methods for the determination of residues in support of operator, worker, resident and bystander exposure studies (KCP 5.1)

Not relevant. No operator, worker, resident and bystander exposure studies performed.

A 2.1.1.6 Description of analytical methods for the determination of residues in ecotoxicology studies (KCP 5.1)

A 2.1.1.6.1 Analytical method for the determination of AE F 108565 in test water from aquatic toxicity tests

A 2.1.1.6.1.1 Method validation

Comments of zRMS:	<p>Chemical analysis of the freshly prepared and aged (96 hours old) test solutions was performed for the metabolite of deltamethrin - AE F108565 using HPLC/UV. LOD: 0.31 mg/L in the aqueous sample LOQ: 0.51 mg/L in the aqueous sample No calibration curve was presented in the report. The repeatability precision is expressed by a mean CV of duplicate determinations < 20% for all concentration levels. The accuracy is within 80 - 120% recovery with a CV < 20%. The number of recovery replicates is outside the minimum acceptable of five (n ≥5) according to SANCO/3029/99 rev.4. Therefore, it cannot be concluded the method is validated for the determination of the concentration of AE F108565 (metabolite of deltamethrin) in test solutions. <u>Remark:</u> The method is not satisfactorily validated in accordance with SANCO/3029/99 rev. 4. for the determination of AE F108565 in test solution.</p>
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Reference:	KCP 5.1.2.6/01
Title:	Acute toxicity to Oncorhynchus mykiss (rainbow trout) AE F108565 (metabolite of deltamethrin) substance, pure Code: AE F108565 00 1B99 0001
Report:	:2001; C010902; M-199816-01-1
Authority registration No:	
Guideline(s):	OECD No. 203; US-EPA E § 72-1; EUC.1 US EPA OPPTS 850.1075
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	This method does not meet all required guideline criteria (SANCO/3029/99 rev 4).
Duplication (if vertebrate study):	No

Materials and methods

Chemical analysis of the freshly prepared and aged (96 hours old) test solutions was performed for the active ingredient AE F108565 using High Performance Liquid Chromatography with ultraviolet detection (HPLC/UV). The concentrations were analysed prior dilution.

The analytical method was validated during the development with respect to linearity range, selectivity, accuracy and the validity monitored during the study period with respect to LOD (limit of detection), LOQ (limit of quantification), precision and accuracy.

Results and discussions

The results of the method validation are summarized in the tables below.

Table A 10: Recovery results from method validation of AE F108565 using the analytical method

Matrix	Analyte	Fortification level (mg/L) (n = 2)	Mean recovery (%)	RSD (%)	Mean RSD (%)
Water	AE F108565	9.88	97.9	3.2	4.5
		17.78		0.6	
		31.62		1.1	
		55.33		1.2	
		98.80		1.8	

Table A 11: Characteristics for the analytical method used for validation of AE F108565 residues in water

	AE F108565
Specificity	<p>The representative chromatograms show well-resolved peaks for AE F108565. The identity of the determined compound is established by</p>

	cochromatography with the corresponding certified reference item.
Calibration (type, number of data points)	No calibration curve presented in the report.
Calibration range	linear working range of the detector response of 25 µg/L to 1000 µg/L.
Assessment of matrix effects is presented	No permanent interferences of the determined compound with matrix or solvent blanks above the LOQ were identified.
Limit of determination/quantification	LOD: 0.31 mg/L in the aqueous sample LOQ: 0.51 mg/L in the aqueous sample

Conclusion

The validation results and chromatograms demonstrate sufficient reliability of the method for the desired application: The lowest concentration level is above the LOQ and all concentration of the analyte solution prepared for HPLC are within the linearity range. The repeatability precision is sufficient expressed by a mean RSD of duplicate determinations < 20% for all concentration levels. The accuracy is within 80 - 120% recovery with a RSD < 20%. The specificity of the method is sufficient: The chromatograms display no matrix interference > LOQ of the determined compound of which the identity is established by co-chromatography with the corresponding certified reference item.

A 2.1.1.6.2 Analytical method for the determination of deltamethrin, emulsifiable concentrate 100 g/L (AE F032640) in test water from aquatic toxicity tests (fish)

A 2.1.1.6.2.1 Method validation

Comments of zRMS:	Chemical analysis of the freshly prepared and aged (24 hours old) test solutions was performed for deltamethrin using HPLC/UV. LOD: 9.38 µg/L in the aqueous sample LOQ: 15.63 µg/L in the aqueous sample No calibration curve was presented in the report. The repeatability precision is expressed by a mean CV of duplicate determinations < 20% for all concentration levels. The accuracy is within 80 - 120% recovery with a CV < 20%. The number of recovery replicates is outside the minimum acceptable of five (n ≥ 5) according to SANCO/3029/99 rev.4. Therefore, it cannot be concluded the method is validated for the determination of the concentration of deltamethrin in test solutions. <u>Remark:</u> The method is not satisfactorily validated in accordance with SANCO/3029/99 rev. 4. for the determination of deltamethrin in test solution.
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Reference:	KCP 5.1.2.6/02
Title:	Static-renewal acute toxicity to <i>Oncorhynchus mykiss</i> (rainbow trout) Deltamethrin emulsifiable concentrate 100 g/L Code: AE F032640 00 EC11 A308
Report:	: 2000; C007498; M-196047-01-1
Authority registration No:	
Guideline(s):	EU (=EEC): 92/69, C.1; OECD: 203; USEPA (=EPA): E § 72-1
Deviations:	--
GLP/GEP:	yes
Acceptability:	This method does not meet all required guideline criteria (SANCO/3029/99 rev 4).
Duplication (if vertebrate study):	No

Materials and methods

Chemical analysis of the freshly prepared and aged (24 hours old) test solutions was performed for all test concentrations of and above 0.56 µg/L. Samples were taken from the test chambers and analysed for the active ingredient AE F032640 using High Performance Liquid Chromatography with ultraviolet detection (HPLC/UV). The concentrations were analysed prior extraction.

The analytical method was validated during the development with respect to linearity range, selectivity, accuracy and the validity monitored during the study period with respect to LOD (limit of detection), LOQ

(limit of quantification), precision and accuracy.

Results and discussions

The results of the method validation are summarized in the tables below.

Table A 12: Recovery results from method validation of AE F032640 using the analytical method

Matrix	Analyte	Fortification level (mg/L) (<i>n</i> = 2)	Mean recovery (%)	RSD (%)	Mean RSD (%)
Fresch water	AE F032640	58.80	94.1	7.7	6.7
		105.00		9.1	
		189.00		6.2	
		336.00		4.1	
		588.00		5.4	
Aged water	AE F032640	58.80	103.1	10.8	3.8
		105.00		6.4	
		189.00		7.1	
		336.00		4.4	
		588.00		2.9	

Table A 13: Characteristics for the analytical method used for validation of AE F032640 residues in water

	AE F032640
Specificity	The identity of the determined compound is established by cochromatography with the corresponding certified reference item.
Calibration (type, number of data points)	No calibration curve presented in the report.
Calibration range	linear working range of the detector response from 0 to 2150 µg/L
Assessment of matrix effects is presented	Deviations on the results of the individual test concentrations analysis occurred due to strong matrix effects on the Chromatography by disturbing the peak shape as well as by irregularly appearing matrix interferences. Where a blank control signal > LOQ was identified according to the attached table the blank value was subtracted from the corresponding sample values. However, due to the bad peak shape and the irregularly appearing interferences a differentiation between both effects for corresponding peak integration and/or control blank subtraction was difficult in several cases.
Limit of determination/quantification	LOD: 9.38 µg/L in the aqueous sample LOQ: 15.63 µg/L in the aqueous sample

Conclusion

The validation results and chromatograms demonstrate sufficient reliability of the method for the desired application: The lowest concentration level is above the LOQ and all concentration/s of the analyte solution prepared for HPLC are within the linearity range. The repeatability precision is sufficient expressed by a mean RSD of duplicate determinations < 20% for all concentration levels. The accuracy is within 80 - 120% recovery with a RSD < 20%. The specificity of the method is demonstrated by identification of the determined compound by co-chromatography with the corresponding certified reference substance.

A 2.1.1.6.3 Analytical method 01306 for the determination of deltamethrin and two metabolites in sediment

A 2.1.1.6.3.1 Method validation

Comments of zRMS:	<p>The analytical method 01306 was validated for the determination of deltamethrin and its metabolites, α-R-deltamethrin and trans-deltamethrin in sediment by HPLC-MS/MS.</p> <p>The limit of quantitation (LOQ) for each single analyte is 0.2 µg/kg in soil. The limit of determination (LOD) for each single analyte is 0.07 µg/kg.</p> <p>Mean recoveries for each fortification level and the overall mean recovery were within the 70 - 110% range. Relative standard deviations were below 20% for all analyte in sediment. Only one MRM transition was monitored for deltamethrin and its metabolites, α-R-deltamethrin and trans-deltamethrin, m/z 523 → 281 for quantitation. According to the SANCO/825/00, rev.8.1 confirmatory method is required to demonstrate the selectivity of the primary method for all representative sample matrices.</p> <p>The method has been satisfactorily validated in accordance with SANCO 3029/99/rev.4.</p> <p>The study is acceptable.</p>
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Reference:	KCP 5.1.2.6/03
Title:	Analytical method 01306 for the determination of deltamethrin and the metabolites α -R-deltamethrin and trans-deltamethrin in sediment by HPLC-MS/MS
Report:	Freitag, T.; Koch, V.; 2011; MR-10/154; M-418179-01-1
Authority registration No:	
Guideline(s):	EU Council Directive 91/414/EEC amended by Commission Directive 96/68/EC European Commission Guidance Document for Generating and Reporting Methods of Analysis in Support of Pre-Registration data Requirements for Annex II (part A, Section 4) and Annex III (part A, section 5) of directive 91/414, SANCO/3029/99 Guidance document on residue analytical methods; SANCO/825/00 rev. 7, European Commission, Directorate General Health and Consumer Protection, 2004-03-17 US EPA Residue Chemistry Test Guideline OPPTS 860.1340: Residue Analytical Method
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The method 01306 describes the determination of deltamethrin and the metabolites α -R-deltamethrin and trans-deltamethrin in sediment by HPLC-MS/MS.

Sediment samples are extracted by shaking with a mixture of acetone/formic acid (100+1, v+v). Possible matrix effects of deltamethrin and its metabolites, α -R-deltamethrin and trans-deltamethrin are eliminated by using an internal standard solution of isotopically labeled reference items. This solution is added to the sample solutions after extraction. Then a subsample is filtrated to remove fine particles of the soil. Identification and quantitation of the test items is done by high performance liquid chromatography using MS/MS detection in the Multiple Reaction Monitoring mode.

This method (01306) was used in support of the ecotoxicological study listed below:

- “*Chironomus riparius* 28-day chronic toxicity test with deltamethrin (tech.) in a water-sediment system using spiked sediment”; Bruns, E.; 2012; Report No: EBDAL036; [M-425202-01-1](#)

Results and discussions

The results of the method validation are summarized in the tables below.

Table A 14: Recovery results from method validation of deltamethrin and the isomers α -R-deltamethrin and trans-deltamethrin using the analytical method 01306

Matrix	Analyte	Fortification level [µg/kg]	Mean recovery [%]	RSD [%]	<i>n</i>	Overall mean recovery [%]	Overall RSD [%]
Sediment	Deltamethrin	0.2	100	8.6	5	100	6.2
		2	100	3.6	5		
		0.2	86	15.4	5	93	12.8

	α -R-Deltamethrin	2	99	5.8	5		
	trans-Deltamethrin	0.2	96	11.4	5	97	8.0
		2	98	3.7	5		

Table A 15: Characteristics for the analytical method used for validation of cis-deltamethrin and the isomers α -R-deltamethrin and trans-deltamethrin residues in sediment

	deltamethrin and the metabolites α -R-deltamethrin and trans-deltamethrin
Specificity	The high selectivity of the method resulted from the HPLC peak retention time in combination with MS/MS detection using two characteristic mass transitions to monitor the analyte: one transition for quantitation and one transition for qualitative confirmation: m/z 298 \rightarrow 144 (quantitation) m/z 298 \rightarrow 100 (confirmation) One MRM transitions were monitored for deltamethrin and its metabolites, α -R-deltamethrin and trans-deltamethrin, m/z 523 \rightarrow 281 for quantitation.
Calibration (type, number of data points)	Individual calibration data in solvent is provided in the study report. Quadratic regression: y = -1.779*10 ⁻⁵ x ² + 0.102 x + 0.00057 (deltamethrin) y = -1.462*10 ⁻⁵ x ² + 0.118 x + 0.00555 (α -R-deltamethrin) y = -9.076*10 ⁻⁶ x ² + 0.107 x + 0.00066 (trans-deltamethrin) Correlation coefficient r 0.9999 (1/x weighted, deltamethrin) 0.9994 (1/x weighted, α -R-deltamethrin) 0.9996 (1/x weighted, trans-deltamethrin) 7 concentrations were measured.
Calibration range	0.2 – 200 µg/L (solvent standards)
Assessment of matrix effects is presented	Apparent residues in control samples were below 0.3 × LOQ. The HPLC-MS/MS method is highly specific and an additional confirmatory method is not necessary.
Limit of determination/quantification	LOD: 0.07 µg/kg for each single analyte LOQ: 0.2 µg/kg for each single analyte

Conclusion

In conclusion, the results show that the assay method presented above is satisfactory for the determination of deltamethrin and its metabolites, α -R-deltamethrin and trans-deltamethrin in sediment at the indicated concentration range between 0.2 – 2 µg/kg.

Concurrent validation parameter from the respective study reports

Comments of zRMS:	Acceptable.
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Reference:	KCP 5.1.2.6/04
Title:	Chironomus riparius 28-day chronic toxicity test with deltamethrin (tech.) in a water-sediment system using spiked sediment
Report:	Bruns, E.; 2012; EBDAL036; M-425202-01-1
Authority registration No:	
Guideline(s):	OECD Guideline 218: Sediment-Water Chironomid Toxicity Test Using Spiked Sediment (adopted 13 April 2004)
Deviations:	none
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Bruns, E.; 2012; [M-425202-01-1](#), Appendix A of the report

Recovery experiments were conducted concurrently with the analysis of the samples. They were performed

to verify the integrity of the analysed residues. These concurrent recoveries were performed with control soil Höfchen.

Table A 16: Concurrent recovery rates of deltamethrin and the metabolites α -R-deltamethrin and trans-deltamethrin (analysis in soil samples) using the analytical method 01306

Matrix	Analyte	Fortification level [$\mu\text{g/kg}$]	Mean recovery [%]	RSD [%]	<i>n</i>	Overall mean recovery [%]	Overall RSD [%]
Soil	deltamethrin	0.2	90	26.3*	4	98	16.9
		2	94	13.1	4		
		100	109	2.5	4		
	trans-deltamethrin	0.2	98	11.2	5	96	12.0
		2	89	17.6	5		
		100	102	2.0	5		
	α -R - deltamethrin	0.2	84	16.6	5	95	15.2
		2	89	2.8	5		
		100	111	4.9			

*: RSD above 20% will be accepted, the overall Mean is acceptable.

A 2.1.1.6.4 Analytical method 01307 for the determination of cis-deltamethrin and its isomers in test water

A 2.1.1.6.4.1 Method validation

Comments of zRMS:	<p>The analytical method 01307 was validated for the determination of deltamethrin and its metabolites, α-R-deltamethrin and trans-deltamethrin in test water from aquatic toxicity tests by HPLC-MS/MS.</p> <p>The limit of quantitation (LOQ) for deltamethrin, α-R-isomer of deltamethrin and trans-isomer of deltamethrin is 0.125 $\mu\text{g/L}$ and the limit of detection (LOD) is 0.0625 $\mu\text{g/L}$.</p> <p>Mean recoveries for each fortification level and the overall mean recovery were within the 70 - 110% range. Relative standard deviations were below 20% for all analyte in test water samples.</p> <p>Only one MRM transition was monitored for deltamethrin and its metabolites, α-R-deltamethrin and trans-deltamethrin, m/z 523 \rightarrow 281 for quantitation. According to the SANCO/825/00, rev.8.1 confirmatory method is required to demonstrate the selectivity of the primary method for all representative sample matrices.</p> <p>This method has been satisfactorily validated in accordance with SANCO 3029/99/rev.4.</p> <p>The study is acceptable.</p>
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Reference:	KCP 5.1.2.6/05
Title:	Method 01307 for the determination of deltamethrin, α -R-isomer of deltamethrin and trans-isomer of deltamethrin in test water from aquatic toxicity tests by HPLC-MS/MS
Report:	Braune, M.; 2011; 01307; M-410093-01-1
Authority registration No:	
Guideline(s):	not specified
Deviations:	not specified
GLP/GEP:	no
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The method 01307 describes the determination of deltamethrin, α -R-isomer of deltamethrin and trans-isomer of deltamethrin in test water from aquatic toxicity tests by HPLC-MS/MS and provides validation data for test water for Multiple Reaction Monitoring (MRM) transition using electrospray ionisation in the positive mode.

The water samples are analysed after addition of acetonitrile and formic acid by direct injection into an HPLC-MS/MS instrument. For quantitation the MRM transition m/z 523 to m/z 281 is monitored for deltamethrin, α -R-isomer of deltamethrin and trans-isomer of deltamethrin.

This method (01307) was used in support of the ecotoxicological study listed below:

- “*Chironomus riparius* 28-day chronic toxicity test with deltamethrin (tech.) in a water-sediment system using spiked sediment”; Bruns, E.; 2012; Report No: EBDAL036; [M-425202-01-1](#)

Results and discussions

As the water samples were analysed by direct injection into the HPLC-MS/MS system recovery data cannot be calculated as stated in the guidance document on pesticide residue analytical methods (SANCO/825/00 rev.8.1).

Because of the direct measurement of fortified samples without separate extraction and clean-up steps it is not possible to determine recovery rates and an estimate of the accuracy of the analytical technique was made by an assessment of the linearity of calibration and by determination of the reproducibility of sample analysis.

The repeatability for cis-deltamethrin, α -R- deltamethrin and trans-deltamethrin was determined based on 8 - 10 injections of a standard solution of 0.125 μ g/L and 8 - 10 injections of a standard solution of 1.25 μ g/L in test water/ acetonitrile/ formic acid.

The results of the method validation are summarized in the tables below.

Table A 17: Method validation of cis-deltamethrin and the isomers α -R-deltamethrin and trans-deltamethrin using the analytical method 01307

Sample concentration [µg/L]	Peak area [area counts]						Retention time		
	Single values				Mean	RSD [%]	Mean [min]	RSD [%]	
<i>deltamethrin</i>									
0.125	4703	4778	5260	5414	5031	5.4	9.27	0.2	
	5219	5150	4994	4732					
1.25	43710	45456	45711	47378	46439	4.8	9.24	0.4	
	49548	47264	48964	43479					
<i>α-R deltamethrin</i>									
0.125	6715	6526	6947	6873	7283	6979	4.2	9.64	0.2
	7447	6889	7344	6774	6994				
1.25	62650	59279	60692	63417		60942	6.1	9.60	0.5
	64020	62618	62310	52549					
<i>trans-deltamethrin</i>									
0.125	2182	2067	2331	2159	2463	2258	6.4	9.06	0.2
	2483	2360	2258	2131	2143				
1.25	22074	22719	22900	23688		22978	5.4	9.03	0.4
	24569	23554	23751	20565					

Table A 18: Characteristics for the analytical method used for validation of cis-deltamethrin and the isomers α -R-deltamethrin and trans-deltamethrin residues in sediment

	cis-deltamethrin and the isomers α -R-deltamethrin and trans-deltamethrin
Specificity	The high selectivity of the method resulted from the HPLC separation in combination with MS/MS detection.
Calibration (type, number of data points)	Individual calibration data in solvent is provided in the study report. Linear regression: $y = 5.062 \cdot 10^4 x + 532.9$ (deltamethrin) $y = 6.247 \cdot 10^4 x + 1195$ (α -R-isomer of deltamethrin) $y = 2.564 \cdot 10^4 x - 76.21$ (trans-isomer of deltamethrin) Correlation coefficient r 0.99896 (1/x weighted, deltamethrin) 0.99932 (1/x weighted, α -R-isomer of deltamethrin) 0.99870 (1/x weighted, trans-isomer of deltamethrin) ≥ 6 concentrations were measured.

Calibration range	0.0625 – 6.25 µg/L
Assessment of matrix effects is presented	The HPLC-MS/MS method is highly specific and an additional confirmatory method is not necessary.
Limit of determination/quantification	LOD: 0.0625 µg/L for each single analyte LOQ: 0.125 µg/L for each single analyte

Conclusion

In conclusion, the results show that the assay method (01307) presented above is satisfactory for the determination of cis-deltamethrin, and its isomers α -R-deltamethrin and trans-deltamethrin in test water from aquatic toxicity tests.

Concurrent validation parameter from the respective study reports

Comments of zRMS:	Acceptable.
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Bruns, E.; 2012; [M-425202-01-1](#), Appendix B of the report

The method was validated concurrently with the test solution analyses. For this purpose standard injections of cis-deltamethrin and its isomers α -R-deltamethrin and trans-deltamethrin were evaluated.

Table A 19: Method validation of cis-deltamethrin and the isomers α -R-deltamethrin and trans-deltamethrin using the analytical method 01307

Sample concentration [µg/L]	Peak area [area counts]		Retention time	
	Mean	RSD [%]	Mean [min]	RSD [%]
<i>cis-deltamethrin</i>				
0.2035	13296	2.7	10.49	0.3
0.2035	7374	7.1	11.12	6.5
2.035	67323	5.2	10.57	1.0
<i>α-R-deltamethrin</i>				
0.2022	14608	1.3	10.79	0.3
0.2022	8614	8.8	11.40	6.1
2.022	79902	5.6	10.87	1.0
<i>trans-deltamethrin</i>				
0.2007	6371	4.8	10.32	0.3
0.2007	3521	8.7	10.93	6.5
2.007	33866	5.4	10.39	1.0

A 2.1.1.6.5 Analytical method for the determination of AE F108565 in test water from aquatic toxicity tests (Daphnia)

A 2.1.1.6.5.1 Method validation

Comments of zRMS:	<p>Chemical analysis of the freshly prepared and aged (48 hours old) test solution was performed for metabolite of deltamethrin (AE F108565) using HPLC/UV.</p> <p>LOD: 0.05 mg/L in the aqueous sample</p> <p>LOQ: 0.08 mg/L in the aqueous sample</p> <p>No calibration curve was presented in the report.</p> <p>The repeatability precision is expressed by a mean CV of duplicate determinations < 20% for all concentration levels. The accuracy is within 80 - 120% recovery with a CV < 20%.</p> <p>The number of recovery replicates is outside the minimum acceptable of five (n ≥5) according to SANCO/3029/99 rev.4.</p> <p><u>Remark:</u></p> <p>The method is not satisfactorily validated in accordance with SANCO/3029/99 rev. 4. for the determination of metabolite of deltamethrin (AE F108565) in test solution.</p>
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Reference:	KCP 5.1.2.6/06
Title:	Acute toxicity to Daphnia magna (Waterflea) AE F108565 (Metabolite of deltamethrin) substance, pure Code: AE F108565 00 1B99 0001
Report:	; 2001; C010889; M-199793-01-1
Authority registration No:	
Guideline(s):	OECD No. 202; US-EPA E § 72-2 EUC.2; US EPA OPPTS 850.1010
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	This method does not meet all required guideline criteria (SANCO/3029/99 rev 4).
Duplication (if vertebrate study):	

Materials and methods

Chemical analysis of the freshly prepared and aged (48 hours old) test solution was performed for the active ingredient AE F108565 using High Performance Liquid Chromatography with ultraviolet detection (HPLC/UV). The concentrations were analysed prior dilution.

The analytical method was validated during the development with respect to linearity range, selectivity, accuracy and the validity monitored during the study period with respect to LOD (limit of detection), LOQ (limit of quantification), precision and accuracy.

Results and discussions

The results of the method validation are summarized in the tables below.

Table A 20: Recovery results from method validation of AE F108565 using the analytical method

Matrix	Analyte	Fortification level (mg/L) (n = 2)	Mean recovery (%)	RSD (%)	Mean RSD (%)
Water	AE F108565	0.99	94.0	7.4	0.4
		1.78		6.1	
		3.16		2.1	
		5.53		1.1	
		9.88		1.7	
		17.78		2.0	
		31.62		0.4	
		55.83		1.8	
		98.80		1.0	

Table A 21: Characteristics for the analytical method used for validation of AE F108565 residues in water

	AE F108565
Specificity	The representative chromatograms show well-resolved peaks for AE F108565. The identity of the determined compound is established by cochromatography with the corresponding certified reference item.
Calibration (type, number of data points)	No calibration curve presented in the report.
Calibration range	linear working range of the detector response of 25 µg/L to 1000 µg/L.
Assessment of matrix effects is presented	No permanent interferences of the determined compound with matrix or solvent blanks above the LOQ were identified. For the lowest concentration level of 1 mg/L nominal test item, matrixinterferences led to exceeding results (136.9% of the nominal concentration) despite subtraction of the control blank value.
Limit of determination/quantification	LOD: 0.05 mg/L in the aqueous sample LOQ: 0.08 mg/L in the aqueous sample

Conclusion

The validation results and chromatograms demonstrate sufficient reliability of the method for the desired application: The lowest concentration level is above the LOQ and all concentrations of the analyte solution prepared for HPLC are within the linearity range. The repeatability precision is sufficient expressed by a mean RSD of duplicate determinations < 20% for all concentration levels. The accuracy is within 80 - 120% recovery with a RSD < 20%. The specificity of the method is sufficient: The chromatograms display no matrix interference > LOQ of the determined compound except for the lowest concentration level on day 2 and their identity is established by co-chromatography with the corresponding certified reference item.

A 2.1.1.6.6 Analytical method for the determination of deltamethrin, emulsifiable concentrate 100 g/L (AE F032640) in test water from aquatic toxicity tests (Daphnia)

A 2.1.1.6.6.1 Method validation

Comments of zRMS:	<p>Chemical analysis of the freshly prepared and aged (48 hours old) test solutions was performed for deltamethrin using GC/ECD.</p> <p>LOD: 0.7 ng/L in the aqueous sample</p> <p>LOQ: 1.1 ng/L in the aqueous sample</p> <p>Mean recovery: 101.4%, CV = 5.6%</p> <p>No calibration curve was presented in the report.</p> <p>The repeatability precision is expressed by a mean CV of duplicate determinations < 20% for all concentration levels. The accuracy is within 80 - 120% recovery with a CV < 20%.</p> <p>The number of recovery replicates is outside the minimum acceptable of five (n ≥ 5) according to SANCO/3029/99 rev.4.</p> <p><u>Remark:</u></p> <p>The method is not satisfactorily validated in accordance with SANCO/3029/99 rev. 4. for the determination of deltamethrin in test solution.</p>
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Reference:	KCP 5.1.2.6/07
Title:	Acute toxicity to Daphnia magna (waterflea) Deltamethrin emulsifiable concentrate 100 g/L Code: AE F032640 00 EC11 A308
Report:	Sowig, P.; Gosch, H.; Weller, O.; 2000; C006590; M-194240-01-1
Authority registration No:	
Guideline(s):	EU (=EEC): C.2; OECD: No.202; USEPA (=EPA): E § 72-2
Deviations:	--
GLP/GEP:	yes
Acceptability:	This method does not meet all required guideline criteria (SANCO/3029/99 rev 4).
Duplication (if vertebrate study):	

Materials and methods

Chemical analysis of the freshly prepared test solutions was performed for the nominal concentrations and of the aged (48 hours old) test solutions. Samples were taken from the test chambers and analysed for the active ingredient AE F032640 by gas chromatographic determination with ECD detection.

The analytical method was validated during the development with respect to linearity range, selectivity, accuracy and the validity monitored during the study period with respect to LOD (limit of detection), LOQ (limit of quantification), precision and accuracy.

Results and discussions

The results of the method validation are summarized in the tables below.

Table A 22: Recovery results from method validation of AE F032640 using the analytical method

Matrix	Analyte	Fortification level (ng/L) (n = 2)	Mean recovery (%)	RSD (%)	Mean RSD (%)
Water	AE F032640	10.5	101.4	2.1	5.6
		18.9		5.3	
		105.0		1.7	
		588.0		1.9	

Table A 23: Characteristics for the analytical method used for validation of AE F032640 residues in water

	AE F032640
Specificity	An electron capture detector (ECD) is highly sensitive for halogenated compounds, as AE F032640. The identity of the determined compound is established by cochromatography with the corresponding certified reference item.
Calibration (type, number of data points)	No calibration curve presented in the report.

Calibration range	linear working range of the detector response from 1 to 21 µg/L
Assessment of matrix effects is presented	The chromatograms of the control test water show small interferences at the retention time of AE F032640. These interferences however, are not regarded as contamination by the test substance due to the fact that mainly concentrations of the interferences were below the LOD (0.7 ng/L) and the general strong base line noise of the complicated matrix according to the extreme trace level achieved by the highly sensitive ECD detection. No permanent interferences of the determined compound with matrix or solvent blanks above the LOQ were identified.
Limit of determination/quantification	LOD: 0.7 ng/L in the aqueous sample LOQ: 1.1 ng/L in the aqueous sample

Conclusion

The validation results and chromatograms demonstrate sufficient reliability of the method for the desired application: The lowest concentration level is above the LOQ and all concentrations of the analyte solution prepared for GC are within the linearity range. The repeatability precision is sufficient expressed by a mean RSD of duplicate determinations < 20 % for all concentration levels. The accuracy is within 80 - 120 % recovery with a RSD < 20 %. The specificity of the method is sufficient: The chromatograms display no matrix interference > LOQ of the determined compound and their identity is established by cochromatography with the corresponding certified reference substance.

A 2.1.1.6.7 Analytical method for the determination of deltamethrin, emulsifiable concentrate 100 g/L (AE F032640) in test water from aquatic toxicity tests (Algae)

A 2.1.1.6.7.1 Method validation

Comments of zRMS:	Chemical analysis of the freshly prepared and aged (96 hours old) test solutions was performed for deltamethrin using HPLC/UV. LOD: 0.04 mg/L in the aqueous sample LOQ: 0.07 mg/L in the aqueous sample Mean recovery: 95.3%, CV = 1.1% No calibration curve was presented in the report. The repeatability precision is expressed by a mean CV of duplicate determinations < 20% for all concentration levels. The accuracy is within 80 - 120% recovery with a CV < 20%. The number of recovery replicates is outside the minimum acceptable of five (n ≥ 5) according to SANCO/3029/99 rev.4. <u>Remark:</u> The method is not satisfactorily validated in accordance with SANCO/3029/99 rev. 4. for the determination of deltamethrin in test solution.
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Reference:	KCP 5.1.2.6/08
Title:	Algal growth inhibition - Pseudokirchneriella subcapitata Deltamethrin emulsifiable concentrate 100 g/L Code: AE F032640 00 EC11 A308
Report:	Weller, O.; Gosch, H.; Sowig, P.; 2000; C007531; M-196114-01-1
Authority registration No:	
Guideline(s):	OECD: No.201; US-EPA- J§123-2 EU C.3; US EPA OPPTS Guidelines 850.5400
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	This method does not meet all required guideline criteria (SANCO/3029/99 rev 4).
Duplication (if vertebrate study):	

Materials and methods

Chemical analysis of the freshly prepared and aged (96 hours old) test solutions was performed for the active ingredient AE F032640 using High Performance Liquid Chromatography with ultraviolet detection

(HPLC/UV). The concentrations were analysed prior dilution.

The analytical method was validated during the development with respect to linearity range, selectivity, accuracy and the validity monitored during the study period with respect to LOD (limit of detection), LOQ (limit of quantification), precision and accuracy.

Results and discussions

The results of the method validation are summarized in the tables below.

Table A 24: Recovery results from method validation of AE F032640 using the analytical method

Matrix	Analyte	Fortification level (mg/L) (<i>n</i> = 2)	Mean recovery (%)	RSD (%)	Mean RSD (%)
Water	AE F032640	1.05	95.3	4.6	1.1
		3.36		1.4	
		10.50		9.0	

Table A 25: Characteristics for the analytical method used for validation of AE F032640 residues in water

	AE F032640
Specificity	The identity of the determined compound is established by cochromatography with the corresponding certified reference item.
Calibration (type, number of data points)	No calibration curve presented in the report.
Calibration range	linear working range of the detector response from 0 to 2150 µg/L
Assessment of matrix effects is presented	No permanent interferences of the determined compound with matrix or solvent blanks above the LOQ were identified.
Limit of determination/quantification	LOD: 0.04 mg/L in the aqueous sample LOQ: 0.07 mg/L in the aqueous sample

Conclusion

The validation results and chromatograms demonstrate sufficient reliability of the method for the desired application: The lowest concentration level is above the LOQ and all concentrations of the analyte solution prepared for HPLC are within the linearity range. The repeatability precision is sufficient expressed by a mean RSD of duplicate determinations < 20 % for all concentration levels. The accuracy is within 80-120 % recovery with a RSD < 20 %. The specificity of the method is sufficient: The chromatograms display no matrix interference > LOQ of the determined compound and their identity is established by co-chromatography with the corresponding certified reference substance.

A 2.1.1.6.8 Analytical method for the determination of deltamethrin in water

A 2.1.1.6.8.1 Method validation

Comments of zRMS:	Accepted.
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Reference:	KCP 5.1.2.6/09
Title:	Biological effects and fate of deltamethrin EW 015 in outdoor mesocosm ponds
Report:	[REDACTED] ; 2005; HBF/BT 07; M-246137-01-2
Authority registration No:	
Guideline(s):	OECD Guidance Doc. "Freshwater Lentic Field Tests", 2004 (Draft) ; Guidance Doc. on Testing Procedures for Pesticides in Freshwater Microcosms (SETAC 1991) Community-Level Aquatic System Studies Interpretation Criteria (SETAC 2002)
Deviations:	none
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	No

Materials and methods

During the course of both studies the water samples were analysed according to method 00886:

- "Method for the Determination of Deltamethrin in Surface Water by HPLC-MS/MS", Dr. B. Brumhard, Bayer CropScience AG Report No. MR 097/04, 2005; [M-248040-01-1](#).

The method 00886 is already summarized in chapter [A 2.1.2.5.2](#).

Concurrent validation parameter from the respective study report

[REDACTED] 2005; [M-246137-01-1](#)

The limit of quantitation for deltamethrin according to this method is 0.005 µg/L with direct injection of 250 µL of the sample. During the study, the method was validated concurrently with the sample analyses of the study by evaluation of the standard injections.

Table A 26: Method validation for deltamethrin (standard injections)

Concentration [µg/L]	Peak area [area counts]			Retention time	
	n	Mean	RSD [%]	Mean [min]	RSD [%]
0.0059	14	0.036	15.6	1.65	0.6
0.059	14	0.300	3.3	1.68	<0.1
0.59	6	3.410	2.1	1.64	<0.1
0.0059	22	0.036	14.2	1.69	0.6
0.059	22	0.310	6.5	1.69	0.6
0.0059	18	0.080	25.0	1.70	1.2
0.059	18	0.350	5.7	1.73	0.6
0.0059	16	0.033	13.5	1.69	<0.1
0.059	16	0.320	3.1	1.67	0.6
0.0059	12	0.043	7.9	1.72	0.6
0.059	12	0.320	3.1	1.71	0.6
0.0052	13	0.049	8.0	1.71	0.6
0.052	13	0.460	2.2	1.70	0.6

A 2.1.1.6.9 Analytical method 00877 for the determination of deltamethrin in sediment

A 2.1.1.6.9.1 Method validation

Comments of zRMS:	Accepted.
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Reference:	KCP 5.1.2.6/09
Title:	Biological effects and fate of deltamethrin EW 015 in outdoor mesocosm ponds
Report:	: 2005; HBF/BT 07; M-246137-01-2
Authority registration No:	
Guideline(s):	OECD Guidance Doc. "Freshwater Lentic Field Tests", 2004 (Draft) ; Guidance Doc. on Testing Procedures for Pesticides in Freshwater Microcosms (SETAC 1991) Community-Level Aquatic System Studies Interpretation Criteria (SETAC 2002)
Deviations:	none
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	No

Materials and methods

The sediment samples were analysed according to the following method:

- - “Analytical method 00877 for the determination of total residues of deltamethrin (AE F032640) in / on soil and sediment by HPLC-MS/MS”; Brumhard, B.; 2005; [M-247896-01-1](#)

This method is already summarized in chapter [A 2.1.2.4.1](#).

Concurrent validation parameter from the respective study report

The limit of quantitation (LOQ) of the method is 0.1 µg/kg for deltamethrin.

The limit of detection (LOD) of the method is 0.03 µg/kg for deltamethrin.

Recovery experiments were conducted concurrently with the analysis of the samples. They were performed to verify the integrity of the analysed residues. These concurrent recoveries were performed with control sediment of the trial investigated in this study. For evaluation of the recovery experiments the measured residue concentrations in the recovery samples were corrected for the blank value in the respective control sample.

Table A 27: Concurrent recovery rates of deltamethrin during analysis of sediment samples using the analytical method 00877

Matrix	Fortification level (µg/kg)	Single Recovery (%)	Mean Recovery (%)
Control Sediment	0.1	122 / 94.9 / 108 / 99.7 / 104 / 95.6 / 95.0 / 88.3 / 98.0 / 91.4 / 88.6 / 95.0 / 104 / 91.2 / 107 / 88.9 / 82.9 / 102 / 89.4 / 103 / 93.5/91.1	98.0
	1.0	105/108/102/104/103/105/96.2 / 94.1 / 92.8 / 96.4 / 97.1 / 94.1 / 93.0 / 104 / 111 / 92.7 / 102 / 93.9 / 97.5 / 98.3 / 97.3/103/97.0/91.8/95.9	

A 2.1.1.6.10 Analytical method 00877 for the determination of deltamethrin in sediment

A 2.1.1.6.10.1 Method validation

Comments of zRMS:	Accepted.
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Reference:	KCP 5.1.2.6/10
Title:	Analysis of deltamethrin concentrations in sediment samples of ECT study no. P1MA
Report:	Brumhard, B.; Loehrwald, K.H.; 2007; MR-07/297; M-291818-01-1
Authority registration No:	
Guideline(s):	not specified
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The sediment samples were analysed according to the following method:

- - “Analytical method 00877 for the determination of total residues of deltamethrin (AE F032640) in / on soil and sediment by HPLC-MS/MS”; Brumhard, B.; 2005; [M-247896-01-1](#)

This method is already summarized in chapter [A 2.1.2.4.1](#).

Concurrent validation parameter from the respective study report

The limit of quantitation (LOQ) of the method is 0.1 µg/kg for deltamethrin.

The limit of detection (LOD) of the method is 0.03 µg/kg for deltamethrin.

Recovery experiments were conducted concurrently with the analysis of the samples. They were performed to verify the integrity of the analysed residues.

Table A 28: Concurrent recovery rates of deltamethrin during analysis of sediment samples using the analytical method 00877

Matrix	Fortification level (µg/kg)	Single Recovery (%)	Mean Recovery (%) ± RSD (%)
Sediment	0.1	104	106 ± 2.7
		109	
		104	
	1.0	101	100 ± 1.2
		99	
		99	

This method was used in support of the following study:

- - “Amendment No. 1 to the Report: Deltamethrin EW 15 G: Acute and chronic Effects to Different Life Stages of the Isopod *Asellus aquaticus* L. in a Natural Water-Sediment System”; Jergentz, S.; 2007a; Report No.: P1MA; Doc. No.: [M-291885-02-1](#).

A 2.1.1.6.11 Analytical method 00886/M001 for the determination of deltamethrin in water

A 2.1.1.6.11.1 Method validation

Comments of zRMS:	Accepted.
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Reference:	KCP 5.1.2.6/11
Title:	Analysis of deltamethrin concentrations in water samples of ECT study no. P1MA
Report:	Krebber, R.; Braune, M.; 2007; MR-07/295; M-291848-01-1
Authority registration No:	
Guideline(s):	not specified
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

During the course of the study the water samples were analysed according to method 00886/M001:

- “Modification M001 of analytical method 00886 for the determination of total residues of deltamethrin (AE F032640) in surface water by HPLC-MS/MS”, R. Krebber and M. Braune, Bayer CropScience AG Report No. MR-07/296; [M-291746-01-1](#).

This method is already summarized in chapter [A 2.1.2.5.3](#).

Concurrent validation parameter from the respective study report

The analytical method was validated within the present study at fortification levels of 2 and 10 ng/L using the internal standard procedure. The limit of quantitation (LOQ) of the method is 2 ng/L. The limit of detection (LOD) of the method was 0.3 x LOQ for deltamethrin in water. Linearity was determined in the concentration range of 2 to 100 ng/L. The correlation coefficient was 0.9997. 5 concentrations measured.

Table A 29: Method validation for deltamethrin in test water using the analytical method 00886/M001

Sample concentration [ng/L]	Peak area [area counts]			Retention time	
	Single values	Mean	RSD [%]	Mean [min]	RSD [%]
2	0.02137 / 0.02233 / 0.02264 / 0.02148 / 0.02217 / 0.02156 / 0.02109 / 0.02224 / 0.02251 / 0.02195	0.02193	2.4	8.14	0.2
10	0.09592 / 0.096955 / 0.09126 / 0.1002 / 0.09664 / 0.09883 / 0.09467 / 0.09578 / 0.09221 / 0.09051	0.09530	3.3	8.12	0.1

This method was used in support of the following study:

- “Amendment No. 1 to the Report: Deltamethrin EW 15 G: Acute and chronic Effects to Different Life Stages of the Isopod *Asellus aquaticus* L. in a Natural Water-Sediment System”; Jergentz, S.; 2007a; Report No.: P1MA; Doc. No.: [M-291885-02-1](#).

A 2.1.1.6.12 Analytical method 01347 for the determination of deltamethrin residues in/ on bees (insects), flowers/ blossoms, green material, honey/ nectar, pollen and wax

A 2.1.1.6.12.1 Method validation

Comments of zRMS:	<p>The analytical method 01347 was validated for the determination of deltamethrin residues in/on bees (insects), flowers/blossoms, green material, honey/nectar, pollen and wax by HPLC-ESI-MS/MS using stable isotopic labelled internal standards.</p> <p>This method determines the sum of deltamethrin isomers.</p> <p>The limit of quantitation (LOQ) for deltamethrin is 0.01 mg/kg in all matrices tested.</p> <p>The limit of determination (LOD) was estimated for the linearity and the control chromatograms and was set to 0.0025 mg/kg.</p> <p>Mean recoveries for each fortification level and the overall mean recovery were within the 70 - 110% range for all matrices. Relative standard deviations were below 20% for all analytes and sample materials.</p> <p>Two MRM transitions were monitored for the analyte and each matrix tested m/z 523 → 281 for the MRM and m/z 525 → 283 for the MRM.</p> <p>The results of the method validation were confirmed using a MRM transition for confirmation.</p> <p>The method meets all guideline criteria (SANCO/825/00/rev. 8.1 and SANCO/3029/99 rev. 4) to determine residues of deltamethrin in/on bees (insects), flowers/blossoms, green material, honey/nectar, pollen and wax at 0.01 mg/kg with exception of wax samples at the LOQ level for the 2nd MRM.</p> <p>The study is acceptable.</p>
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Reference:	KCP 5.1.2.6/12
Title:	Residue analytical method 01347 for the determination of residues of deltamethrin by HPLC with electrospray and MS/MS - detection
Report:	Schoening, R.; Willmes, J.; 2013; MR-012/067; M-444791-01-1
Authority registration No:	
Guideline(s):	<p>Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC</p> <p>European Commission Guidance Document for Generating and Reporting Methods of Analysis in Support of Pre-Registration data Requirements for Annex II (part A, Section 4) and Annex III (part A, section 5) of directive 91/414, SANCO/3029/99 rev. 4, 11/07/00</p> <p>Guidance document on residue analytical methods, SANCO/825/00/rev. 8.1, European Commission, Directorate General Health and Consumer Protection 16/11/2010</p> <p>US EPA Residue Chemistry Test Guideline OCSPP 860.1340: Residue Analytical Method</p>
Deviations:	not specified
GLP/GEP:	no yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The analytical method 01347 was developed for the determination of deltamethrin by HPLC with electrospray and MS/MS-detection.

Deltamethrin was extracted from the sample material using a mixture of dichloromethane/ n-hexane/ acetone (1/1/1, v/v/v). After filtration an aliquot of this solution was evaporated to the aqueous remainder and clean-up on a ChemElut® column or by liquid/ liquid partition for wax. After elution of the residues with dichloromethane or separation with acetonitrile the extract was evaporated to dryness and re-dissolved in water/ acetonitrile (1/9, v/v) + 10 mmol ammonium formate/L + 100 µL/L formic acid. The residues were quantified by reversed phase HPLC with ESI MS/MS-detection using internal standards.

The method 01347 is used in support of the following studies:

- “Assessment of side effects on the honeybee (*Apis mellifera* L.), exposed to *Phacelia tanacetifolia*, sprayed sequentially with deltamethrin during flowering in a long-term field study in North Alsace, France”, Rexer, H. U.; 2013, [M-452717-01-1](#)

Including a separate analytical report in A16:

“Analytical phase report - Assessment of side effects on the honeybee (*Apis mellifera* L.), exposed to *Phacelia tanacetifolia*, sprayed sequentially with deltamethrin during flowering in a long-term field study in North Alsace, France”, Schoening, R., Diehl, P., 2013, [M-451145-01-1](#)

-“Assessment of side effects on the honeybee (*Apis mellifera* L.), exposed to *Phacelia tanacetifolia*, sprayed sequentially with deltamethrin during flowering in a long-term field study in Mid Alsace, France”, Rexer, H. U.; 2013, [M-452723-01-1](#)

Including a separate analytical report in A16:

“Analytical phase report - Assessment of side effects on the honeybee (*Apis mellifera* L.), exposed to *Phacelia tanacetifolia*, sprayed sequentially with deltamethrin during flowering in a long-term field study in Mid Alsace, France”, Schoening, R., Diehl, P., 2013, [M-451154-01-1](#)

Results and discussions

Table A 30: Recovery results from method validation of deltamethrin using the analytical method 01347

Matrix	Analyte	Fortification level (µg/kg) (<i>n</i> = 5)	Mean recovery (%)	RSD (%)	Overall mean [%] and RSD [%]
1 st MRM transition					
Bees (insects)	deltamethrin	10	95	4.2	99 ± 4.6
		100	102	1.6	
Green material		10	99	5.3	98 ± 5.1
		100	96	5.1	
Flowers/ blossoms		10	95	7.3	98 ± 5.4
		100	100	1.8	
Nectar/ honey		10	97	4.0	97 ± 6.2
		100	97	8.4	
Pollen		10	76	7.6	83 ± 10.8
		100	90	6.0	
Wax		10	86	7.3	87 ± 5.6
		100	87	4.3	
2 nd MRM transition					
Bees (insects)	deltamethrin	10	93	4.6	97 ± 5.7
		100	101	2.5	
Green material		10	100	1.2	97 ± 4.4
		100	94	4.7	
Flowers/ blossoms		10	99	6.5	100 ± 4.5
		100	100	1.8	
Nectar/ honey		10	93	6.5	93 ± 7.8
		100	93	9.7	
Pollen		10	80	1.6	84 ± 5.6
		100	88	3.2	
Wax*		10	86	6.7	83 ± 6.4
		100	80	4.4	

* The evaluation of the 2nd MRM at the LOQ level (0.01 mg/kg) for wax is not according to the guideline (signal to noise >3/1). Therefore the confirmation of the residues of deltamethrin at the LOQ level is not possible for wax.

Table A 31: Characteristics for the analytical method used for validation of deltamethrin residues in pure solvent

	Deltamethrin
Specificity	mass spectrum is provided blank value < 30 % LOQ
Calibration (type, number of data points)	individual calibration data is presented calibration line equations: y = 0.922 x + 0.00134 (1st MRM transition) y = 0.954 x + 0.000849 (2nd MRM transition) Correlation coefficients r: 0.9995 (1/x weighted, 1st MRM transition) 0.9998 (1/x weighted, 2nd MRM transition) number of data points: 6
Calibration range	0.1 - 50 µg/L
Assessment of matrix effects is presented	Possible matrix effects of deltamethrin are eliminated by using an internal standard solution of the isotopically labelled analytical standard.
Limit of determination/quantification	LOQ = 10 µg/kg (in all sample materials) LOD = 2.5 µg/kg

Conclusion

The method 01347 meets all guideline criteria to determine residues of deltamethrin in/ on bees (insects), flowers/ blossoms, green material, honey /nectar, pollen and wax at 0.01 mg/kg with exception of wax samples at the LOQ level for the 2nd MRM. The evaluation of the 2nd MRM at the LOQ level (0.01 mg/kg) for wax is not according to the guideline (signal to noise >3/1). Therefore the confirmation of the residues of deltamethrin at the LOQ level is not possible for wax.

Concurrent validation parameter from the respective study reports

Schoening, R.; Diehl, P.; 2013; [M-451145-01-1](#)

The method 01347 was validated concurrently with the test solution analyses.

Table A 32: Recovery results from method validation of deltamethrin using the analytical method 01347

Matrix	Analyte	Fortification level (µg/kg) (n = 5)	Mean recovery (%)	RSD (%)	Overall mean [%] and RSD [%]
Pollen	deltamethrin	10	78	3.7	82 ± 6.2
		100	85	4.9	
Nectar		10	90	2.8	95 ± 6.4
		100	100	2.1	
Beewax		10	94	8.9	90 ± 7.9
		100	86	2.1	
Flowers/ blossoms		10 (n = 1)	102	-	90 ± 12.0
		100 (n = 1)	85	-	
		1000 (n = 1)	82	-	

Linearity of deltamethrin with internal standard in pure solvent (0.1 – 50 µg/L):

Linear concentration range: 0.1 – 50 µg/L

Regression equation: y = 0.0933 x + 0.00245; r = 0.9999 (1/x weighted)

Concurrent validation parameter from the respective study reports

Schoening, R.; Diehl, P.; 2013; [M-451154-01-1](#)

The method 01347 was validated concurrently with the test solution analyses.

Table A 33: Recovery results from method validation of deltamethrin using the analytical method 01347

Matrix	Analyte	Fortification level (µg/kg) (<i>n</i> = 5)	Mean recovery (%)	RSD (%)	Overall mean [%] and RSD [%]
Pollen	deltamethrin	10	79	2.7	85 ± 7.8
		100	91	1.8	
10		90	6.1	95 ± 6.9	
100		100	1.2		
Beewax		10	101	2.2	92 ± 10.7
		100	8.3	4.0	
Flowers/ blossoms		10 (<i>n</i> = 1)	84	-	85 ± 9.5
		100 (<i>n</i> = 1)	94	-	
		1000 (<i>n</i> = 1)	78	-	

Linearity of deltamethrin with internal standard in pure solvent (0.1 – 50 µg/L):

Linear concentration range: 0.1 – 50 µg/L

Regression equation: $y = 0.851x + 0.00121$; $r = 0.9995$ (1/x weighted)

A 2.1.1.6.13 Analytical method 01347 (modified) for the determination of deltamethrin in employed feeding solutions

A 2.1.1.6.13.1 Method validation

Comments of zRMS:	<p>The objective of study P672134735 was to determine the concentration of deltamethrin in the employed feeding solutions.</p> <p>The limit of quantitation (LOQ) for deltamethrin was 0.01 mg/kg (=10 µg/kg) for the sample material aqueous sugar solution, corresponding to the lowest fortification level of successfully conducted recovery experiments. The limit of detection (LOD) was estimated to be at least 30% of the LOQ.</p> <p>All results of the method validation were in accordance with the general requirements for residue analytical methods; therefore, the modified analytical method 01347 was validated successfully and it is suitable for the detection of deltamethrin in employed feeding solutions.</p> <p>The modification is acceptable.</p>
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Reference:	KCP 5.1.2.6/13
Title:	Determination of deltamethrin in feeding solutions from a 10d continuous honeybee feeding study (Study Number: S13-00151; Eurofins)
Report:	Schoening, R.; Willmes, J.; 2013; MR-13/135; M-469484-01-1
Authority registration No:	
Guideline(s):	not specified
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

This modified analytical method 01347 is described in Appendix A 3 of the report of Kling, A., 2014 ([M-477250-01-1](#)) and was developed to determine deltamethrin in employed feeding solutions by HPLC with ESI MS/MS-detection in support of this chronic toxicity study to honey bees (*Apis mellifera* L.).

In the original method 01347 (Schoening, R.; Willmes, J.; 2013; Residue analytical method 01347 for the determination of residues of deltamethrin by HPLC with electrospray and MS/MS - detection; [M-444791-01-1](#)) deltamethrin was extracted from the sample material using a mixture of dichloromethane/ n-hexane/ acetone (1/1/1, v/v/v). After filtration an aliquot of this solution was evaporated to the aqueous remainder and clean-up on a ChemElut® column or by liquid/ liquid partition for wax. After elution of the residues with dichloromethane or separation with acetonitrile the extract was evaporated to dryness and re-dissolved in water/ acetonitrile. The residues were quantified by reversed phase HPLC with ESI MS/MS-detection using internal standards.

Due to the fact that the concentration in the feeding solutions used in the respective study were at a very high level the method 01347 was modified. It was therefore only necessary to take an aliquot of the feeding solution and to dilute the sample. Thereafter, aliquots of the diluted samples were subjected to reversed phase High Performance Liquid Chromatography (HPLC) coupled with electrospray and mass spectrometry (MS/MS) detection without a further clean-up step.

Results and discussions

Table A 34: Recovery results from method validation of deltamethrin using the analytical method 01347 (modified)

Matrix	Analyte	Fortification level (mg/kg)	Mean recovery (%)	RSD (%)	Overall mean and RSD [%]
Aqueous sugar solution	deltamethrin	0.01 (n=5)	97	1.9	99 ± 2.0
		0.10 (n=5)	100	1.6	
		200 (n=3)	99	1.5	

Table A 35: Characteristics for the analytical method used for validation of deltamethrin residues in employed feeding solutions

	Deltamethrin
Specificity	blank value < LOQ
Calibration (type, number of data points)	individual calibration data is presented Two calibration lines were investigated for covering the large linear range: 1. $y = 0.942471 x + 0.00115$, $r = 0.9998$ (1/x weighted) 2. $y = 0.956695 x - 0.00536$, $r = 0.9998$ (1/x weighted) 5 -7 number of data points per regression curve
Calibration range	Linear range 1 0.00005/0.01 – 0.50/0.01 µg/mL (analyte conc./ internal standard conc.)

	Deltamethrin
Specificity	blank value < LOQ
	Linear range 2 0.0005/0.01 – 0.50/0.01 µg/mL (analyte conc./ internal standard conc.)
Assessment of matrix effects is presented	Possible matrix effects of deltamethrin are eliminated by using an internal standard solution of the isotopically labelled analytical standard.
Limit of determination/quantification	LOQ = 10 µg/kg (aqueous sugar solution)

Conclusion

The present validation data for this analytical method (01347, modified) show that the method is suitable for the detection of deltamethrin in employed feeding solutions.

A 2.1.1.6.14 Analytical method for the determination of deltamethrin in freshwater

A 2.1.1.6.14.1 Method validation

Comments of zRMS:	The method is not satisfactorily validated in accordance with SANCO/3029/99 rev. 4. for the determination of deltamethrin in freshwater.
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Reference:	KCP 5.1.2.6/14
Title:	LX165-08 (deltamethrin technical) - Toxicity to the freshwater green alga, <i>Selenastrum capricornutum</i>
Report:	Giddings, J. M.; Bayne, M. C. R.; Mitchell, K. L.; Shepherd, S. P.; 1990; A47090; M-131038-01-1
Authority registration No:	
Guideline(s):	OECD: 201
Deviations:	--
GLP/GEP:	yes
Acceptability:	This method does not meet all required guideline criteria (SANCO/3029/99 rev 4).
Duplication (if vertebrate study):	

Materials and methods

The analytical method was developed for the determination of deltamethrin in freshwater by GC-ECD in support of this toxicity study to the freshwater green alga *Selenastrum capricornutum*.

Each sample was shaken with the appropriate volume of hexane. The layers were allowed to separate and the organic phase was dried through sodium sulphate and collected into round bottom flasks. The extract was brought to dryness by rotary evaporation. Each sample was brought to a final volume with hexane for GC analysis.

Results and discussions

Table A 36: Recovery results from method validation of deltamethrin using the analytical method

Matrix	Analyte	Fortification level (µg/L) (<i>n</i> = 3)	Concentration recovered (µg/L)	Percent recovered (%)
freshwater	deltamethrin	1.00	1.02	102
			0.975	97.5
			1.10	110
		0.10	0.103	103
			0.0959	95.9
			0.0930	93.0
		0.025	0.0252	101
			0.0222	88.7
			0.0255	102
		0.010	0.0106	106
			0.00977	97.7
			0.0107	107
Average recovery			100	6.08

Table A 37: Characteristics for the analytical method used for validation of deltamethrin residues in freshwater

	deltamethrin
Specificity	blank value < minimal detectable concentration
Calibration (type, number of data points)	individual calibration data is presented number of data points: 5; $r = 0.999449$
Calibration range	5.0 – 100 µg/L
Limit of determination/quantification	Minimal detectable concentration = 0.0123 µg/L (for a 1000 mL sample)

Conclusion

The present validation data for this analytical method show that the method is suitable for the detection of deltamethrin in freshwater in support of ecotoxicological studies.

A 2.1.1.7 Description of analytical methods for the determination of residues in support of physical and chemical properties tests (KCP 5.1)

The analytical method used for the generation of pre-authorization data is the same as the one described in part B section 5.2.1

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)

A 2.1.2.1.1 Analytical method 00086/M089

A 2.1.2.1.1.1 Method validation

Comments of zRMS:	<p>The the multi method DFG S 19 (L 00.0034) (BCS Method ID 00086/M089) was validated for the the determination of residues of cis-deltamethrin (AE F032640) in tomato (fruit), orange (fruit), barley (grain), dried bean (seed) and oilseed rape (seed).</p> <p>The limit of quantitation (LOQ) for cis-deltamethrin is 0.01 mg/kg in all matrices tested.</p> <p>For all matrices, analysis of control specimens by GC-MSD indicated that residues of the test substance were below 30% of the LOQ.</p> <p>Mean recoveries for each fortification level and the overall mean recovery were within the 70 - 110% range for all matrices. Relative standard deviations were below 20% for cis-deltamethrin and all sample materials.</p> <p>Three ions (253, 251, 181) were monitored to fulfil the requirement for validation of this confirmatory method.</p> <p>The residue definition for monitoring is cis-deltamethrin. The analytical method is suitable to support this residue definition.</p> <p>The method meets all guideline criteria (SANCO/825/00/rev. 8.1 and SANCO/3029/99 rev. 4) to determine residues of cis-deltamethrin in plant matrices such as tomato (fruit), orange (fruit), barley (grain), dried bean (seed) and oilseed rape (seed) with satisfactory accuracy, precision and repeatability.</p> <p>The study is acceptable.</p>
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Reference:	KCP 5.2.1/01
Title:	Validation of enforcement method DFG S19 (L 00.00-34) (BCS method ID 00086/M089) for the determination of cis-deltamethrin (AE F032640) in/on foodstuff of plant origin
Report:	Weber, H.; 2009; S09-00553; M-351076-01-1
Authority registration No:	
Guideline(s):	<p>EU Directive 91/414/EEC as amended by 96/46/EC 4.2.1</p> <p>Guidance document SANCO/3029/99 rev. 4 of 11/07/00 of the European Commission</p> <p>Guidance document SANCO/0825/00 rev. 7 of 17/03/04 of the European Commission</p> <p>BBA Guideline: Residue Analytical Methods for Post-Registration Control Purposes of July 21, 1998</p>
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The purpose of this study was to validate the multi method DFG S 19 (L 00.0034) (BCS Method ID 00086/M089) for the determination of residues of cis-deltamethrin (AE F032640) in tomato (fruit), orange (fruit), barley (grain), dried bean (seed) and oilseed rape (seed).

A series of recovery experiments were performed by fortifying control (untreated) specimens of the matrices tomato (fruit), orange (fruit), oilseed rape (seed), dry bean (seed) and barley (grain).

The validation followed the procedures as described in the multi method DFG S 19 (L 00.0034) [1] as well as the guideline SANCO/825/00 rev.7 (17/03/04).

Cis-deltamethrin was extracted from tomato (fruit), orange (fruit), dry bean (seed) and barley (grain) specimens with acetone/water (2/1, v/v). Thereafter, ethyl acetate/cyclohexane (1/1, v/v) and sodium chloride were added for liquid-liquid partition. An aliquot of the organic phase was evaporated to dryness. From oilseed rape (seeds), cis-deltamethrin was extracted with acetonitrile/acetone (9/1, v/v) in the presence of synthetic calcium silicate (trade name Calflo E) and Celite. The organic phase was filtered and evaporated to dryness.

For all matrices the evaporated extract was cleaned up by gel permeation chromatography (GPC) on Bio Beads S-X3 polystyrene gel using a mixture of ethyl acetate/cyclohexane (1/1, v/v) as eluant. The collected extracts were further cleaned on a mini silicagel column and analysed for residues of deltamethrin by gas chromatography with mass selective detection (GC-MSD).

Three ions were monitored to fulfil the requirement for validation of this confirmatory method. Using GC-

MSD, the ions 253, 251 and 181 were used for the determination of cis-deltamethrin in tomato (fruit), orange (fruit), oilseed rape (seed), dried bean (seed) and barley (grain). Control specimens were analysed in duplicate and fortified specimens were analysed in quintuple for each fortification level.

Results and discussions

For cis-deltamethrin in tomato (fruit), orange (fruit), oilseed rape (seed), dried beans (seed) and barley (grain) the limit of quantitation (LOQ) was 0.01 mg/kg.

Fortification experiments were performed for tomato (fruit), orange (fruit), dried bean (seed) and oilseed rape (seed) at the limits of quantitation (LOQ) and tenfold LOQ. For barley (grain), fortification experiments were performed at the LOQ, tenfold LOQ and two hundred fold LOQ.

The linearity of the detector response was confirmed by injecting eight external standard solutions in the range between of 0.00500 to 1.25 µg/mL of deltamethrin. Correlation coefficients R were ≥ 0.9960 for the three monitored ions.

For all matrices, analysis of control specimens by GC-MSD indicated that residues of the test substance were below 30% of the LOQ.

Mean recovery values obtained for tomato (fruit), orange (fruit), oilseed rape (seed), dry bean (seed) and barley (grain) specimens for all fortification levels comply with the standard acceptance criteria of SANCO Guideline 825/00.

Furthermore, as required by the standard acceptance criteria the overall relative standard deviation and the relative standard deviation for each fortification level were $\leq 20\%$.

Matrix effects were tested by evaluating the results with solvent standards and with matrix-matched standards. For cis-deltamethrin, signal suppression or enhancement below 10% were observed for all matrices. Therefore solvent standards were used for the analysis.

Cis-deltamethrin in calibration solution is stable during storage under refrigerator conditions for at least 25 days

Cis-deltamethrin in extract is stable during storage under refrigerator conditions for at least 23 days

Table A 38: Recovery results from method validation of cis-deltamethrin using the analytical method in different plant matrices

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
cis-deltamethrin					
tomato (fruit)	0.01	5	78	3.9	m/z=253
	0.10	5	84	11	m/z=253
	0.01	5	88	11	m/z=251
	0.10	5	85	12	m/z=251
	0.01	5	81	4.5	m/z=181
	0.10	5	85	11	m/z=181
orange (fruit)	0.01	5	96	6.2	m/z=253
	0.10	5	88	4.5	m/z=253
	0.01	5	95	4.9	m/z=251
	0.10	5	88	5.5	m/z=251
	0.01	5	92	5.0	m/z=181
	0.10	5	90	5.6	m/z=181
dried beans (seed)	0.01	5	101	10	m/z=253
	0.10	5	89	5.3	m/z=253
	0.01	5	98	8.4	m/z=251
	0.10	5	90	5.2	m/z=251
	0.01	5	97	10	m/z=181
	0.10	5	89	5.1	m/z=181
barley (grain)	0.01	5	94	10	m/z=253
	0.10	5	79	8.6	m/z=253
	2.0	5	78	9.0	m/z=253
	0.01	5	88	18	m/z=251
	0.10	5	81	7.0	m/z=251
	2.0	5	80	9.0	m/z=251
	0.01	5	94	9.4	m/z=181
	0.10	5	81	9.0	m/z=181
	2.0	5	80	8.9	m/z=181
oilseed rape (seed)	0.01	5	86	6.1	m/z=253
	0.10	5	74	4.5	m/z=253
	0.01	5	81	8.3	m/z=251
	0.10	5	74	4.2	m/z=251
	0.01	5	82	5.3	m/z=181
	0.10	5	74	4.7	m/z=181

Table A 39: Characteristics for the analytical method used for validation of cis-deltamethrin in different plant matrices

	cis-deltamethrin
Specificity	mass spectrum is provided in Appendix 3 of the method report blank value < 30 % LOQ)

	cis-deltamethrin
Calibration (type, number of data points)	A one point external standard calibration was carried out.individual calibration data presented in Appendix 2 of the repport calibration line equation presented for each m/z number of data points>5 (8) m/z=253→R = 0.9963 m/z=251→R = 0.9960 m/z=181→R = 0.9967
Calibration range	External standard with one point calibration in the range between of 0.0050 to 1.25 µg/mL of cis-deltamethrin
Assessment of matrix effects is presented	yes
Limit of determination/quantification	LOQ = 0.01 mg/kg

Conclusion

The results demonstrate that the multi method DFG S 19 (L 00.0034) (BCS Method ID 00086/M089) permits the determination of residues of cis-deltamethrin in tomato (fruit), orange (fruit), oilseed rape (seed), dry bean (seed) and barley (grain). The validation proved that the method is valid for the determination of residues of cis-deltamethrin in plant matrices. The method has proven its applicability as an enforcement method.

A 2.1.2.1.1.2 Independent laboratory validation

Comments of zRMS:	The Bayer CropScience method 00086/M0089 based on DFG method S19 was independently validated successfully for the determination of residues of cis-deltamethrin in plant materials by GC/MS, exemplified for tomato (fruit), barley (grain), orange (fruit), dry beans (seed) and oilseed rape (seed), all with a limit of quantitation (LOQ) of 0.01 mg/kg. Specimens were fortified (5 replicates per matrix and fortification level) at the LOQ and at the 10-fold LOQ, and for barley grain at the 200-fold LOQ. For all three MS ions monitored, apparent residues in all blank control specimens were below 20% of the LOQ. The average recoveries were within the acceptable range of 70% to 110% with relative standard deviations (RSD) ≤ 20%. The study is acceptable.
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Reference:	KCP 5.2.1/02
Title:	Independent laboratory validation of the DFG method S19 (BCS method 00086/M089) for the determination of residues of cis-deltamethrin (AE F032640) in plant materials, using GC/MS
Report:	Merdian, H.; 2009; P/B 1681 G; M-356306-01-1
Authority registration No:	
Guideline(s):	EC Directive 91/414/EEC, EC Guidance document on residue analytical methods, SANCO/825/00 rev. 7, 17/03/04 and the OECD Guidance Document on Pesticide Residue Analytical Methods (ENV/JM/Mono (2007) 17, 2007-08-13)
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The objective was to independently validate Bayer CropScience method 00086/M0089 based on DFG method S19 for the determination of residues of cis-deltamethrin in plant materials by GC/MS, exemplified for tomato (fruit), barley (grain), orange (fruit), dry beans (seed) and oilseed rape (seed), all with a limit of

quantitation (LOQ) of 0.01 mg/kg.

Residue analysis was performed according to the original method validation report, with minor modifications indicated and explained in the report. These minor modifications became necessary due to slightly different laboratory routines and are considered insignificant.

Extraction was done following extraction procedures (modules E1 for tomato, E2 for bean and grain, E3 for orange, and E7 for oilseed rape seed), with subsequent clean-up according to module GPC and mini silica gel chromatography, and gas chromatography with mass selective detection (GC/MS), monitoring three ions for the determination and confirmation (253, 251 and 181 m/z).

Results and discussions

As demonstrated by the independent laboratory validation results, the method allows the determination of cis-deltamethrin with a limit of quantification (LOQ) of 0.01 mg/kg.

Apparent residues in all blank control specimens were below 20 % of the LOQ.

Specimens were fortified (5 replicates per matrix and fortification level) at the LOQ and at the 10-fold LOQ, and for barley grain at the 200-fold LOQ. Additional specimens were kept untreated as blank controls. The linearity of the detector response was confirmed by injecting seven external standard solutions in the range between of 0.005 to 0.500 µg/mL of deltamethrin. Correlation coefficients R were ≥ 0.9960 for the three monitored ions. Correlation coefficients R were ≥ 0.980 for the three monitored ions.

For all three MS ions monitored, apparent residues in all blank control specimens were below 20 % of the LOQ.

The average recoveries were within the acceptable range of 70 % to 110 % with relative standard deviations (RSD) ≤ 20 %.

All standard solutions were stored refrigerated in amber glass bottles when not in use. The solutions were stable for approximately one month as demonstrated by consistent GC/MS results obtained during the study. Summaries of the independent laboratory validation results are given below:

Table A 40: Recovery results from method validation of cis-deltamethrin using the analytical method in different plant matrices

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
cis-deltamethrin					
tomato (fruit)	0.01	5	97	3	m/z=253
	0.10	5	89	13	m/z=253
	0.01	5	97	3	m/z=251
	0.10	5	91	11	m/z=251
	0.01	5	91	4	m/z=181
	0.10	5	89	12	m/z=181
orange (fruit)	0.01	5	98	10	m/z=253
	0.10	5	90	15	m/z=253
	0.01	5	98	8	m/z=251
	0.10	5	92	13	m/z=251
	0.01	5	99	7	m/z=181
	0.10	5	91	17	m/z=181
dried beans (seed)	0.01	5	96	5	m/z=253
	0.10	5	83	13	m/z=253
	0.01	5	94	10	m/z=251
	0.10	5	84	15	m/z=251
	0.01	5	97	5	m/z=181
	0.10	5	84	12	m/z=181

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
barley (grain)	0.01	5	97	7	m/z=253
	0.10	5	90	20	m/z=253
	2.0	5	82	4	m/z=253
	0.01	5	96	10	m/z=251
	0.10	5	90	19	m/z=251
	2.0	5	83	3	m/z=251
	0.01	5	98	6	m/z=181
	0.10	5	90	16	m/z=181
	2.0	5	84	5	m/z=181
oilseed rape (seed)	0.01	5	97	6	m/z=253
	0.10	5	98	7	m/z=253
	0.01	5	94	9	m/z=251
	0.10	5	98	5	m/z=251
	0.01	5	98	7	m/z=181
	0.10	5	101	4	m/z=181

Table A 41: Characteristics for the analytical method used for validation of cis-deltamethrin in different plant matrices

	cis-deltamethrin
Specificity	mass spectrum is provided in Figure 3 of the method report blank value < 20 % of the LOQ)
Calibration (type, number of data points)	A one point external standard calibration for cis-deltamethrin was carried out. individual calibration data presented in Figure 2 of the method report calibration line equation presented for each m/z in Figure 1 of the method report number of data points>5 (7) m/z=253→R = 0.9848 m/z=251→R = 0.9800 m/z=181→R = 0.9902
Calibration range	External standard with one point calibration in the range between of 5.0 to 500 ng/mL of cis-deltamethrin
Assessment of matrix effects is presented	yes
Limit of determination/quantification	LOQ = 0.01 mg/kg

Conclusion

PTRL Europe performed the independent laboratory validation (ILV) of the DFG method S19 originally validated by Harald Weber (Specht Study No.: BAY-0902V, Bayer CropScience Project No.: P682097524, 07-Jul-09).

The method was independently validated successfully for the determination of residues of cis-deltamethrin in/on plant matrices by GC/MS, exemplified for tomato (fruit), barley (grain), orange (fruit), dry beans (seed) and oilseed rape (seed), demonstrating the LOQ of 0.01 mg/kg.

It is concluded that DFG method S19 fulfils the reproducibility requirements as defined in the Council Directive 91/414/EEC, in the EC Guidance document on residue analytical methods (SANCO/825/00 rev. 7 17/03/04) and in the OECD Guidance Document on Pesticide Residue Analytical Methods (ENV/JM/Mono (2007) 17, 2007-08-13) and is, therefore, applicable as an enforcement method.

A 2.1.2.1.1.3 Confirmatory method (if required)

No confirmatory method is required because of the specificity of the detection methods (three transition monitored:

Comments of zRMS:	Accepted. See point A 2.1.1.1.1.3.
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A 2.1.2.1.1.4 Extraction efficiency

Refer to point [A 2.1.1.1.1.3](#)

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

A 2.1.2.2.1 Analytical method DFG S 19

A 2.1.2.2.1.1 Method validation

Comments of zRMS:	<p>The multi method DFG method S 19 (BCS Method ID 00086/M090) was validated for the the determination of residues of cis-deltamethrin (AE F032640) in milk, egg, bovine muscle, liver, kidney and fat.</p> <p>The limit of quantitation (LOQ) for cis-deltamethrin is 0.01 mg/kg in all matrices tested.</p> <p>For all matrices, analysis of control specimens by GC-MSD indicated that residues of the test substance were below 30% of the LOQ.</p> <p>Mean recoveries for each fortification level and the overall mean recovery were within the 70 - 110% range for all matrices. Relative standard deviations were below 20% for cis-deltamethrin and all sample materials.</p> <p>Three ions (253, 251, 181) were monitored to fulfil the requirement for validation of this confirmatory method.</p> <p>The residue definition for monitoring is cis-deltamethrin. The analytical method is suitable to support this residue definition.</p> <p>The method meets all guideline criteria (SANCO/825/00/rev. 8.1 and SANCO/3029/99 rev. 4) to determine residues of cis-deltamethrin in animal matrices such as milk, egg, bovine muscle, liver, kidney and fat with satisfactory accuracy, precision and repeatability.</p> <p>The study is acceptable.</p>
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Reference:	KCP 5.2.2/01
Title:	Validation of enforcement method DFG S19 (L 00.00-34) (BCS method ID 00086/M090) for the determination of residues cis-deltamethrin (AE F032640) in/on foodstuff of animal origin
Report:	Weber, H.; 2009; S09-00551; M-351080-01-1
Authority registration No:	
Guideline(s):	<p>EU Directive 91/414/EEC as amended by 96/46/EC 4.2.1</p> <p>Guidance document SANCO/3029/99 rev. 4 of 11/07/00 of the European Commission</p> <p>Guidance document SANCO/0825/00 rev. 7 of 17/03/04 of the European Commission</p> <p>BBA Guideline: Residue Analytical Methods for Post-Registration Control Purposes of</p> <p>July 21, 1998</p>
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The purpose of this study was the examination of the applicability of the DFG Method S 19 (BCS Method ID 00086/M090) for the determination of residues of cis-deltamethrin (AE F032640) in milk, egg, bovine muscle, liver, kidney and fat. This examination followed the extended and revised version of the DFG

Method S 19, published as ‘Modular Multiple Analytical Method for the Determination of Pesticide Residues in Foodstuffs, L 00.00-34’, as part of the Official Collection of Test Methods under Article 64 of the LFGB (German Food, Commodity and Feed Code).

A series of recovery experiments were performed by fortifying control (untreated) specimens of the matrices milk, egg, bovine muscle, liver, kidney and fat. The validation followed the procedures as described in the multi method DFG S 19 (L 00.0034) [1] as well as the guideline SANCO/825/00 rev.7 (17/03/04).

Cis-deltamethrin was extracted from milk (whole milk, 3.5 % fat), poultry egg (yolk and egg white, without shell), bovine muscle, liver (from cattle) and kidney (from cattle) specimens with acetone/water (2/1, v/v). Thereafter, ethyl acetate/cyclohexane (1/1, v/v) and sodium chloride were added for liquid-liquid partition. An aliquot of the organic phase was evaporated to dryness.

For the analysis of cis-deltamethrin in fat the samples were dissolved in ethyl acetate/cyclohexane (1/1, v/v) and directly cleaned by gel permeation chromatography (GPC).

For all other matrices the evaporated extract was cleaned up by gel permeation chromatography (GPC) on Bio Beads S-X3 polystyrene gel using a mixture of ethyl acetate/cyclohexane (1/1, v/v) as eluant. The collected extracts were further cleaned on a mini silicagel column and analysed for residues of cis-deltamethrin by gas chromatography with mass selective detection (GC-MSD).

Using GC-MSD, three ions were monitored to fulfil the requirement for validation of this confirmatory method. Ions m/z 253 (quantification) and m/z 251 and 181 m/z (confirmation) were used for the determination of cis-deltamethrin in milk, egg, bovine muscle, liver, kidney and fat. Control specimens were analysed in duplicate and fortified specimens were analysed in quintuple for each fortification level.

Results and discussions

For cis-deltamethrin in milk, egg, bovine muscle, liver, kidney and fat the limit of quantitation (LOQ) was 0.01 mg/kg.

Fortification experiments were performed for milk, egg, bovine muscle, liver, kidney and fat at the limits of quantitation (LOQ) and tenfold LOQ.

The linearity of the detector response was confirmed by injecting nine external standard solutions in the range between of 0.00250 to 1.25 $\mu\text{g/mL}$ of cis-deltamethrin. Correlation coefficients R were ≥ 0.9968 for the three monitored ions.

For all matrices, analysis of control specimens by GC-MSD indicated that residues of the test substance were below 30% of the LOQ.

Mean recovery values obtained for milk, egg, bovine muscle, liver, kidney and fat specimens for all fortification levels comply with the standard acceptance criteria of SANCO Guideline 825/00.

Furthermore, as required by the standard acceptance criteria, the overall relative standard deviation and the relative standard deviation for each fortification level were $\leq 20 \%$.

Matrix effects were tested by evaluating the results with solvent standards and with matrix-matched standards. For cis-deltamethrin, signal suppression or enhancement below 10% were observed for all matrices. Therefore solvent standards were used for the analysis.

Stabilities of cis-deltamethrin in the calibration solution and in selected extracts were assessed at the end of the study. The results prove that stability of the Cis-deltamethrin in calibration solution is stable during storage under refrigerator conditions for at least 25 days and stability of Cis-deltamethrin in extract is stable during storage under refrigerator conditions for at least 24 days

Table A 42: Recovery results from method validation of cis-deltamethrin using the analytical method

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
cis-deltamethrin					
milk	0.01	5	84	15	m/z=253
	0.10	5	87	15	m/z=253
	0.01	5	86	13	m/z=251
	0.10	5	88	15	m/z=251
	0.01	5	86	17	m/z=181
	0.10	5	87	15	m/z=181
egg	0.01	5	94	7.5	m/z=253
	0.10	5	88	9.0	m/z=253
	0.01	5	91	6.2	m/z=251
	0.10	5	86	7.9	m/z=251
	0.01	5	96	7.7	m/z=181
	0.10	5	86	8.0	m/z=181
bovine muscle	0.01	5	78	15	m/z=253
	0.10	5	82	8.5	m/z=253
	0.01	5	78	14	m/z=251
	0.10	5	82	10	m/z=251
	0.01	5	81	15	m/z=181
	0.10	5	83	9.2	m/z=181
liver	0.01	5	84	16	m/z=253
	0.10	5	85	13	m/z=253
	0.01	5	85	16	m/z=251
	0.10	5	87	15	m/z=251
	0.01	5	84	18	m/z=181
	0.10	5	87	14	m/z=181
kidney	0.01	5	80	13	m/z=253
	0.10	5	85	13	m/z=253
	0.01	5	77	14	m/z=251
	0.10	5	85	14	m/z=251
	0.01	5	83	11	m/z=181
	0.10	5	86	14	m/z=181
fat	0.01	5	95	6.2	m/z=253
	0.10	5	81	4.8	m/z=253
	0.01	5	81	3.4	m/z=251
	0.10	5	80	5.0	m/z=251
	0.01	5	92	10	m/z=181
	0.10	5	80	4.9	m/z=181

Table A 43: Characteristics for the analytical method used for validation of cis-deltamethrin residues in different animal matrices

	cis-deltamethrin
Specificity	mass spectrum is provided in Appendix 3 of the method report blank value < 30 % LOQ)
Calibration (type, number of data points)	individual calibration data presented in Appendix 2 of the report calibration line equation presented for each m/z number of data points>5 (9) m/z=253→R = 0.9968 m/z=251→R = 0.9968 m/z=181→R = 0.9975 A one point external standard caliabrathion was carried out.
Calibration range	External standard with one point calibration in the range between of 0.0025 to 1.25 µg/mL of cis-deltamethrin
Assessment of matrix effects is presented	yes
Limit of determination/quantification	LOQ = 0.01 mg/kg

Conclusion

The results demonstrate that the multi method DFG S 19 (L 00.0034) (BCS Method ID 00086/M090) permits the determination of residues of cis-deltamethrin in milk, egg, bovine muscle, liver, kidney and fat. The validation proved that the method is valid for the determination of residues of cis-deltamethrin in animal matrices. The method can therefore be considered valid and applicable as enforcement method.

A 2.1.2.2.1.2 Independent laboratory validation

Comments of zRMS:	<p>The Bayer CropScience method 00086/M0090 based on DFG method S19 was independently validated successfully for the determination of residues of cis-deltamethrin in animal matrices by GC/MS, exemplified for whole milk, hen's egg, bovine muscle, liver, kidney and fat all with a limit of quantitation (LOQ) of 0.01 mg/kg.</p> <p>For independent laboratory validation (ILV), specimens were fortified (5 replicates per matrix and fortification level) at the LOQ and at the 10-fold LOQ.</p> <p>For all three MS ions monitored, apparent residues in all blank control specimens were below 20% of the LOQ.</p> <p>The average recoveries were within the acceptable range of 70% to 110% with relative standard deviations (RSD) \leq 20%.</p> <p>The study is acceptable.</p>
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Reference:	KCP 5.2.2/02
Title:	Independent laboratory validation of the DFG method S19 (BCS method 00086/M089) for the determination of residues of cis-deltamethrin (AE F032640) in foodstuffs of animal origin, using GC/MS
Report:	Merdian, H.; 2009; P/B 1682 G; M-356331-01-1
Authority registration No:	
Guideline(s):	EC Directive 91/414/EEC, EC Guidance document on residue analytical methods, SANCO/825/00 rev. 7 17/03/04 and the OECD Guidance Document on Pesticide Residue Analytical Methods (ENV/JM/Mono (2007) 17, 2007-08-13)
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The objective was to independently validate Bayer CropScience method 00086/M090 based on DFG method S19 for the determination of residues of cis-deltamethrin in animal matrices by GC/MS, exemplified for whole milk, hen's egg, bovine muscle, liver, kidney and fat all with a limit of quantitation (LOQ) of 0.01 mg/kg.

Extraction was done following extraction modules E 1 (milk, egg, muscle, liver and kidney) and E 6 (fat), with subsequent clean-up according to module GPC and mini silica gel chromatography, and gas chromatography with mass selective detection (GC/MS), monitoring three ions for the determination and confirmation (253, 251 and 181 m/z).

Results and discussions

For independent laboratory validation (ILV), specimens were fortified (5 replicates per matrix and fortification level) at the LOQ and at the 10-fold LOQ. Additional specimens were kept untreated as blank controls.

A one-point external standard calibration for cis-deltamethrin was carried out. Peak area in counts from injection of known standards versus standard concentrations in ng/mL was used to quantify the residues in the samples.

Calibration functions obtained from injections of calibration solutions containing eight different concentrations ranging from 2.0 to 500 ng/mL were used to show the linearity of the detector response.

Regression coefficients (r^2) were \geq 0.993 for all three fragment ions.

As demonstrated by the independent laboratory validation results, the method allows the determination of cis-deltamethrin with a limit of quantification (LOQ) of 0.01 mg/kg. For all three MS ions monitored, apparent residues in all blank control specimens were below 20 % of the LOQ.

The average recoveries were within the acceptable range of 70 % to 110 % with relative standard deviations (RSD) \leq 20 %.

Summaries of the independent laboratory validation results are given below:

Table A 44: Recovery results from method validation of cis-deltamethrin using the analytical method in different animal matrices

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
cis-deltamethrin					
Hen's Egg	0.01	5	108	4	m/z=253
	0.10	5	93	14	m/z=253
	0.01	5	110	3	m/z=251
	0.10	5	94	10	m/z=251
	0.01	5	109	2	m/z=181
	0.10	5	93	12	m/z=181
Whole Milk	0.01	5	91	3	m/z=253
	0.10	5	101	8	m/z=253
	0.01	5	95	4	m/z=251
	0.10	5	103	5	m/z=251
	0.01	5	95	3	m/z=181
	0.10	5	105	9	m/z=181
Bovine Muscle	0.01	5	102	6	m/z=253
	0.10	5	105	5	m/z=253
	0.01	5	102	4	m/z=251
	0.10	5	105	9	m/z=251
	0.01	5	103	5	m/z=181
	0.10	5	105	10	m/z=181
Bovine Liver	0.01	5	104	3	m/z=253
	0.10	5	103	3	m/z=253
	0.01	5	103	3	m/z=251
	0.10	5	103	3	m/z=251
	0.01	5	106	5	m/z=181
	0.10	5	102	3	m/z=181
Bovine Kidney	0.01	5	94	7	m/z=253
	0.10	5	107	9	m/z=253
	0.01	5	96	9	m/z=251
	0.10	5	100	7	m/z=251
	0.01	5	97	14	m/z=181
	0.10	5	100	7	m/z=181
Bovine Fat	0.01	5	104	4	m/z=253
	0.10	5	101	11	m/z=253
	0.01	5	97	6	m/z=251
	0.10	5	99	8	m/z=251
	0.01	5	98	3	m/z=181
	0.10	5	96	14	m/z=181

Table A 45: Characteristics for the analytical method used for validation of cis-deltamethrin in different animal matrices

	cis-deltamethrin
Specificity	mass spectrum is provided in Figure 3 of the method report blank value < 20 % LOQ)
Calibration (type, number of data points)	A one point external standard calibration individual was carried out. Calibration data presented in Figure 2 of the method report calibration line equation presented for each m/z in Figure 1 of the method report number of data points>5 (8) m/z=253→R = 0.9981 m/z=251→R = 0.9950 m/z=181→R = 0.9934
Calibration range	External standard with one point calibration in the range between of 0.002 to 0.50µg/mL of cis-deltamethrin
Assessment of matrix effects is presented	yes
Limit of determination/quantification	LOQ = 0.01 mg/kg

Conclusion

PTRL Europe performed the independent laboratory validation (ILV) of the DFG method S19 originally validated by Harald Weber (Specht Study No.: BAY-0903V, Bayer CropScience Project No.: P682097525, 07-Jul-09). The method was independently validated successfully for the determination of residues of cis-deltamethrin in/on animal matrices by GC/MS, exemplified for whole milk, hen's egg, bovine muscle, liver, kidney and fat, demonstrating the LOQ of 0.01 mg/kg.

It is concluded that DFG method S19 fulfils the reproducibility requirements as defined in the Council Directive 91/414/EEC, in the EC Guidance document on residue analytical methods (SANCO/825/00 rev. 7 17/03/04) and in the OECD Guidance Document on Pesticide Residue Analytical Methods (ENV/JM/Mono (2007) 17, 2007-08-13) and is, therefore, applicable as an enforcement method.

A 2.1.2.2.1.3 Confirmatory method (if required)

No confirmatory method is required

Comments of zRMS:	Accepted. See point A 2.1.1.1.1.3
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A 2.1.2.2.1.4 Extraction efficiency

Refer to [A 2.1.1.1.1.3](#)

A 2.1.2.3 Description of Methods for the Analysis of Body Fluids and Tissues (KCP 5.2)

A 2.1.2.3.1 Analytical method 01127 for the determination of deltamethrin in blood

A 2.1.2.3.1.1 Method validation

Comments of zRMS:	The analytical method 01127 was successfully validated for the determination of residues of deltamethrin in blood by HPLC-MS/MS. Two MRM transitions were monitored for deltamethrin (m/z 523 → m/z 281 for quantitation and m/z 523 → m/z 181 for confirmation). The limit of quantitation (LOQ) for deltamethrin in cattle blood was 50 µg/L. Mean recoveries for each fortification level and the overall mean recoveries were within the 70% - 110% range for deltamethrin for both MRM transitions. Relative standard deviations were below 20%. The study is acceptable.
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Reference:	KCP 5.2.3/01
Title:	Analytical method 01127 for the determination of cyfluthrin and deltamethrin in blood by HPLC-MS/MS
Report:	Krebber, R.; 2009; MR-08/176; M-348630-01-1
Authority registration No:	
Guideline(s):	SANCO/825/00 rev. 7 of March 17, 2004; BBA Guideline: Residue Analytical Methods for Post-Registration Control Purposes of July 21, 1998; EU: 96/46/EC amending Council Directive 91/414/EEC of 16 July 1996
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

This method describes the determination of deltamethrin (among other analytes not reported here) in cattle blood by HPLC-MS/MS and provides validation data for Multiple Reaction Monitoring (MRM) using electrospray in the positive mode. The sample is extracted and deproteinized by mixing with acetonitrile and subsequent centrifugation. The supernatant is diluted with water and the determination is performed by direct injection in an HPLC-MS/MS instrument. Two MRM transitions were monitored for deltamethrin (m/z 523 \rightarrow m/z 281 for quantitation and m/z 523 \rightarrow m/z 181 for confirmation). Quantification is carried out by external calibration using matrix-matched standards.

An aliquot of the sample solution was injected into the high performance liquid chromatograph and subjected to reversed phase chromatography coupled with tandem mass spectrometry (MS/MS) with electrospray ionisation. The MS/MS instrument was operated in the Multiple Reaction Monitoring mode (MRM). The pseudomolecular ions of the analytes ($[M+H]^+$, $[M-H]^-$ or any adducts) were selected by the first quadrupole. These precursor ions were impulsed with nitrogen in the collision cell (second quadrupole) and the resulting fragment ions (product ions) were separated according to their m/z ratio in the third quadrupole. Two of these product ions per analyte were selected: one product ion (MRM-transition) serving for quantitation and the second for confirmation.

Results and discussions

The results of the method validation are summarized in the tables below.

Table A 46: Recovery results from method validation of deltamethrin using the analytical method 01127

Matrix	Analyte	Fortification level ($\mu\text{g/L}$) (n = 5)	Recoveries (%) (single values)					Mean (%)	RSD (%)	Overall mean (%)	RSD (%)
Cattle blood	deltamethrin (m/z 523 \rightarrow m/z 281, quantitation)	50	111	116	118	117	107	114*	4.2	111*	4.1
		500	107	109	110	108	106	108	1.4		
	deltamethrin (m/z 523 \rightarrow m/z 181, confirmation)	50	109	117	116	116	101	112*	6.0	110	4.8
		500	107	108	109	106	105	107	1.6		

* The mean recovery rate is slightly above the usual acceptance limit of 110%. This is a result of an inaccuracy of the extract volume which is used for calculation. The extract volume is assumed as 1 mL (0.1 mL blood + 0.9 mL acetonitrile). The real volume is less, between 0.8 and 0.9 mL. Therefore the recovery rates rose to values above 100%. In order to enable a simple and fast analysis these higher recovery rates can be accepted.

Table A 47: Characteristics for the analytical method used for validation of deltamethrin residues in cattle blood

	Deltamethrin
Specificity	mass spectrum is provided blank value < 30% LOQ Two MRM transitions were successfully validated. Therefore the HPLC-MS/MS method is highly specific and an additional confirmatory method is not necessary. No signals/peaks interfering with the detection of the analytes were observed in solutions of untreated control specimens.
Calibration (type, number of data points)	individual calibration data is presented calibration line equation (1/x weighted): quantitation: $y = 26958.4 x - 2832.5$, $r = 0.9995$ confirmation: $y = 3017.54 x - 380.025$, $r = 0.9988$ number of data points: ≥ 5
Calibration range	2 – 50 µg/L
Assessment of matrix effects is presented	yes The MS/MS detection of deltamethrin was affected by the matrix. The peak areas of the quantification and confirmatory ion in a matrix matched sample containing 25 µg/L of deltamethrin were about 30% lower than the corresponding peak areas in deionized water. Therefore, quantification was performed using matrix-matched standards.
Limit of determination/quantification	LOQ = 50 µg/L (cattle blood) LOD = 15 µg/L (cattle blood)

Conclusion

The above data is in line with the requirements outlined in the “Guidance document on residue analytical methods, SANCO/825/00 rev. 7”. Method 01127 is therefore suitable for the determination of cis-Deltamethrin in blood matrix representative of body fluids.

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

A 2.1.2.4.1 Analytical method 00877 (including amendment) for the determination of deltamethrin (cis-deltamethrin) and its isomers alpha-R-deltamethrin and trans-deltamethrin in soil and sediment

A 2.1.2.4.1.1 Method validation

Comments of zRMS:	<p>The analytical method 00877 was validated for the determination of the total residue of deltamethrin in soil and sediment by means of HPLC-MS/MS. The total residue is defined as the sum of cis-deltamethrin (AE F032640), α-R-deltamethrin (AE F108569) and trans-deltamethrin (AE F0035073). The method was optimised and validated using cis-deltamethrin.</p> <p>The limit of quantitation of the method is 0.1 µg/kg for cis-deltamethrin.</p> <p>Mean recoveries for each fortification level and the overall mean recoveries were within the 70% - 110% range for deltamethrin. Relative standard deviations were below 20%.</p> <p>For confirmation of deltamethrin identity the mass fragments monitored were 523 m/z → 281 m/z. The mass fragments identified for the internal standard ([phenoxy-¹³C₆]deltamethrin) were 529 m/z → 281 m/z.</p> <p>This method has been satisfactorily validated in accordance with SANCO 3029/99/rev.4 and SANCO/825/00.</p>
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Reference:	KCP 5.2.4/01
Title:	Analytical method 00877 for the determination of total residues of deltamethrin (AE F032640) in / on soil and sediment by HPLC-MS/MS
Report:	Brumhard, B.; 2005; C047210; M-247896-01-1
Authority registration No:	
Guideline(s):	--
Deviations:	--
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Reference:	KCP 5.2.4/02
Title:	Analytical method 00877 for the determination of total residues of Deltamethrin (AE F032640) in/on soil and sediment by HPLC-MS/MS
Report:	Brumhard, B.; 2009; 00877; M-246580-02-1
Authority registration No:	
Guideline(s):	EC Guidance Document on Residue Analytical Methods, SANCO/825/00 rev.7 of March 17,2004 BBA Guideline: Residue Analytical Methods for Post-Registration Control Purposes of July 21, 1998 Commission Directive 96/46/EC amending Council Directive 91/414/EEC of 16 July 1996 US EPA OPPTS 835.6100, 835.6200
Deviations:	With the exception of recognised differences that exist between the GLP principles/standards of OECD and those FIFRA and JMAFF (for instance, authority granted agency inspectors).
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The analytical method 00877 was developed for the determination of deltamethrin (cis-deltamethrin) and its isomers alpha-R-deltamethrin and trans-deltamethrin in soil and sediment. The method was optimised and validated using cis-deltamethrin. Residues were extracted from soil with acetonitrile/10 mM ammonium acetate solution (9/1, v/v) using a microwave extractor. A stable isotopically labelled analyte was added to the extract. After centrifugation at > 12000 G to remove fine soil particles, the extract was analysed without further clean up by HPLC-MS/MS in positive ion mode. Residues were quantified using an internal standard of isotopically labelled [phenoxy-¹³C₆]deltamethrin to eliminate possible matrix effects. The MRM transitions, m/z 523 → 281 for cis-deltamethrin and m/z 529 → 281 for [phenoxy-¹³C₆]deltamethrin, were monitored for each matrix tested.

Results and discussions

The results of the method validation are summarized in the tables below.

Table A 48: Recovery results from method validation of deltamethrin using the analytical method 00877

Matrix	Analyte	Fortification level (µg/kg) (n = 5)	Mean recovery (%)	RSD (%)	Overall mean recovery (%)	Overall RSD (%)
Höfchen soil	Deltamethrin m/z 523 → 281	0.1	94.6	3.8	97.6	4.1
		1.0	101	1.5		
Laacher Hof		0.1	91.0	7.7	97.0	8.2
		1.0	103	1.7		
Sediment		0.1	102	5.2	102	3.8

Matrix	Analyte	Fortification level (µg/kg) (n = 5)	Mean recovery (%)	RSD (%)	Overall mean recovery (%)	Overall RSD (%)
		1.0	101	2.1		
Overall Mean		0.1	95.9	7.3	98.8	5.9
		1.0	102	2.0		

Table A 49: Characteristics for the analytical method used for validation of deltamethrin residues in soil

	deltamethrin
Specificity	mass spectrum is provided blank value < 30% LOQ
Calibration (type, number of data points)	individual calibration data is presented calibration line equation: $y = 0.509282 x + 0.00420206$ correlation coefficient $r = 0.9999$ number of data points: 8
Calibration range	0.015 – 5 µg/L in solvent standards, corresponding to a soil concentration of 0.03 – 10 µg/kg
Assessment of matrix effects is presented	Yes Possible matrix effects with deltamethrin were eliminated by using an internal standard solution of an isotopically labelled analytical standard.
Limit of determination/quantification	cis-deltamethrin: LOQ = 0.1 µg/kg LOD = 0.03 µg/kg

Conclusion

The method 00877 is suitable to determine residues of cis-deltamethrin (deltamethrin), as well as its isomers (trans-deltamethrin and alpha-R-deltamethrin) in soil and sediment. The method was optimised and validated using cis-deltamethrin. The LOQ of the method is 0.1 µg/kg and the LOD is 0.03 µg/kg for deltamethrin. This method further fulfils the requirements for the SANCO/825/00 rev. 8.1 and is therefore suitable as enforcement method in soil.

A 2.1.2.4.2 Analytical method 01358 for the determination of cis-deltamethrin residues in/on soil/sediment

A 2.1.2.4.2.1 Method validation

Comments of zRMS:	<p>The analytical method 01358 was successfully validated for the determination of residues of cis-deltamethrin in three different soils by HPLC-MS/MS.</p> <p>Two MRM transitions were monitored for each soil tested m/z 523 → 281 for quantitation and m/z 525 → 283 for confirmation of cis-deltamethrin. Therefore, the HPLC- MS/MS method is highly specific and an additional confirmatory method is not necessary.</p> <p>The limit of quantitation (LOQ) for each single analyte was 0.2 µg/kg in soil. The limit of determination (LOD) for each single analyte was 0.07 µg/kg.</p> <p>Mean recoveries for each fortification level and the overall mean recoveries were within the 70% - 110% range for all soils tested. Relative standard deviations were below 20%.</p> <p>The analytical method meets all guideline criteria according to SANCO/825/00 rev. 8.1 and SANCO/3029/99 rev. 4.</p> <p>The study is acceptable.</p>
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Reference:	KCP 5.2.4/03
Title:	Analytical method 01358 for the determination of cis-deltamethrin in soil by HPLC-MS/MS
Report:	Freitag, T.; 2013; MR-13/002; M-451547-01-1
Authority registration No:	
Guideline(s):	<p>Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC</p> <p>European Commission Guidance Document for Generating and Reporting Methods of Analysis in Support of Pre-Registration data Requirements for Annex II (part A, Section 4) and Annex III (part A, section 5) of directive 91/414, SANCO/3029/99 rev. 4, 11/07/00</p> <p>Guidance document on residue analytical methods, SANCO/825/00/rev. 8.1, European Commission, Directorate General Health and Consumer Protection 16/11/2010</p> <p>US EPA Residue Chemistry Test Guideline OCSPP 860.1340: Residue Analytical Method</p>
Deviations:	not applicable
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The analytical method 01358 developed for the determination of cis-deltamethrin residues in/on soil is proposed as new enforcement method for soil (or sediment, if needed).

Soil samples of 20 g were extracted four times in a laboratory rotating mixer with a total of 100 mL of acetone/formic acid (100/1). The extracts were subjected to a liquid/liquid partition step on a ChemElut *CE 1010 column. After clean up and evaporation to dryness the residues were resolved and subsamples of the extracts are centrifuged to remove fine particles of the soil. Identification and quantitation of the active substance is done by high performance liquid chromatography using MS/MS detection in the Multiple Reaction Monitoring mode.

The method was validated using three different soils "Höfchen", "Laacher Hof", and "Dollendorf".

Two MRM transitions were monitored for each soil tested m/z 523 → 281 for quantitation and m/z 525 → 283 for confirmation of cis-deltamethrin.

Results and discussions

The results of the method validation are summarized in the tables below.

Table A 50: Recovery results from method validation of cis-deltamethrin using the analytical method 01358

Matrix	Analyte	Fortification level (µg/kg) (n = 5)	Mean recovery (%)	RSD (%)	Overall mean recovery (%)	Overall RSD (%)
soil Höfchen	cis- deltamethrin m/z 523 → 281	0.2	75	10.5	78	12.5
		2	81	14.0		
soil Dollendorf		0.2	81	14.8	81	10.6
		2	80	5.7		
soil Laacher Hof		0.2	96	13.8	97	9.6
		2	97	4.4		
soil Höfchen	cis- deltamethrin m/z 70 → 43	0.2	86	19.7	85	15.5
		2	84	12.1		
soil Dollendorf		0.2	72	8.0	75	7.3
		2	78	4.1		
soil Laacher Hof		0.2	101	12.8	99	9.1
		2	97	2.2		

Table A 51: Characteristics for the analytical method used for validation of cis-deltamethrin residues in soil

	cis-deltamethrin
Specificity	mass spectrum is provided blank value < 30% LOQ
Calibration (type, number of data points)	individual calibration data is presented calibration line equations: quantitation (m/z 523 → 281): soil Höfchen: $y = 14872.1 x + 606.636$, $r = 0.9920$ soil Laacher Hof: $y = 13690.8 x + 234.938$, $r = 0.9922$ soil Dollendorf: $y = 11186.6 x + 118.005$, $r = 0.9990$ confirmation (m/z 525 → 283) : soil Höfchen: $y = 8072.27 x - 102.905$, $r = 0.9940$ soil Laacher Hof: $y = 7430.17 x + 694.573$, $r = 0.9935$ soil Dollendorf: $y = 6219.77 x + 435.711$, $r = 0.9982$ number of data points: ≥ 6
Calibration range	0.125 – 20 µg/L (matrix standards)
Assessment of matrix effects is presented	matrix matched standards were used
Limit of determination/quantification	LOQ = .2 µg/kg (soil) LOD = 0.07 µg/kg

Conclusion

The method meets all guideline criteria to determine residues of cis-deltamethrin in soil at 0.2 µg/kg and 2 µg/kg for the quantifier mass transition. It is proposed as the new enforcement method for soil (or sediment, if needed). This method further fulfils the requirements for the SANCO/825/00 rev. 8.1 and is therefore suitable as enforcement method in soil/sediment.

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

A 2.1.2.5.1 Analytical method 01383 for the determination of cis-deltamethrin residues in drinking and surface water

A 2.1.2.5.1.1 Method validation

Comments of zRMS:	<p>The analytical method 01383 was successfully validated for the determination of residues of cis-deltamethrin in surface water by HPLC-MS/MS using two MRM transitions. Two MRM transitions were monitored for deltamethrin (m/z 523 → m/z 281 for quantitation and m/z 523 → m/z 181 for confirmation), so an additional confirmatory method is not necessary. In the SANCO/825/00 rev. 8.1 it is stated that <i>“Provided that a method has been successfully validated for surface water at the LOQ required for drinking water, no further validation in drinking water is required.”</i></p> <p>The limit of quantitation (LOQ) for deltamethrin is 0.05 µg/L in surface water. Because of the direct measurement of the samples recovery rates cannot be calculated. Thus precision data are presented.</p> <p>The relative standard deviations for the peak areas were below 20% for all MRM transitions. The analytical method meets all guideline criteria to determine concentrations of deltamethrin in drinking and surface water at 0.05 µg/L according to SANCO/825/00 rev. 8.1 and SANCO/3029/99 rev. 4.</p> <p>The study is acceptable.</p>
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Reference:	KCP 5.2.5/01
Title:	Analytical method 01383 for the determination of deltamethrin in drinking and surface water by HPLC-MS/MS
Report:	Krebber, R.; Braune, M.; 2013; MR-13/053; M-464818-01-1
Authority registration No:	
Guideline(s):	<p>Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC</p> <ul style="list-style-type: none"> • EC Guidance Document on Residue Analytical Methods, SANCO/825/00 rev. 8.1 of November 16, 2010 • European Commission Guidance Document for Generating and Reporting Methods of Analysis in Support of Pre-Registration data Requirements for Annex II (part A, Section 4) and Annex III (part A, section 5) of directive 91/414, SANCO/3029/99 rev. 4, July 11, 2000
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The analytical method 01383 developed for the determination of cis-deltamethrin residues in drinking and surface water is proposed as new enforcement method for water. A validation for drinking water is not necessary because the limit of quantitation for surface water is below the drinking water limit (i.e. < 0.1 µg/L).

Water samples were investigated after addition of acetonitrile and formic acid by direct injection into the HPLC-MS/MS instrument using the positive ion mode for deltamethrin without further clean-up. Concentrations were quantified using external matrix-matched standard solutions.

Two MRM transitions were monitored for deltamethrin (m/z 523 → m/z 281 for quantitation and m/z 523 → m/z 181 for confirmation).

Results and discussions

The results of the method validation are summarized in the tables below.

Because of the direct measurement of the samples, recovery rates cannot be calculated. Thus precision data are presented.

Table A 52: Recovery/ precision results from method validation of cis-deltamethrin using the analytical method 01383

Matrix	Analyte	Fortification level (µg/L) (n = 10)	Mean value (peak area)	RSD (%)
Surface water	cis-deltamethrin m/z 523 → 281 (quantitation)	0.05	11381	2.1
		0.5	102355	3.7
	cis-deltamethrin m/z 523 → 181 (confirmation)	0.05	1149	3.4
		0.5	10122	3.0

Table A 53: Characteristics for the analytical method used for validation of cis-deltamethrin residues in surface water

	cis-deltamethrin
Specificity	mass spectrum is provided blank value < 30% LOQ no signals/peaks interfering with the detection of the analyte
Calibration (type, number of data points)	individual calibration data is presented calibration line equations (1/x weighted): m/z 523 → 281 (quantitation): $y = 2.71 \cdot 10^5 x - 503$, $r = 0.9997$ m/z 523 → 181 (confirmation): $y = 2.64 \cdot 10^4 x + 170$, $r = 0.9996$ number of data points: ≥ 6
Calibration range	0.014 – 8 µg/L (standard solutions in a mixture of surface water / acetonitrile / formic acid (800/200/0.2, v/v/v)) corresponding to 0.017 - 10 µg/L in surface water
Assessment of matrix effects is presented	yes The MS/MS detection is affected by the matrix. Matrix effects can be eliminated by using matrix-matched standard solutions.
Limit of determination/quantification	LOQ = 0.05 µg/L (surface water)

Conclusion

The method 01383 meets all guideline criteria of SANCO/825/00 rev. 8.1 to determine concentrations of deltamethrin in drinking and surface water at 0.05 µg/L. It is proposed as the new enforcement method for water samples. Therefore, an independent laboratory validation of method no. 01383 was performed, which is summarized in the following.

A 2.1.2.5.1.2 Independent laboratory validation for method 01383

Comments of zRMS:	<p>The method 01383 was independently validated for the determination of deltamethrin in surface water, using LC/MS/MS (LOQ: 0.05 µg/L).</p> <p>Two MRM transitions were monitored for deltamethrin. The results of the independent method validation were confirmed using a 2nd MRM transition for confirmation.</p> <p>The method was shown to be selective and yields accurate and repeatable results.</p> <p>The validation data can be considered sufficient according to SANCO/825/00 rev. 8.1 for ground and drinking water. All validation parameters were within the required range.</p> <p>The study is acceptable.</p>
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Reference:	KCP 5.2.5/02
Title:	Independent laboratory validation of BCS analytical method no. 01383 for the determination of deltamethrin in surface water, using LC/MS/MS
Report:	Stanislawski, T.; 2013; P 3021 G; M-471762-01-1
Authority registration No:	
Guideline(s):	<p>Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC</p> <p>European Commission Guidance Document for Generating and Reporting Methods of Analysis in Support of Pre-Registration data Requirements for Annex II (part A, Section 4) and Annex III (part A, section 5) of directive 91/414, SANCO/3029/99 rev. 4, 11/07/00</p> <p>Guidance document on Pesticide Residue Analytical Methods, SANCO/825/00/rev. 8.1, European Commission, Directorate General Health and Consumer Protection 16/11/2010</p> <p>Commission Regulation (EU) No. 283/2013 of 1 March 2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market.</p>
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The analytical method no. 01383 was validated for the determination of cis-deltamethrin in surface water. Water samples were determined after addition of acetonitrile and formic acid by direct injection into the LC-MS/MS instrument using the positive ion mode for deltamethrin without further clean-up. The solution was subjected to HPLC-MS/MS and the concentrations were quantified using matrix matched standards.

Two MRM transitions were monitored for deltamethrin, m/z 523 → 281 as 1st MRM (quantification) and m/z 523 → 181 as 2nd MRM (confirmation).

Results and discussions

The results of the method validation are summarized in the tables below.

Because of the direct measurement of the samples recovery rates cannot be calculated. Thus precision data are presented.

Table A 54: Recovery/ precision results from independent laboratory validation of cis-deltamethrin using the analytical method 01383

Matrix	Analyte	Fortification level (µg/L) (n = 5)	Mean value (peak area)	RSD (%)
Surface water	cis-deltamethrin m/z 523 → 281 (quantitation)	0.05	7611	6.5
		0.5	86110	4.0

Matrix	Analyte	Fortification level (µg/L) (n = 5)	Mean value (peak area)	RSD (%)
	cis-deltamethrin m/z 523 → 181 (confirmation)	0.05	866	5.5
		0.5	8828	4.0

Table A 55: Characteristics for the analytical method used for independent laboratory validation of cis-deltamethrin residues in surface water

	cis-deltamethrin
Specificity	mass spectrum is provided blank value < 30% LOQ no signals/peaks interfering with the detection of the analyte
Calibration (type, number of data points)	individual calibration data is presented calibration line equations (1/x weighted): m/z 523 → 281 (quantitation): $y = 1.95 \cdot 10^5 x - 102$, $r = 0.9998$ m/z 523 → 181 (confirmation): $y = 2.01 \cdot 10^4 x + 66.3$, $r = 0.9999$ number of data points: 7
Calibration range	0.012 – 8 µg/L (standard solutions in a mixture of surface water / acetonitrile / formic acid (800/200/0.2, v/v/v)), corresponding to 0.015 - 10 µg/L in surface water
Assessment of matrix effects is presented	Matrix effects were be eliminated by using matrix-matched standard solutions.
Limit of determination/quantification	LOQ = 0.05 µg/L (surface water)

Conclusion

The method 01383 meets all guideline criteria of SANCO/825/00/rev. 8.1 to determine concentrations of deltamethrin in surface water at 0.05 µg/L. It can be used as enforcement method for water samples.

A 2.1.2.5.2 Analytical method 00886 for the determination of deltamethrin (cis-deltamethrin) and its isomers α -R-deltamethrin and trans-deltamethrin in surface water

A 2.1.2.5.2.1 Method validation

Comments of zRMS:	<p>The method 00886 was validated for the determination of total residues of deltamethrin in surface water by means of HPLC-MS/MS. The total residue is defined as the sum of cis-deltamethrin (AE F032640), α-R-deltamethrin (AE F108569) and trans-deltamethrin (AE F0035073).</p> <p>It is known that cis-deltamethrin can be transformed by chemical or biological processes to its diastereomers α-R-deltamethrin and trans-deltamethrin. For ecotoxicological risk assessment purposes α-R- and trans-deltamethrin are assumed to have the same biological/pesticidal activity as cis-deltamethrin. This method is able to quantify cis-deltamethrin as well as its isomers trans-deltamethrin and α-R-deltamethrin. The method was optimised and validated using cis-deltamethrin.</p> <p>For confirmation of deltamethrin identity the mass fragments monitored were 523 m/z \rightarrow 281 m/z. The mass fragments identified for the internal standard ([phenoxy-¹³C₆]deltamethrin) were 529 m/z \rightarrow 281 m/z.</p> <p>The limit of quantitation for cis-deltamethrin in surface water is 0.005 µg/L.</p> <p>The limit of detection in surface water is 0.002 µg/L.</p> <p>The individual and average recoveries at each fortification level were within the range of 70 – 110% for deltamethrin. The RSD values were below 20%.</p> <p>This method has been satisfactorily validated in accordance with SANCO 3029/99/rev.4.</p> <p>The study is acceptable.</p>
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Reference:	KCP 5.2.5/03
Title:	Analytical method 00886 for the determination of total residues of deltamethrin (AE F032640) in surface water by HPLC-MS/MS
Report:	Brumhard, B.; 2005; C047388; M-248040-01-1
Authority registration No:	
Guideline(s):	--
Deviations:	--
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The analytical method was developed for the determination of deltamethrin (cis-deltamethrin) and its isomers α -R-deltamethrin and trans-deltamethrin in surface water. The method was optimised and validated using deltamethrin. Water samples were diluted with 20% acetonitrile, and then ammonium acetate added to give a 10 mM solution. A stable isotopically labelled analyte was added to the sample, which was then analysed directly by HPLC-MS/MS in positive ion mode. Residues were quantified using an internal standard of isotopically labelled [phenoxy-¹³C₆]deltamethrin to minimise possible matrix effects. The MRM transitions, m/z 523 \rightarrow 281 for cis-deltamethrin and m/z 529 \rightarrow 281 for [phenoxy-¹³C₆]deltamethrin, were monitored for identification and quantification.

Results and discussions

The results of the method validation are summarized in the tables below.

Table A 56: Recovery results from method validation of cis-deltamethrin using the analytical method 00886

Matrix	Analyte	Fortification level (µg/L) (n = 10)	Mean recovery (%)	RSD (%)	Overall mean recovery (%)	Overall RSD (%)
River water	cis-deltamethrin m/z 523 \rightarrow 281	0.0059	100	5.7	100	4.2
		0.059	100	1.8		

Table A 57: Characteristics for the analytical method used for validation of cis-deltamethrin residues in surface water

	cis-deltamethrin
Specificity	mass spectrum is provided blank value < 30% LOQ
Calibration (type, number of data points)	individual calibration data is presented calibration line equation (1/x weighted): $y = 0.746692 x + 0.0053296$ correlation coefficient $r = 0.99905$ number of data points: 6
Calibration range	0.004 – 118.1 µg/L
Assessment of matrix effects is presented	yes The MS/MS detection of cis-deltamethrin was affected by the matrix. Possible matrix effects were minimised by using an internal standard solution of an isotopically labelled analytical standard
Limit of determination/quantification	LOQ = 0.005 µg/L (surface water) LOD = 0.002 µg/L

Conclusion

The method is suitable to determine residues of deltamethrin, as well as its isomers trans-deltamethrin and α -R-deltamethrin in surface water. The method was optimised and validated using deltamethrin. The LOQ of the method is 0.005µg/L and the LOD is 0.002 µg/L for deltamethrin.

A 2.1.2.5.3 Analytical method 00886/M001 for the determination of deltamethrin residues in surface water

A 2.1.2.5.3.1 Method validation

Comments of zRMS:	<p>The method 00886 developed for <u>total residues of deltamethrin</u> in surface water was modified. The analytical method 00886/M001 was validated for the determination of <u>deltamethrin</u> residues in surface water.</p> <p>The limit of quantitation (LOQ) for deltamethrin was 2 ng/L.</p> <p>For confirmation of deltamethrin identity the mass fragments monitored were 523 m/z → 281 m/z. The mass fragments identified for the internal standard ([phenoxy-¹³C₆]deltamethrin) were 529 m/z → 281 m/z.</p> <p>The individual and average recoveries at each fortification level were within the range of 70 – 110% for deltamethrin. The RSD values were below 20%.</p> <p>This method has been satisfactorily validated in accordance with SANCO 3029/99/rev.4.</p> <p>The study is acceptable.</p>
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Reference:	KCP 5.2.5/04
Title:	Modification M001 of analytical method 00886 for the determination of total residues of deltamethrin (AE F032640) in surface water by HPLC-MS/MS
Report:	Krebber, R.; Braune, M.; 2007; 00886/M001; M-291746-01-1
Authority registration No:	
Guideline(s):	US EPA OPPTS 835.6100, 835.6200
Deviations:	not specified
GLP/GEP:	no
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The analytical method 00886/M001 was validated for the determination of deltamethrin residues in surface water. It is a modification of the method developed for total residues of deltamethrin in surface water. Water

samples were adjusted to pH 4 with formic acid, and then diluted with acetonitrile (1:1, v/v). A stable isotopically labelled analyte was added to the sample, which was then analysed directly by HPLC-MS/MS in positive ion mode. Residues were quantified using an internal standard of isotopically labelled [phenoxy-¹³C₆]deltamethrin.

The MRM transitions, m/z 523 → 281 for deltamethrin and m/z 529 → 281 for [phenoxy-¹³C₆]deltamethrin, were monitored for identification and quantification.

Results and discussions

The results of the method validation are summarized in the tables below.

Table A 58: Recovery results from method validation of deltamethrin using the analytical method 0086/M001

Matrix	Analyte	Fortification level (µg/L) (n = 10)	Mean recovery (%)	RSD (%)	Overall mean recovery (%)	Overall RSD (%)
Surface Water	Deltamethrin m/z 523 → 281	0.002	105	2.4	101	4.6
		0.01	98	3.3		

Table A 59: Characteristics for the analytical method used for validation of deltamethrin residues in water

	deltamethrin
Specificity	mass spectrum is provided No residues of deltamethrin were detected in the test water control samples.
Calibration (type, number of data points)	individual calibration data is presented calibration line equation (1/x weighted): $y = 0.00195024 x + 0.957351$ correlation coefficient $r = 0.9995$ number of data points: 5
Calibration range	2 – 100 ng/L (solvent standards)
Assessment of matrix effects is presented	yes The MS/MS detection of deltamethrin was not affected by the matrix.
Limit of determination/quantification	LOQ = 0.002 µg/L (test water) LOD = 0.001 µg/L

Conclusion

The method is suitable to determine residues of deltamethrin in surface water. The LOQ of the method is 0.002 µg/L and the LOD is 0.001 µg/L.

A 2.1.2.6 Description of Methods for the Analysis of Air (KCP 5.2)

No new or additional studies have been submitted.

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

None

A 2.2 Analytical methods for Flupyradifurone

A 2.2.1 Methods used for the generation of pre-authorization data (KCP 5.1)

A 2.2.1.1 Description of analytical methods for the determination of residues in plant matrices (KCP 5.1)

A 2.2.1.1.1 Analytical method 1 (Method 01304)

The analytical method 01304 was fully validated for the determination of residues of flupyradifurone and its metabolite difluoroacetic acid (DFA) in the representative crop matrices dried bean seed, cereal forage, orange fruit, soybean seed, tomato fruit and wheat grain, as reported in the DAR (NL, 2015) and the EFSA Conclusion on the peer review (EFSA Journal 2015;13(2):4020). For the crop submitted in this application, additional validations were conducted with a limited dataset of recoveries during the conduct of the residue studies. Information on the additional recoveries is given below.

A 2.2.1.1.1 Method validation

Comments of zRMS:	<p>Full validation data is documented in method 01304 for matrices representing the 5 major crop groups, including dry seeds of beans, forage, orange fruit, soybean seeds, tomato fruit, and wheat grain.</p> <p>For the matrices relevant to residue studies, but not included in the original validation, a limited set of additional validation recoveries were analyzed within the course of these studies.</p> <p>The individual and average recoveries at each fortification level and overall per matrix were within the range of 70 – 110% for all analytes. The RSD values were below 20%.</p> <p>All method validation data complies with the current guideline requirements for data collection methods. The validation of method 01304 for the determination of parent flupyradifurone and its metabolite DFA can therefore be considered successful for the additionally tested matrices (primary and rotational crops, processed commodities).</p> <p>Accepted.</p>
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Primary crop studies

Reference:	KCP 5.1.2.5/07
Title:	Determination of the residues of BYI 02960 and deltamethrin in/on rape after spray application of deltamethrin & flupyradifurone EC 085 in Spain and Portugal
Report:	Miara, C.; Nayyar, B.; Kowalski, N.; 2018; 16-2169; M-645539-01-1
Authority registration No:	
Guideline(s):	<p>Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market</p> <p>OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009)</p> <p>US EPA OCSPP 860.1500, Crop Field Trial</p>
Deviations:	None
GLP/GEP:	Yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/08
Title:	Determination of the residues of BYI 02960 and deltamethrin in/on rape after spray application of deltamethrin & flupyradifurone EC 085 in Spain, Portugal, southern France and Italy
Report:	Miara, C.; Nayyar, B.; Kowalski, N.; 2018; 16-2131; M-643446-01-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP 860.1500, Crop Field Trial
Deviations:	None
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/03
Title:	Determination of the residues of BYI 02960 and deltamethrin in/on rape after spray application of deltamethrin & flupyradifurone EC 085 in Germany, Belgium and northern France
Report:	Kaussmann, M.; Kerkerling, S.; 2018; 16-2044; M-641044-01-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP 860.1500, Crop Field Trial
Deviations:	None
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Rotational crop studies

Reference:	KCP 5.1.2.5/09
Title:	Determination of the residues of BYI 02960 in/on potato and soil after spraying of BYI 02960 SL 200 in the field in Germany, the Netherlands, Italy and Spain
Report:	Freitag, T.; 2018; 16-2510; M-613149-01-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guidelines for the Testing of Chemicals. Residues in Rotational Crops (Limited Field Studies). 504. 2007-01-08 OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1900, Field Accumulation in Rotational Crops US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations:	None
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/10
Title:	Determination of the residues of BYI 02960 in/on the field rotational crop rape and soil after spray application of BYI 02960 SL 200 to bare soil in the field in Belgium and the Netherlands - Final report
Report:	Freitag, T.; Effertz, C.; 2018; 16-2511; M-617178-02-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guidelines for the Testing of Chemicals. Residues in Rotational Crops (Limited Field Studies). 504. 2007-01-08 OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1900, Field Accumulation in Rotational Crops US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations:	None
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/11
Title:	Determination of the residues of BYI 02960 in/on the field rotational crop rape and soil after spray application of BYI 02960 SL 200 to bare soil in the field in Italy and Portugal
Report:	Kaussmann, M.; van Berkum, S.; 2018; 16-2521; M-613466-02-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guidelines for the Testing of Chemicals. Residues in Rotational Crops (Limited Field Studies). 504. 2007-01-08 OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1900, Field Accumulation in Rotational Crops US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations:	Yes, but acceptable
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/12
Title:	Determination of the residues of BYI 02960 in/on the field rotational crop barley and soil after spray application of BYI 02960 SL 200 to bare soil in the field in United Kingdom and the Netherlands
Report:	Freitag, T.; Kaussmann, M.; 2018; 16-2512; M-612254-01-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guidelines for the Testing of Chemicals. Residues in Rotational Crops (Limited Field Studies). 504. 2007-01-08 OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1900, Field Accumulation in Rotational Crops US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations:	Yes, but acceptable
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/13
Title:	Determination of the residues of BYI 02960 in/on the field rotational crop maize/corn and soil after spray application of BYI 02960 SL 200 to bare soil in the field in France (South) and Portugal - Final report
Report:	Freitag, T.; van Berkum, S.; 2018; 16-2524; M-617943-01-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guidelines for the Testing of Chemicals. Residues in Rotational Crops (Limited Field Studies). 504. 2007-01-08 OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1900, Field Accumulation in Rotational Crops US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations:	none
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/14
Title:	Determination of the residues of BYI 02960 in/on the field rotational crop strawberry and soil after spray application of BYI 02960 SL 200 to bare soil in the field in Belgium and the Netherlands
Report:	Freitag, T.; Hoffmeister, R.; 2018; 16-2515; M-617563-01-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guidelines for the Testing of Chemicals. Residues in Rotational Crops (Limited Field Studies). 504. 2007-01-08 OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1900, Field Accumulation in Rotational Crops US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations:	None
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/15
Title:	Determination of the residues of BYI 02960 in/on the field rotational crop cauliflower, broccoli and soil after spray application of BYI 02960 SL 200 to bare soil in the field in Belgium, the Netherlands, Italy and Spain
Report:	Freitag, T.; Effertz, C.; 2018; 16-2516; M-617941-02-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guidelines for the Testing of Chemicals. Residues in Rotational Crops (Limited Field Studies). 504. 2007-01-08 OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1900, Field Accumulation in Rotational Crops US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations:	None
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Processing studies

Reference:	KCP 5.1.2.5/16
Title:	BYI 02960 200 SL - Magnitude of the residue in/on soybean processed commodities
Report:	Lenz, C.; 2012; RARVY029; M-428939-01-2
Authority registration No:	
Guideline(s):	EPA Ref.: OPPTS 860.1500, Crop Field Trials PMRA Ref.: DACO 7.4.5. Processed Food/Feed OECD Test Guideline 508: Residues in Processed Commodities (Adopted Oct., 3 2008)
Deviations:	Weather data, pesticide history data, irrigation records, maintenance chemical applications, field sample weights, cultural practices records, soil characterization and plot slope information were not collected under GLP. A protocol amendment identifying the analytical method to be used in the study was not signed until after sample analyses were initiated.
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/17
Title:	BYI 02960 200 SL - Magnitude of the residue in cotton processed commodities (crop subgroup 20C)
Report:	Lenz, C.; Beedle, E.; 2012; RARVY033; M-433122-01-1
Authority registration No:	
Guideline(s):	EPA Ref.: OPPTS 860.1520, Processed Food/Feed PMRA Ref.: DACO 7.4.5. Processed Food/Feed OECD Test Guideline 508: Residues in Processed Commodities (Adopted Oct., 3 2008)
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/18
Title:	BYI 02960 200 SL - Magnitude of the residue in/on potato processed commodities
Report:	Lenz, C.; 2012; RARVY038; M-430542-01-2
Authority registration No:	
Guideline(s):	EPA Ref.: OPPTS 860.1520, Processed Food/Feed PMRA Ref.: DACO 7.4.5. Processed Food/Feed OECD Test Guideline 508: Residues in Processed Commodities (Adopted Oct., 3 2008)
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/19
Title:	Determination of the residues of BYI 02960 in/on potato and the processed fractions (tuber, washed; peel washed; tuber, peeled; tuber, cooked; tuber with peel, cooked; fibre; pulp, dry; starch; waste; waste, dried; flakes; and crisps (Am.: chips)) after spray application of BYI 02960 SL 200 in the field in Germany and the Netherlands
Report:	Freitag, T.; Hoffmeister, R.; 2016; 13-3149; M-546878-01-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC, EC Guidance working document 7029/VI/95 rev.5 (1997-07-22), OECD 508, Adopted 2008-10-03, OECD Guideline for the Testing of Chemicals, Magnitude of Pesticide Residues in Processed Commodities US EPA OCSPP Guideline No. 860.152
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/20
Title:	Processing study - Determination of the residues of BYI 02960 in/on spring barley and the processed fractions (malt sprouts; brewer's malt; brewer's grain, hops draff; brewer's yeast; beer; pearl barley; pearl barley rub off) after spraying of BYI 02960 SL 200 in the field in Germany
Report:	Schulte, G.; Ruhl, S.; 2012; 10-3410; M-439853-01-1
Authority registration No:	
Guideline(s):	EU-Ref: Council Directive 91/414/EEC of July 15, 1991, Annex II, part A, section 6 and Annex III, part A, section 8 Residues in or on Treated Products, Food and Feed, EC Guidance working document 7029/VI/95 rev.5 (1997-07-22) EC Guidance working document 7035/VI/95 rev.5 (1997-07-22) OECD Guideline for the Testing of Chemicals, Magnitude of the Pesticide Residues in Processed Commodities, 508 (2008-10-03) US EPA Ref: OCSP 860.1520. SUPP
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/21
Title:	Processing study - Determination of the residues of BYI 02960 in/on wheat and the processed fractions (semolina; semolina bran; whiteflour bran; white flour; white bread; whole meal; wholemeal bread and wheat germ) after spraying of BYI 02960 SL 200 in the field in Germany
Report:	Schulte, G.; Bauer, J.; 2012; 10-3409; M-440307-01-1
Authority registration No:	
Guideline(s):	EU-Ref: Council Directive 91/414/EEC of July 15, 1991, Annex II, part A, section 6 and Annex III, part A, section 8 Residues in or on Treated Products, Food and Feed EC guidance working document 7029/VI/95 rev. 5 (1997-07-22) EC guidance working document 7035/VI/95 rev. 5 (1997-07-22) OECD Guideline for the Testing of Chemicals, Magnitude of the Pesticide Residues in Processed Commodities, 508 (2008-10-03) US EPA Ref: OCSSP Guideline No. 860. 1520. SUPP
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/22
Title:	BYI 02960 200 SL - Magnitude of the residue in/on wheat processed commodities
Report:	Lenz, C.; Fischer, D. R.; 2012; RARVY031; M-427047-01-2
Authority registration No:	
Guideline(s):	OPPTS 860.1520, Processed Food/Feed PMRA Ref.: DACO 7.4.5. Processed Food/Feed OECD Test Guideline 508: Residues in Processed Commodities (Adopted Oct. 3, 2008)
Deviations:	Weather data, pesticide history data, irrigation records, maintenance chemical applications, field sample weights, and cultural practices records were not collected under GLP.
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/23
Title:	BYI 02960 200 SL - Magnitude of the residue in/on field corn processed commodities
Report:	Lenz, C.; 2012; RARVY030; M-424774-01-1
Authority registration No:	
Guideline(s):	OPPTS 860.1520, Processed Food/Feed PMRA Ref.: DACO 7.4.5, Processed Food/Feed OECD Test Guideline 508: Residues in Processed Commodities (adopted Oct., 3 2008)
Deviations:	weather data, pesticide history data, irrigation records, maintenance chemical applications, field sample weights, cultural practices records and soil characterization information were not collected under GLP.
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Results and discussions

For matrices relevant in the residue studies submitted in this dRR, but not included in the original validation of method 01304, additional validation set were conducted in the course of the residue studies. These additional validation recoveries are presented in [Table A 60](#), if not already evaluated at EU level.

Table A 60: Recovery results from method validation of flupyradifurone using the analytical method 01304 in various primary, rotational crops and processed commodities

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
Flupyradifurone					
Strawberry / fruit	0.01	3	103	4.2	m/z 289 → 126 (16-2515)
	0.10	3	103	1.9	
Soybean /seed, dry	0.01	7	97	4.7	m/z 289 → 126 (RARVY029)
	1.0	3	93	5.3	
Soybean / aspirated grain fractions	0.25	3	86	8.1	m/z 289 → 126 (RARVY029)
	15	3	92	6.6	
Soybean / meal	0.01	3	91	19.6	m/z 289 → 126 (RARVY029)
	1.0	3	94	10.1	
Soybean / hull	0.01	3	93	16.1	m/z 289 → 126 (RARVY029)
	1.0	3	89	2.3	
Soybean / oil, refined	0.01	3	92	11.3	m/z 289 → 126 (RARVY029)
	1.0	3	102	8.6	
Soybean / milk	0.01	3	98	2.7	m/z 289 → 126 (RARVY029)
	1.0	3	98	1.0	
Soybean / defatted flour	0.01	3	111	5.8	m/z 289 → 126 (RARVY029)
	1.0	3	93	7.2	

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
<i>Flupyradifurone</i>					
Broccoli / curd	0.01	3	93	1.6	m/z 289 → 126 (16-2516)
	0.10	3	84	7.0	
Cauliflower / curd	0.01	3	93	1.1	m/z 289 → 126 (16-2516)
	0.10	3	90	2.8	
Potato / tuber	0.01	3	100	1.2	m/z 289 → 126 (16-2510)
	0.10	3	96	0.6	
Potato / peel, washed	0.01	3	93	0.6	m/z 289 → 126 (13-3149)
	0.10	3	93	2.7	
Potato / tuber, cooked	0.01	3	92	0.6	m/z 289 → 126 (13-3149)
	0.10	3	93	1.1	
Potato / starch	0.01	3	94	1.6	m/z 289 → 126 (13-3149)
	0.10	3	95	1.2	
Potato / flakes	0.01	3	77	6.6	m/z 289 → 126 (13-3149)
	0.10	3	78	10.8	
Potato / crisps	0.01	3	87	3.0	m/z 289 → 126 (13-3149)
	0.10	3	89	2.8	
Potato / washings	0.01	3	98	14	m/z 289 → 126 (RARVY038)
	0.10	3	88	8	
Potato / crisps	0.01	3	90	23	m/z 289 → 126 (RARVY038)
	0.10	3	78	2	
Potato / flakes	0.01	3	88	15	m/z 289 → 126 (RARVY038)
	0.50	3	96	12	
Potato / wet peel	0.01	3	89	6	m/z 289 → 126 (RARVY038)
	0.10	3	90	7	
Potato / starch	0.01	3	91	14	m/z 289 → 126 (RARVY038)
	0.50	3	97	10	
Potato / tuber with peel, cooked (boiled)	0.01	3	88	19	m/z 289 → 126 (RARVY038)
	0.10	3	82	5	
Potato / tuber peeled	0.10	3	98	-	m/z 289 → 126 (RARVY038)
Potato cooked, (steamed), peeled, mashed	0.01	3	91	7	m/z 289 → 126 (RARVY038)
	0.10	3	85	5	
Potato cooking (boiling) water	0.01	3	90	11	m/z 289 → 126 (RARVY038)
	0.10	3	90	4	
Barley / green material	0.01	3	103	4.6	m/z 289 → 126 (16-2512)
	0.10	3	99	3.8	
Barley / grain	0.01	3	106	7.1	

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
Flupyradifurone					
	0.10	3	103	3.1	m/z 289 → 126 (16-2512)
Barley / straw	0.01	3	93	5.4	m/z 289 → 126 (16-2512)
	0.50	3	94	3.1	
Maize/corn / green material	0.01	3	94	4.6	m/z 289 → 126 (16-2524)
	0.10	3	82	14.1	
Maize/corn / kernel	0.01	3	109	1.4	m/z 289 → 126 (16-2524)
	0.10	3	101	3.6	
Barley, beer	0.01	5	98	4.5	m/z 289 → 126 (10-3410)
	0.10	3	94	2.7	
Barley, brewer's yeast	0.01	5	105	4.2	m/z 289 → 126 (10-3410)
	0.10	3	108	2.3	
Barley, grain	0.01	1	107	-	m/z 289 → 126 (10-3410)
	0.10	1	109	-	
	5.0	1	89	-	
Barley, malt sprouts	0.01	5	77	10.9	m/z 289 → 126 (10-3410)
	0.10	3	83	3.9	
Hop, hops draff	0.10	5	97	9.8	m/z 289 → 126 (10-3410)
	1.0	3	103	2.0	
Maize/corn / grain	0.01	7	97	8.4	m/z 289 → 126 (RARVY030)
	1.0	3	91	5.6	
Maize/corn / Aspirated Grain Fractions	0.01	4	93	8.9	m/z 289 → 126 (RARVY030)
	1.0	3	107	8.9	
Maize/corn / Bran	0.01	3	103	7.6	m/z 289 → 126 (RARVY030)
	1.0	3	87	7.0	
Maize/corn / Flour	0.01	3	92	13.3	m/z 289 → 126 (RARVY030)
Maize/corn / Forage	0.01	3	96	5.7	m/z 289 → 126 (RARVY030)
	2.0	3	89	5.9	
	15.0	3	88	3.5	
Maize/corn / Germ Dry Milling	0.01	3	95	5.0	m/z 289 → 126 (RARVY030)
Maize/corn / Germ Wet Milling	0.01	3	90	5.8	m/z 289 → 126 (RARVY030)
	1.0	3	85	6.7	
Maize/corn / Grits	0.01	3	89	14.7	m/z 289 → 126 (RARVY030)
Maize/corn / Meal Dry Milled	0.01	3	83	15.0	m/z 289 → 126 (RARVY030)
	1.0	3	96	2.4	
Maize/corn /	0.01	3	96	19.1	m/z 289 → 126

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
Flupyradifurone					
Oil Dry Milled	1.0	3	103	1.0	(RARVY030)
Maize/corn / Oil Wet Milled	0.01	3	87	8.8	m/z 289 → 126 (RARVY030)
	1.0	3	106	3.3	
Maize/corn / Silage	0.01	3	103	11.5	m/z 289 → 126 (RARVY030)
	2.0	3	97	3.9	
	10.0	3	96	6.1	
Maize/corn / Starch	0.01	3	95	9.1	m/z 289 → 126 (RARVY030)
	1.0	3	95	3.7	
Maize/corn / Steep Water	0.01	3	96	6.1	m/z 289 → 126 (RARVY030)
	1.0	3	103	2.4	
Wheat / Aspirated Grain Fractions	0.200	3	99	5.3	m/z 289 → 126 (RARVY031)
	40.000	3	100	4.5	
Wheat / Bran	0.010	3	96	17.9	m/z 289 → 126 (RARVY031)
	4.000	3	103	4.4	
Wheat / Cooking Water	0.010	3	100	4.9	m/z 289 → 126 (RARVY031)
	0.200	3	93	3.3	
Wheat / Germ	0.010	3	97	17.7	m/z 289 → 126 (RARVY031)
	4.000	3	104	8.6	
Wheat / Gluten	0.010	3	113	4.9	m/z 289 → 126 (RARVY031)
	1.000	3	99	9.0	
	4.000	3	96	3.1	
Wheat / Grain	0.010	7	93	18.4	m/z 289 → 126 (RARVY031)
	2.500	3	98	7.7	
Wheat / Pasta Fresh	0.010	4	89	17.7	m/z 289 → 126 (RARVY031)
	4.000	3	106	5.2	
Wheat / Shorts	0.010	3	91	4.9	m/z 289 → 126 (RARVY031)
	4.000	3	107	9.4	
Wheat / Starch	0.010	3	99	3.5	m/z 289 → 126 (RARVY031)
	0.200	3	96	16.3	
Wheat / White Bread	0.010	2	108	-	m/z 289 → 126 (RARVY031)
Wheat / White Flour	0.010	3	103	6.4	m/z 289 → 126 (RARVY031)
	4.000	3	112	5.9	
Wheat / Whole meal flour	0.010	2	110	-	m/z 289 → 126 (RARVY031)
Wheat / Whole meal Bread	0.010	2	104	-	m/z 289 → 126 (RARVY031)
	4.000	3	88	3.4	
Wheat / grain	0.01	5	99	6.3	m/z 289 → 126

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
Flupyradifurone					
	0.50	3	89	2.3	(10-3409)
Wheat / meal ⁽³⁾	0.50	3	91	2.8	m/z 289 → 126 (10-3409)
Wheat / semolina bran	0.01	5	110	5.1	m/z 289 → 126 (10-3409)
Wheat / wholemeal bread	0.01	5	102	2.8	m/z 289 → 126 (10-3409)
	0.50	3	96	1.2	
Rape / green material	0.01	3	105	2.0	m/z 289 → 126 (16-2511)
	0.10	3	96	1.6	
	0.01	3	105	2.0	m/z 289 → 126 (16-2521)
	0.10	3	96	1.6	
	0.01	3	92	7.1	m/z 289 → 126 (16-2044)
	0.10	3	93	2.8	
	0.01	3	101	2.1	m/z 289 → 126 (16-2131)
	0.10	3	97	4.3	
	0.01	3	104	1.1	m/z 289 → 126 (16-2169)
	0.10	3	96	1.6	
Rape / seed	0.01	3	99	2.7	m/z 289 → 126 (16-2511)
	0.10	3	101	2.5	
	0.01	3	99	2.7	m/z 289 → 126 (16-2521)
	0.10	3	101	2.5	
	0.01	3	96	3.2	m/z 289 → 126 (16-2044)
	0.10	3	96	4.9	
	0.01	3	101	4.0	m/z 289 → 126 (16-2131)
	0.10	3	94	9.0	
	0.01	3	100	1.5	m/z 289 → 126 (16-2169)
	0.10	3	92	1.3	
Rape / straw	0.01	3	89	1.7	m/z 289 → 126 (16-2044)
	0.10	3	92	3.8	
	0.01	3	98	3.1	m/z 289 → 126 (16-2131)
	0.10	3	108	1.4	
	0.01	3	92	2.3	m/z 289 → 126 (16-2169)
	0.10	3	83	6.3	
Cotton / seed undelinted	0.01	3	105	10.1	m/z 289 → 126 (RARVY033)
	3.0	3	99	1.0	
Cotton / crude oil, neutralized	0.01	4	99	16.8	m/z 289 → 126 (RARVY033)
Cotton / meal	0.01	3	105	8.7	m/z 289 → 126

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
Flupyradifurone					
	1.0	3	105	2.9	(RARVY033)
Cotton / hull	0.01	3	92	5.5	m/z 289 → 126 (RARVY033)
	1.0	3	99	8.6	
Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
DFA					
Strawberry / fruit	0.02	3	104	3.5	m/z 95 → 51 (16-2515)
	0.20	3	97	1.6	
Soybean /seed, dry	0.050	7	78	7.6	m/z 289 → 126 (RARVY029)
	1.0	3	81	6.5	m/z 289 → 126 (RARVY029)
Soybean / aspirated grain fractions	0.05	3	101	3.0	m/z 95 → 51 (RARVY029)
	0.25	3	90	5.6	m/z 95 → 51 (RARVY029)
Soybean / meal	0.050	3	73	2.8	m/z 95 → 51 (RARVY029)
	1.0	3	78	16.0	m/z 95 → 51 (RARVY029)
Soybean / hull	0.050	3	84	0.7	m/z 95 → 51 (RARVY029)
	1.0	3	78	3.2	m/z 95 → 51 (RARVY029)
Soybean / oil, refined	0.050	3	104	4.5	m/z 95 → 51 (RARVY029)
	1.0	3	106	8.1	m/z 95 → 51 (RARVY029)
Soybean / milk	0.050	3	95	3.2	m/z 95 → 51 (RARVY029)
	1.0	3	102	4.9	m/z 95 → 51 (RARVY029)
Soybean / defatted flour	0.050	3	72	4.9	m/z 95 → 51 (RARVY029)
	1.0	3	77	8.7	m/z 95 → 51 (RARVY029)
Broccoli / curd	0.02	3	100	2.1	m/z 95 → 51 (16-2516)
	0.20	3	84	7.3	
Cauliflower / curd	0.02	3	100	2.1	m/z 95 → 51 (16-2516)
	0.20	3	90	1.3	
Potato / tuber	0.02	3	101	2.6	m/z 95 → 51 (16-2510)
	0.20	3	93	1.2	
Potato / peel, washed	0.02	3	117 ⁽¹⁾	3.7	m/z 95 → 51 (13-3149)
	0.20	3	100	1.2	
Potato / tuber,	0.02	3	113 ⁽¹⁾	4.0	m/z 95 → 51

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
DFA					
cooked	0.20	3	95	0.6	(13-3149)
Potato / starch	0.02	3	105	2.7	m/z 95 →51 (13-3149)
	0.20	3	95	3.0	
Potato / flakes	0.02	3	106	6.3	m/z 95 →51 (13-3149)
	0.20	3	66 ⁽⁵⁾	4.6	
Potato / crisps	0.02	3	118 ⁽¹⁾	0.5	m/z 95 →51 (13-3149)
	0.20	3	83	6.3	
Potato / washings	0.05	3	92	5	m/z 95 →51 (RARVY038)
	0.10	3	84	1	
Potato / crisps	0.05	3	80	3	m/z 95 →51 (RARVY038)
	0.10	3	77	6	
Potato / flakes	0.05	3	86	13	m/z 95 →51 (RARVY038)
	0.50	3	78	1	
Potato / wet peel	0.05	3	90	1	m/z 95 →51 (RARVY038)
	0.10	3	84	2	
Potato / starch	0.05	3	101	6	m/z 95 →51 (RARVY038)
	0.50	3	93	4	
Potato / tuber with peel, cooked (boiled)	0.05	3	82	5	m/z 95 →51 (RARVY038)
	0.10	3	78	4	
Potato / tuber peeled	0.10	3	106	-	m/z 95 →51 (RARVY038)
Potato cooked, (steamed), peeled, mashed	0.05	3	90	2	m/z 95 →51 (RARVY038)
	0.10	3	82	2	
Potato cooking (boiling) water	0.05	3	102	2	m/z 95 →51 (RARVY038)
	0.10	3	96	2	
Barley / green material	0.02	3	104	2.5	m/z 95 →51 (16-2512)
	0.20	3	98	3.1	
Barley / grain	0.02	3	94 ⁽²⁾	0.0	m/z 95 →51 (16-2512)
	0.20	3	97	6.2	
Barley / straw	0.10	3	90	1.1	m/z 95 →51 (16-2512)
	1.0	3	89	1.9	
Maize/corn / green material	0.02	3	89	6.3	m/z 95 →51 (16-2524)
	0.20	3	88	3.5	
Maize/corn / kernel	0.02	3	108	0.9	m/z 95 →51 (16-2524)
	0.20	3	87	2.4	
Barley, beer	0.02	5	99	1.5	m/z 95 → 51 (10-3410)
	0.20	3	95	3.2	

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
DFA					
Barley, brewer's yeast	0.02	5	97	3.4	m/z 95 → 51 (10-3410)
	0.20	3	89	2.3	
Barley, grain	0.02	1	114	-	m/z 95 → 51 (10-3410)
	0.50	1	100	-	
	5.0	1	80	-	
Barley, malt sprouts	0.02	5	81 ⁽⁴⁾	7.1	m/z 95 → 51 (10-3410)
	0.20	3	84	2.7	
Hop, hops draff	0.20	5	105	5.8	m/z 95 → 51 (10-3410)
	1.0	3	100	2.6	
Maize/corn / grain	0.05	7	90	11.4	m/z 95 → 51 (RARVY030)
	1.0	3	84	5.3	
Maize/corn / Aspirated Grain Fractions	0.05	4	87	8.1	m/z 95 → 51 (RARVY030)
	1.0	3	99	6.9	
Maize/corn / Bran	0.05	3	85	1.4	m/z 95 → 51 (RARVY030)
	1.0	3	83	4.5	
Maize/corn / Flour	0.05	3	76	2.6	m/z 95 → 51 (RARVY030)
Maize/corn / Forage	0.05	3	105	9.4	m/z 95 → 51 (RARVY030)
	2.0	3	92	4.5	
	15.0	3	88	2.4	
Maize/corn / Germ Dry Milling	0.05	3	82	8.4	m/z 95 → 51 (RARVY030)
Maize/corn / Germ Wet Milling	0.05	3	72	4.4	m/z 95 → 51 (RARVY030)
	1.0	3	72	2.9	
Maize/corn / Grits	0.05	3	81	1.4	m/z 95 → 51 (RARVY030)
Maize/corn / Meal Dry Milled	0.05	3	74	4.7	m/z 95 → 51 (RARVY030)
	1.0	3	87	4.4	
Maize/corn / Oil Dry Milled	0.05	3	95	15.5	m/z 95 → 51 (RARVY030)
	1.0	3	105	0.6	
Maize/corn / Oil Wet Milled	0.05	3	85	4.5	m/z 95 → 51 (RARVY030)
	1.0	3	101	5.2	
Maize/corn / Silage	0.05	3	87	10.6	m/z 95 → 51 (RARVY030)
	2.0	3	99	0.6	
	10.0	3	89	1.7	
Maize/corn / Starch	0.05	3	89	16.4	m/z 95 → 51 (RARVY030)
	1.0	3	82	3.7	
	0.05	3	97	8.3	m/z 95 → 51

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
DFA					
Maize/corn / Steep Water	1.0	3	105	1.1	(RARVY030)
Wheat / Aspirated Grain Fractions	0.200	3	106	5.2	m/z 95 → 51 (RARVY031)
	40.000	3	100	4.1	
Wheat / Bran	0.050	3	92	6.8	m/z 95 → 51 (RARVY031)
	4.000	3	85	2.4	
Wheat / Cooking Water	0.050	3	96	1.6	m/z 95 → 51 (RARVY031)
	0.200	3	99	2.6	
Wheat / Germ	0.050	3	77	2.6	m/z 95 → 51 (RARVY031)
	4.000	3	75	4.3	
Wheat / Gluten	0.050	3	99	16.7	m/z 95 → 51 (RARVY031)
	1.000	3	98	8.7	
	4.000	3	102	0.6	
Wheat / Grain	0.050	7	84	6.9	m/z 95 → 51 (RARVY031)
	2.500	3	84	5.5	
Wheat / Pasta Fresh	0.050	4	95	2.0	m/z 95 → 51 (RARVY031)
	4.000	3	100	5.0	
Wheat / Shorts	0.050	3	85	2.4	m/z 95 → 51 (RARVY031)
	4.000	3	87	2.3	
Wheat / Starch	0.050	3	88	2.3	m/z 95 → 51 (RARVY031)
	0.200	3	84	6.8	
Wheat / White Bread	0.050	2	90	-	m/z 95 → 51 (RARVY031)
Wheat / White Flour	0.050	3	92	6.6	m/z 95 → 51 (RARVY031)
	4.000	3	74	3.9	
Wheat / Whole meal flour	0.050	2	80	-	m/z 95 → 51 (RARVY031)
Wheat / Whole meal Bread	0.050	2	91	-	m/z 95 → 51 (RARVY031)
	4.000	3	83	0.7	
Wheat / grain	0.02	5	89	3.8	m/z 95 → 51 (10-3409)
	0.50	3	75	7.1	
Wheat / meal ⁽³⁾	0.50	3	72	5.6	m/z 95 → 51 (10-3409)
Wheat / semolina bran	0.02	5	87	8.6	m/z 95 → 51 (10-3409)
Wheat / wholemeal bread	0.02	5	84	5.1	m/z 95 → 51 (10-3409)
	0.50	3	77	6.0	
Rape / green material	0.02	3	103	6.5	m/z 95 → 51 (16-2511)
	0.20	3	99	6.6	

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
DFA					
	0.02	3	103	6.5	m/z 95 →51 (16-2521)
	0.20	3	99	6.6	
	0.02	3	100	2.0	m/z 95 →51 (16-2044)
	0.20	3	94	1.8	
	0.02	3	101	2.6	m/z 95 →51 (16-2131)
	0.20	3	98	5.4	
	0.02	3	100	3.1	m/z 95 →51 (16-2169)
	0.20	3	91	1.9	
Rape / seed	0.02	3	97	3.6	m/z 95 →51 (16-2511)
	0.20	3	83	4.8	
	0.02	3	97	3.6	m/z 95 →51 (16-2521)
	0.20	3	83	4.8	
	0.02	3	94	10.8	m/z 95 →51 (16-2044)
	0.20	3	86	2.9	
	0.02	3	81	1.9	m/z 95 →51 (16-2131)
	0.20	3	74	7.8	
	0.02	3	77	1.3	m/z 95 →51 (16-2169)
	0.20	3	76	1.5	
Rape / straw	0.02	3	100	7.0	m/z 95 →51 (16-2044)
	0.20	3	90	0.6	
	0.02	3	96	5.9	m/z 95 →51 (16-2131)
	0.20	3	103	1.5	
	0.02	3	96	2.6	m/z 95 →51 (16-2169)
	0.20	3	85	7.2	
Cotton / seed undelinted	0.050	3	79	16.0	m/z 95 →51 (RARVY033)
	3.0	3	90	2.3	
Cotton / crude oil, neutralized	0.01	4	99	16.8	m/z 95 →51 (RARVY033)
Cotton / meal	0.050	3	77	4.5	m/z 95 →51 (RARVY033)
	1.0	3	83	0.0	
Cotton / hull	0.050	3	72	4.2	m/z 95 →51 (RARVY033)

(1) This value was accepted. According to OECD guidance, recoveries can range between 70 – 120% in a fortification range of >0.01 to ≤0.1 mg/kg.

(2) Residues in control sample were found at 0.00667 mg/kg expressed as parent equivalents. Single recoveries of 128% each were corrected to 94% each. Uncorrected mean recovery: 128%.

(3) Study-independent sample material (wheat meal_2004-10-28) was used for these fortification experiments.

(4) Residues in control sample were found at 0.0367 mg/kg expressed as parent equivalents. Single recoveries were corrected for residues (uncorrected values are given in brackets): 72% (258%), 78% (262%), 84% (268%), 85% (268%), 85% (268%).

(5) This value was accepted as residue values in the sample were always close to the LOQ level

Note: in several cases RSD values were recalculated based on rounded values available in the report.

In the primary studies (oilseed rape) as well as in the rotational crops studies (potato, oilseed rape, barley, maize/corn, strawberry and brassica) and the EU processing studies, the apparent residues in the control samples used for the recoveries were below 30%. Recoveries were not corrected for apparent residues,

except residues of DFA in barley grain in study 16-2512, where residues of DFA in the control sample were found at 0.00667 mg/kg expressed as parent equivalents. Therefore recoveries at 0.02 mg/kg were corrected for apparent residues. The same was true for barley malt sprouts in study 10-3410, where residues of DFA were found at 0.0367 mg/kg expressed as parent equivalents and therefore recoveries were also corrected. For all of these studies the mean recoveries for each fortification level were within the 70 - 110% range. The RSDs were below 20%. ~~The RSDs were always below 20%.~~

In the US studies (processing studies of potato, wheat, maize/corn, and cotton (RARVY038, RARVY031, RARVY030, RARVY033) recoveries were corrected independent on the amount of residues within the control samples as it is common practice in the USA. Details on residues in corresponding control sample used for each recovery are detailed in the study reports. Residues in control samples were clearly <LOQ with only some exceptions as stated below. Therefore any correction results only in a slight difference. Within wheat processing study RARVY031 all control interferences for the wheat grain RAC and all processed commodities were less than their respective determined limits of quantitation (LOQs) for both analytes except for the following: aspirated grain fractions contained BYI 02960 residue ranging from 0.02 to 0.21 mg/kg in both trials. Shorts contained an apparent BYI 02960 residue of 0.01 mg/kg. Aspirated grain fractions also contained DFA residue ranging from 0.15 to 0.43 mg/kg along with an apparent DFA residue of 0.06 mg/kg from gluten. Consequently, the LOQ levels had to be adapted in these matrices. For all US studies the overall mean of the recoveries for each matrix was within the acceptable range of 70 to 120%, and the relative standard deviation (RSD) values were below 20%.

Table A 61: Characteristics for the analytical method 01304 used for validation of flupyradifurone and its metabolite residues

	Flupyradifurone and DFA
Specificity	Mass spectra are provided in Appendix of the original EU reviewed method 01304 blank values < 30% LOQ
Calibration (type, number of data points)	Calibration data presented Calibration line presented number of data points ≥ 5 R > 0.98
Calibration range (maximum range over all studies)	0.0832 ng/mL to 312.5 ng/mL corresponding to 0.002 to 2.5 mg/kg for flupyradifurone and DFA, expressed as parent, standards in solvent with internal standards.
Assessment of matrix effects is presented	No. The use of stable isotopically labelled internal standards compensates for matrix effect.
Lowest limit of quantification (LOQ dependent on matrix, see fortification levels in table above)	Lowest LOQ (lowest validated level): FPF: 0.01 mg/kg (expressed as parent) DFA: 0.02 mg/kg (expressed as parent)

Conclusion

All method validation data are in compliance with the guideline requirements for data generation methods. Method 01304 can therefore be considered successfully validated for the determination of parent flupyradifurone and its metabolite DFA in all additional plant matrices relevant to this submission (primary and rotational crops as well as processed commodities).

A 2.2.1.1.2 Analytical method 2 (Method 01212)

The analytical method 01212 was fully validated for the determination of residues of flupyradifurone and its metabolite difluoroacetic acid (DFA) in the representative plant matrices tomato fruit, grape and bunch of grape, kidney bean dry seed, barley grain and summer rape seed, as reported in the DAR (NL, 2015) and the EFSA Conclusion on the peer review (EFSA Journal 2015;13(2):4020). For the crop submitted in this application, additional validations were conducted with a limited dataset of recoveries during the conduct of the residue studies. The validation data are shown below.

A 2.2.1.1.2.1 Method validation

Comments of zRMS:	<p>Full validation data is documented with the method 01212 itself for matrices representing 5 major crop groups, including tomato (fruit), grapes (bunch of grapes), kidney bean (dry seed), barley (grain) and summer rape (seed).</p> <p>For rape (green material), a limited set (1 control, 3 repetitions each at two fortification levels) of additional validation recoveries and for rape (straw) a full validation (2 controls, 5 repetitions each at two fortification levels) were done within the course of this study.</p> <p>The individual LOQs for BYI 02960 and difluoroacetic acid are 0.01 and 0.02 mg/kg, respectively in the sample materials materials wheat (seed), wheat (green material) and wheat (straw). Thus a theoretical LOQ of 0.03 mg/kg results for the sum of the two analytes. No residues above the LOQ were found in the control samples. The apparent residues in the control samples used for recoveries at LOQ level were below 30% of the LOQ except for difluoroacetic acid:</p> <ul style="list-style-type: none"> - control 15-2132-01-0024E: DFA was found at 35% of LOQ - control 15-2132-02-0024E: DFA was found at 40% of LOQ. <p>The recoveries conducted with these affected control samples were corrected.</p> <p>For BYI 02960 and its metabolite difluoroacetic acid the average recoveries per fortification level were within the acceptable range of 70 – 110% and the RSD values were below 20% for all compounds and for all sample materials.</p> <p>All method validation data are in compliance with the guideline requirements for data collection methods.</p> <p>The validation of method 01212 can therefore be considered successful for the new matrices.</p>
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Reference:	KCP 5.1.2.5/02
Title:	Amendment no. 1: Determination of the residues of BYI 02960 and deltamethrin in/on rape after spray application of deltamethrin & flupyradifurone EC 085 in France (North), Germany and Belgium
Report:	Schulte, G.; 2017; 15-2132; M-578527-02-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations:	yes, see report
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Results and discussions

For matrices relevant in the residue studies submitted in this dRR, but not included in the original validation of method 01212, a limited dataset of validation recoveries (at least three repetitions at two fortification levels) was conducted. These additional validation recoveries are presented in [Table A 62](#), if not already evaluated at EU level.

Table A 62: Recovery results from method validation of flupyradifurone using the analytical method 01212 in oilseed rape green material and straw

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
Flupyradifurone					
Rape / green material	0.01	4	98	1.3	m/z 289 → 126 (15-2132)
	0.10	4	99	1.5	
Rape / straw	0.01	5	105	3.3	m/z 289 → 126 (15-2132)
	0.10	5	102	3.0	

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
DFA					
Rape / green material	0.02	4	106	2.7	m/z 95 →51 (15-2132)
	0.20	3	97	1.0	
Rape / straw	0.02	5	96 ⁽¹⁾	4.2	m/z 95 →51 (15-2132)
	0.20	5	99	2.2	

⁽¹⁾ This result for difluoroacetic acid is the corrected result after control sample value subtraction (40% of the LOQ); uncorrected values are respectively 126, 128, 133, 99, 120, mean recovery: 121%.

In oilseed rape, the apparent residues in the control samples used for the recoveries were below 30% of the LOQ except for DFA in straw (35% and 40% of the LOQ). Therefore for these recovery values, the control sample value was subtracted. Mean recoveries and mean corrected recoveries for each fortification level were within the 70 - 110% range for all matrices. The RSDs were below 20%.

Table A 63: Characteristics for the analytical method 01212 used for validation of flupyradifurone and its metabolite residues

	Flupyradifurone and DFA
Specificity	Mass spectra are provided in Appendix of the original EU reviewed method 01212 blank values < 30% LOQ
Calibration (type, number of data points)	Calibration data presented Calibration line presented number of data points ≥ 5 R > 0.99
Calibration range	0.05 to 50 µg/L (flupyradifurone) and 0.15 to 50 µg/L (DFA, expressed as parent), standards in solvent with internal standards. Corresponding calibration range in mass ratio units for the sample: 0.002 mg/kg to 2 mg/kg (flupyradifurone) and 0.006 to 2 mg/kg (DFA, expressed as parent).
Assessment of matrix effects is presented	No. The use of stable isotopically labelled internal standards compensates for matrix effect.
Limit of determination/quantification	FPF: 0.01 mg/kg (expressed as parent) DFA: 0.02 mg/kg (expressed as parent)

Conclusion

All method validation data are in compliance with the guideline requirements for data generation methods. The validation of method 01212 can therefore be considered successful for oilseed rape green material and straw matrices to determine residues of flupyradifurone and its metabolite DFA, with an LOQ of 0.01 mg/kg for flupyradifurone, and of 0.02 mg/kg for DFA, all expressed in parent compound equivalents.

A 2.2.1.1.3 Analytical method 3 (01304/M001)

The analytical method 01304/M001 (modification of method 01304) was fully validated for the determination of residues of flupyradifurone and its metabolite difluoroacetic acid (DFA) in green and fermented cocoa beans. These crop matrices are of high oil content and therefore the method was also used for the analysis of flupyradifurone and DFA residues in oilseed rape matrices in a storage stability study ([Winter, O.; Amann, S.; Giesler, W.; 2018; M-626405-01-1](#), cf. B7, Appendix A 2.1.1.1.3) and in a residue study ([Block, H.; 2016; M-546226-03-1](#), cf. B7, Appendix A 2.1.3.1.3). Both studies were conducted at Eurofins. A full dataset of recoveries was conducted during the conduct of the storage stability study and a limited validation in the residue study as shown below.

A 2.2.1.1.3.1 Method validation (cocoa beans, green and fermented)

Comments of zRMS:	The modification M001 of the analytical method 01304 was validated for the determination
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	<p>of BYI 02960 and its metabolites difluoroethyl-amino-furanone (DFEAF), difluoroacetic acid (DFA) and 6-chloronicotinic acid (6-CNA) residues in <u>green and fermented cacao beans</u> by HPLC-ESI-MS/MS using internal standards for quantitation..</p> <p>The limit of quantitation (LOQ) is 0.01 mg/kg for BYI 02960 and DFEAF and 0.02 mg/kg for DFA and 6-CNA in cacao beans.</p> <p>Residues in control samples were below 30% of the LOQ.</p> <p>One MRM transition was monitored for BYI 02960, DFEAF, DFA and 6-CNA and each matrix tested. For BYI 02960 m/z 289 → 126, for DFEAF m/z 161 → 98, for DFA m/z 95 → 51 and for 6-CNA m/z 156 → 112. For flupyradifurone and DFEAF, a second MRM transition was measured for confirmation.</p> <p>Mean recoveries for each fortification level and the overall mean recoveries were within the 70 - 110% range for recoveries at all fortification levels for all matrices.</p> <p>Relative standard deviations were below 20% for BYI 02960 and its metabolites DFEAF, DFA and 6-CNA acid in all sample materials.</p> <p>The method meets all guideline criteria to determine residues of BYI 02960 and its metabolites DFEAF, DFA and 6-CNA in/on green and fermented cacao beans.</p> <p>In the study 15-2109 / S15-01020 residues of BYI 02960 and its metabolites DFEAF, DFA and 6-CNA in field samples (spring oilseed rape (whole plant, seeds)) were determined according to the BCS method 01304/M001.</p> <p>A full method validation for 6-CNA and DFA and a reduced validation set for BYI 02960 and DFEAF in oilseed rape seeds and oilseed rape green material was conducted within this study.</p> <p>The limits of quantitation (LOQ) for BYI 02960, DFEAF, DFA and 6-CNA are 0.01 mg/kg, 0.006 mg/kg, 0.007 mg/kg and 0.005 mg/kg, respectively, corresponding to the lowest fortification levels of successfully conducted recovery experiments. These LOQs accord to 0.01 mg/kg for DFEAF and 6-CNA and 0.02 mg/kg for DFA expressed as parent equivalent (BYI 02960).</p> <p>The mean of the concurrent recoveries per fortification level and overall per matrix were for all analytes within the range of 70 – 110%. Wherever applicable (n ≥ 3), the RSD values were below 20%. Therefore, the results are considered acceptable.</p> <p>All method validation data are in compliance with the guideline requirements for data collection methods. The validation of method 01304/M001 can therefore be considered successful for <u>oilseed rape seeds and green material</u>.</p> <p>In the study S17-05312 the residues of flupyradifurone and its metabolites difluoroethyl-amino-furanone (DFEAF), difluoroacetic acid (DFA) and 6-chloronicotinic acid (6-CNA) were determined in <u>oilseed rape (seed and straw)</u> according to BCS Method 01304/M001.</p> <p>The limit of quantification (LOQ) for this study was 0.01 mg/kg for flupyradifurone, DFEAF and 6-CNA expressed as parent equivalents and 0.05 mg/kg for DFA expressed as parent equivalents for each matrix.</p> <p>All method validation data are in compliance with the guideline requirements for data generation methods.</p>
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Reference:	KCP 5.1.2.5/24
Title:	Modification M001 of the analytical method 01304 for the determination of residues of BYI 02960 and its metabolites in plant materials by HPLC-MS/MS
Report:	Schoening, R.; Willmes, J.; 2014; 01304/M001; M-476845-01-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC European Commission Guidance Document for Generating and Reporting Methods of Analysis in Support of Pre-Registration data Requirements for Annex II (part A, Section 4) and Annex III (part A, section 5) of directive 91/414, SANCO/3029/99 rev. 4, 11/07/00 Guidance document on residue analytical methods, SANCO/825/00/rev. 8.1, European Commission, Directorate General Health and Consumer Protection 16/11/2010 US EPA Residue Chemistry Test Guideline OCSPP 860.1340: Residue Analytical Method
Deviations:	not applicable
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/25
Title:	Final report amendment no. 2 to study 15-2109 / S15-01020 - Determination of the residues of flupyradifurone (BYI 02960) in/on spring oilseed rape after seed dressing with BYI 02960 FS 480 in Poland, Denmark and Germany
Report:	Block, H.; 2016; 15-2109; M-546226-03-1
Authority registration No:	
Guideline(s):	REGULATION (EC) No 1107/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC and Regulations (EU) 283/2013 and 284/2013 SANCO/3029/99 rev. 4, applying only for the analytical part of this study OECD 509 Adopted 2009-09-07, OECD GUIDELINE FOR THE TESTING OF CHEMICALS, Crop Field Trial
Deviations:	none
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/26
Title:	Storage stability of deltamethrin and flupyradifurone in oilseed rape (seed and straw)
Report:	Winter, O.; Amann, S.; Giesler, W.; 2018; S17-05312; M-626405-01-1
Authority registration No:	
Guideline(s):	Regulation (EC) No 1107/2009 of the European Parliament and the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC EC Guideline 7032/VI/95, rev. 5, July 1997; Appendix H of working document 1607/VI/97, rev. 2, June 1999 – Storage Stability of Residue Samples OECD 506, 2007; OECD Guideline for the Testing of Chemicals – Stability of Pesticide Residues in Stored Commodities
Deviations:	None
GLP/GEP:	yes
Acceptability:	
Duplication (if vertebrate study):	

Materials and methods

The modification M001 of the data generation method 01304 was validated for the determination of residues of flupyradifurone and its metabolite difluoroacetic acid (DFA) in green and fermented cacao beans (matrix with high oil content). The analytes were extracted two times by blending with acetonitrile/water (4/1, v/v) + 2.2 mL/L formic acid. After centrifugation the clear supernatant was transferred into a volumetric flask and filled up to volume. For DFA an aliquot of the crude extract was diluted with internal standard and acetonitrile/water (4/6, v/v) + 0.11 mL/L formic acid and the residues were quantified using reversed HPLC and MS/MS detection.

For flupyradifurone an aliquot of the crude extract was evaporated to the aqueous remainder and purified using a Chromabond XTR column. After elution of the residues with dichloromethane, the eluate was evaporated to dryness and re-dissolved with acetonitrile/water (2/8, v/v). An aliquot of the solution was diluted with internal standard and acetonitrile/water (4/6, v/v) + 0.11 mL/L formic acid and the residues were quantified using reversed HPLC and MS/MS detection.

In contrast to the original method 01304, centrifugation steps instead of filtration steps were applied and the purification of flupyradifurone was done by liquid-liquid extraction instead of using solid phase extraction, however the extraction steps remained as described in the original method.

Flupyradifurone and its metabolite DFA were stable in standard solutions (prepared in acetonitrile/water (2/8, v/v)+0.1 mL/L acetic acid) for at least 6 months when stored at 4°C ± 3°C in the dark. This was tested in the method 01304 (RV-001-P10-03). Flupyradifurone and DFA were also stable in cacao beans for at least three weeks when stored at 4°C ± 3°C in the dark.

For the determination of flupyradifurone a high performance liquid Chromatograph was used with a reversed phase chromatography system (Phenomenex Gemini 5 µm C18, 150 mm x 2.0 mm, column with a guard column) coupled with tandem mass spectrometry (MS/MS) with electrospray ionisation (Applied Biosystems API 5500 Triple Quadrupole Mass Spectrometer, AB Sciex Instruments, using Analyst version 1.6.1) operated in the positive ion mode. The MS/MS instrument was operated in the Multiple Reaction Monitoring mode (MRM). For the determination of DFA a high performance liquid Chromatograph was used with a different reversed phase chromatography system (ZIC HILIC, 150 mm x 2.1mm, 5 µm column) coupled with tandem mass spectrometry (MS/MS) with electrospray ionisation (Applied Biosystems API 5500 Triple Quadrupole Mass Spectrometer, AB Sciex Instruments, using Analyst version 1.6.1) operated in the negative ion mode. One MRM transition was monitored for quantification, e.g. m/z 289 → 126 for flupyradifurone and m/z 95 → 51 for DFA. For flupyradifurone, a second MRM transition was measured for confirmation.

Note: Method 01304/M001 was developed as a *data collection method* for the determination of the residues of flupyradifurone (parent compound), and its metabolites DFA, DFEAF, and 6-CNA in/on plant

materials. (As 6-CNA and DFEAF are not included in the residue definitions and are therefore not of relevance for this submission, further details relevant to these compounds will not be discussed below. For more details on 6-CNA and DFEAF, please see the original report.)

Results and discussions

The validation described within method 01304/M001 was performed on cacao, green and fermented beans. Mean recoveries for each fortification level were within the 70 - 110% range for both analytes in both matrices. The RSD values were well below 20%. The results are summarized in the table below.

Additional validation recoveries conducted in the oilseed rape matrices were added in the table.

Table A 64: Recovery results from method validation of flupyradifurone and its metabolite DFA using the analytical method 01304/M001

Matrix	Fortification level (mg/kg)	Single recoveries (%)	n	Mean recovery (%)	RSD (%)	Comments
Flupyradifurone						
Cocoa, green bean	0.01	90, 99, 101, 105, 106	5	100	6.4	m/z 289 → 126 (original method)
	0.1	85, 98, 90, 91, 101	5	93	6.9	
Cocoa, fermented bean	0.01	108, 103, 104, 105, 104	5	105	1.8	m/z 289 → 126 (original method)
	0.1	100, 103, 96, 102, 102	5	101	2.8	
Additional validation recoveries						
Rape, green material	0.01	112, 109, 104	3	108	3.7	m/z 289 → 126 (15-2109)
	0.1	83, 104, 87	3	91	12	
Rape, straw (= green material)	0.01	102, 105, 105, 105, 108	5	105	2.0	m/z 289 → 126 (S17-05312)
	0.1	93, 96, 99, 101, 104	5	99	4.3	
Rape, seed	0.01	89, 94, 107	3	97	10	m/z 289 → 126 (15-2109)
	0.1	98, 86, 84	3	89	8.5	
	0.01	84, 94, 97, 100, 101	5	95	7.2	m/z 289 → 126 (S17-05312)
	0.1	82, 89, 90, 91, 92	5	89	4.5	
DFA						
Cocoa, green bean	0.02	80, 92, 83, 93, 93	5	88	7.1	m/z 95 → 51 (original method)
	0.2	89, 102, 101, 99, 100	5	98	5.4	
Cocoa, fermented bean	0.02	90, 81, 101, 99, 99, 88	5	92	9.0	m/z 95 → 51 (original method)
	0.2	100, 105, 100, 97, 100	5	100	2.9	
Additional validation recoveries						
Rape, green material	0.02	97, 94, 99, 100, 99	5	98	2.4	m/z 95 → 51 (15-2109)
	0.2	91, 93, 94, 93, 93	3	93	1.2	
Rape, straw (= green material)	0.05	88, 93, 94, 94, 101	5	94	4.9	m/z 95 → 51 (S17-05312)
	0.50	99, 100, 100, 100, 101	5	100	0.7	
Rape, seed	0.02	79, 80, 83, 84, 81	3	81	2.5	m/z 95 → 51 (15-2109)
	0.2	70, 69, 74, 74, 70	3	71	3.4	
	0.05	86, 89, 95, 95, 96	5	92	4.8	m/z 95 → 51 (S17-05312)
	0.50	87, 87, 89, 93, 95	5	90	4.0	

Remark: Fortification level expressed as flupyradifurone parent equivalents

Table A 65: Characteristics for the analytical method used for validation of f residues in plant commodities with high oil content

	Flupyradifurone (FPF)	DFA
Specificity	blank value < 30% of LOQ, mass spectra are presented within the original method 01304	
Calibration (type, number of data points)	1/x weighted linear regression individual calibration data and calibration line equation presented; number of data points ≥ 5 ; $r \geq 0.999$ (original method)	
Calibration range	0.05-10 ng/mL corresponding calibration range in mass ratio units for the sample: 0.005-1.0 mg/kg (expressed as parent equivalent) standards in solvent with internal standards. (range may differ in single studies with in-study validations)	
Assessment of matrix effects is presented	Matrix effects are compensated by using internal standards	
Lowest limit of quantification (LOQ dependent on matrix, see fortification levels in table above)	LOD: 0.003 mg/kg LOQ: 0.01 mg/kg	LOD: 0.002* LOQ: 0.007*

* LOD/LOQ expressed in DFA equivalents (corresponds to an LOD of 0.006 mg/kg and an LOQ of 0.02 when expressed in flupyradifurone equivalents (molecular weight of flupyradifurone = 288.68 g/mol; molecular weight of DFA = 96.03 g/mol)

Conclusion

The data collection method 01304/M001 meets all necessary performance requirements to determine residues of flupyradifurone and its metabolite DFA in green or fermented cocoa beans being representative for plant matrices with high oil content as well as in rape seed and green material. The LOQ is 0.01 mg/kg for flupyradifurone, and 0.02 mg/kg for DFA when expressed as flupyradifurone and 0.007 mg/kg, when expressed as DFA.

A 2.2.1.1.4 Analytical method 4 (01207)

A 2.2.1.1.4.1 Method validation (tomato fruit, wheat green material and grain, grape bunches, potato tuber and dry peas)

Comments of zRMS:	<p>The analytical method BCS 01207 was validated for the determination of flupyradifurone in/on samples of tomato (fruit), wheat (green material), onion (bulbs), grape (bunches), wheat (grain), potato (tuber), peas (dry peas) and oilseed rape (seeds). The LOQ of BCS Method 01207 is defined as 0.01 mg/kg as validated in study S10-00279. This analyte not validated within study S10-00279 were validated within this study (reduced validation set – 5 samples fortified at 1.0 mg/kg). LOQ: 1 mg/kg. Mean recoveries were within the 70 - 110% range. The RSD values were well below 20%.</p> <p>Amendment No. 3 is written to provide additional information for the validation of flupyradifurone</p> <ol style="list-style-type: none"> 1. On request of the sponsor a full scan spectrum and the product ion spectra of flupyradifurone are added to the report. 2. On request of the sponsor the linearity ranges for flupyradifurone are expressed as mass fractions of the original sample in mg/kg and the percentage of the fortification level at the lower and upper level is calculated for the used linearity curves of flupyradifurone. 3. Starting 2017-01-01 the name of the sponsor changed. <p>Accepted.</p>
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Reference:	KCP 5.1.2.5/05
Title:	Amendment no. 3 to final report - 7 days freezer storage stability study with different combinations of a total of 61 analytes (parent and metabolite molecules) and five matrix types (high water / acidic / starch / protein / oil)
Report:	Lakaschus, S.; Gizler, A.; 2017; S13-03307; M-480441-06-1
Authority registration No:	
Guideline(s):	Commission Regulation (EU) No 544/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for active substances US EPA Residue Chemistry Test Guideline OPPTS 860.1380: Storage Stability Data OECD Test Guideline 506, adopted 16 October 2007
Deviations:	see report
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The data generation method 01207 was validated for the determination of residues of flupyradifurone in tomato fruit, wheat green material and grain, grape bunches, potato tuber and dry peas within the storage stability study S13-03307 ([Lakaschus, S.; Gizler, A.; 2017; M-480441-06-1](#)). A full set of validation data was conducted in the different matrices at the spiking level relevant for the storage stability study (1 mg/kg).

For the analysis of flupyradifurone, the water content of different sample materials was adjusted to 5 g followed by the addition of acetonitrile, leading to a acetonitrile/water ratio of (4/1, v/v) followed by shaking. Thereafter the samples were left to soak under solvent for 15 minutes. After shaking a salt mixture ($\text{Mg}_2\text{SO}_4/\text{NaCl}/\text{Na}_3\text{ citrate } 2 \text{ H}_2\text{O}/\text{Na}_2\text{H citrate } 6 \text{ H}_2\text{O}$) (4/1/1/0.5,w/w/w/w) was added followed by shaking again and centrifugation. A defined aliquot was filled up with methanol/water (1/1, v/v) to a defined volume and internal standard solution was added. The residues of flupyradifurone were quantified using reversed HPLC and MS/MS detection.

For the determination of flupyradifurone a high performance liquid Chromatograph was used with a reversed phase chromatography system (Phenomenex Luna C18) coupled with tandem mass spectrometry (MS/MS) with electrospray ionisation (Applied Biosystems API 5500 Triple Quadrupole Mass Spectrometer, AB Sciex Instruments, using Analyst version 1.6.1) operated in the positive ion mode. The MS/MS instrument was operated in the Multiple Reaction Monitoring mode (MRM). One MRM transition was monitored for quantification, m/z 289 \rightarrow 126, a second one for confirmation, m/z 289 \rightarrow 90.

Results and discussions

The validation described within the storage stability study S13-03307 using method 01207 was performed on tomato, fruit, wheat, green material, wheat grain, grape, bunches, potato tuber and peas, dried. Mean recoveries were within the 70 - 110% range. The RSD values were well below 20%. The results are summarized in the table below.

Table A 66: Recovery results from method validation of flupyradifurone using the analytical method 01207

Matrix	Fortification level (mg/kg)	Single recoveries (%)	n	Mean recovery (%)	RSD (%)	Comments
Flupyradifurone						
Tomato, fruit	1.0	96, 100, 97, 93, 91	5	95	3.7	m/z 289 \rightarrow 126
	1.0	105, 117, 75, 99, 89	5	97	16	m/z 289 \rightarrow 90
Wheat, green material	1.0	107, 100, 114, 97, 85	5	101	11	m/z 289 \rightarrow 126
	1.0	104, 95, 114, 103, 104	5	104	6.5	m/z 289 \rightarrow 90
Wheat grain	1.0	98, 119, 110, 103, 112	5	108	7.5	m/z 289 \rightarrow 126
	1.0	97, 111, 114, 103, 112	5	107	6.7	m/z 289 \rightarrow 90
Grape, bunches	1.0	97, 95, 128, 97, 81	5	100	17	m/z 289 \rightarrow 126

Matrix	Fortification level (mg/kg)	Single recoveries (%)	n	Mean recovery (%)	RSD (%)	Comments
	1.0	104, 104, 131, 95, 80	5	103	18	m/z 289 → 90
Potato tuber	1.0	98, 89, 94, 71, 72	5	85	15	m/z 289 → 126
	1.0	84, 85, 96, 71, 69	5	81	14	m/z 289 → 90
Peas, dried	1.0	97, 96, 102, 105, 96	5	99	4.1	m/z 289 → 126
	1.0	93, 86, 103, 87, 97	5	93	7.6	m/z 289 → 90

Fortification level expressed as flupyradifurone parent equivalents

Table A 67: Characteristics for the analytical method used for validation of residues in different plant commodities

	Flupyradifurone (FPF)
Specificity	blank value < 30% of fortification level of 1.0 mg/kg mass spectra are presented within the report S13-03307
Calibration (type, number of data points)	1/x weighted linear regression individual calibration data and calibration line equation presented; number of data points ≥5; r ≥ 0.99
Calibration range	Accepted calibration range in concentration units : Tomato fruit, wheat green material, bunches of grape and potato tuber: 0.75-10 µg/L corresponding calibration range in mass ratio units for the sample: 0.30-4.0 mg/kg Wheat grain: 0.75-12 µg/L corresponding calibration range in mass ratio units for the sample: 0.30-4.8 mg/kg Dried peas: 1.0-20 µg/L corresponding calibration range in mass ratio units for the sample: 0.40-8.0 mg/kg
Assessment of matrix effects is presented	Matrix effects are compensated by using matrix-matched standards
Limit of quantification	LOQ: 1 mg/kg

Conclusion

The data collection method 01207 (based on QuEChERS) meets all necessary performance requirements to determine residues of flupyradifurone in tomato fruit, wheat, green material and grain, grapes, potatoes and dry peas (pulses) with a limit of quantification of 1 mg/kg (spiking level of the study).

A 2.2.1.2 Description of analytical methods for the determination of residues in animal matrices (KCP 5.1)

A 2.2.1.2.1 Analytical method RV-006-A17-01

A 2.2.1.2.1.1 Method validation

Comments of zRMS:	<p>An analytical method RV-006-A17-01 was validated to determine the residues of difluoroacetic acid in animal matrices using an isotopically labeled internal standard and LC/MS/MS detection.</p> <p>The limit of quantitation (LOQ) was 0.010 mg/kg for difluoroacetic acid in all matrices.</p> <p>The overall means of the recoveries for each matrix at each fortification level were within the acceptable range of 70 to 110%, and the relative standard deviation values were below 20%. The coefficients of determination of the linearity curves were all >0.99.</p> <p>The method are in compliance with the guideline requirements for data generation methods (SANCO/3029/99 rev. 4, 11/07/2000).</p> <p>Accepted.</p>
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Reference:	KCP 5.1.2.5/27
Title:	An analytical method for the determination of residues of difluoroacetic acid in animal matrices using LC/MS/MS
Report:	Kormos, T.; 2017; RV-006-A17-01; M-589558-01-1
Authority registration No:	
Guideline(s):	US EPA Test Guideline OCSPP 860.1340: Residue Analytical Method OECD Guidance Document on Pesticide Residue Analytical Methods, Series on Testing and Assessment Document 72 and Series on Pesticides: Document 39, August 2007 (OECD Guideline, ENV/JM/MONO (2007) 17, Aug 13, 2007) PMRA Residue Chemistry Guidelines, Regulatory Directive 98-02, Section 3, Residue Analytical Method, June 1998
Deviations:	none
GLP/GEP:	no
Acceptability:	yes
Duplication (if vertebrate study):	

Reference:	KCP 5.1.2.5/28
Title:	Difluoroacetic acid - Magnitude of the residue in laying hens
Report:	2017; RARVN150; M-611007-01-1
Authority registration No:	
Guideline(s):	APVMA Residue Guideline No. 23; OPPTS 860.1480; DACO 7.5.1; OECD 505 Residues in Livestock
Deviations:	none
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	No

Reference:	KCP 5.1.2.5/29
Title:	Diffuoroacetic acid - Magnitude of the residue in dairy cows
Report:	[REDACTED]; 2017; RARVN149; M-608471-01-1
Authority registration No:	
Guideline(s):	APVMA Residue Guideline No. 23 OCSPP 860.1480 - Meat/Milk/Poultry/Eggs DACO 7.5.1 - Livestock Feeding Study OECD Guideline 505 - Residues in Livestock
Deviations:	none
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	No

Materials and methods

The analytical method RV-006-A17-01 was developed for the determination of residues of difluoroacetic acid in animal matrices from poultry and cattle.

Residues of difluoroacetic acid are extracted from fat blending the sample in a mixture of acetonitrile/water (85:15, v/v) acidified with 5.0 mL/L formic acid. Heptane is added to the sample, and the sample is blended again. An isotopic internal standard is added to the sample, and the sample is centrifuged. A sample aliquot is cleaned through a C₁₈ and SCX cartridge pre-washed with acetonitrile.

Residues of difluoroacetic acid are extracted from liver, kidney, and muscle blending the sample in a mixture of acetonitrile/water (85:15, v/v) acidified with 5.0 mL/L formic acid. The sample is filtered, an isotopic internal standard is added to the sample, and the sample is brought to volume. A sample aliquot is cleaned through a C₁₈ and SCX cartridge prewashed with acetonitrile.

Residues of difluoroacetic acid are extracted from eggs, egg whites and egg yolks blending the sample in a mixture of acetonitrile/water (80:20, v/v) acidified with 2.2 mL/L formic acid. The sample is filtered, an isotopic internal standard is added to the sample, and the sample is brought to volume. A sample aliquot is cleaned through a C₁₈ and SCX cartridge pre-washed with acetonitrile.

Residues of difluoroacetic acid are extracted from milk, cream, and skim milk by shaking the sample in a mixture of acetonitrile/water (85:15, v/v) acidified with 5.0 mL/L formic acid. An isotopic internal standard is added to the sample, and the sample is centrifuged. A sample aliquot is cleaned through a C₁₈ and SCX cartridge pre-washed with acetonitrile.

All extracts are then diluted with 3 volumes of acetonitrile and analyzed by high performance liquid chromatography/triple stage mass spectrometry (LC-MS/MS) operating in the Multiple Reaction Monitoring mode (MRM) with electrospray ionization (ESI) interface.

Quantitation of the analyte was based on the comparison of peak areas of the analyte and the isotopically labeled internal standard analog.

Standard solutions are prepared with a mixture of acetonitrile/water (1:1, v/v) and calibration solutions are dissolved in acetonitrile/water (95:5, v/v) + 1.5 mL/L formic acid.

The method validation was conducted during livestock feeding studies on poultry ([\[REDACTED\]; 2017; M-611007-01-1](#)) and ruminant ([\[REDACTED\]; 2017; M-608471-01-1](#)).

Results and discussions

The limit of quantification was established at 0.01 mg/kg for difluoroacetic acid in all the investigated matrices (fat, liver, kidney, muscle, eggs, egg whites and egg yolks, milk, cream, skim milk).

The limit of detection (LOD) was determined during the poultry and ruminant feeding studies and is defined as the lowest concentration of an analyte that can be determined to be statistically different from a blank. The LODs were determined from method validation data obtained from control samples fortified at the respective analyte LOQs. The LODs were calculated by multiplying the standard deviation of recovery measurements at the LOQ by $t_{0.99}$ [where $t_{0.99}$ is the one-tailed t-statistic at the 99% confidence level for the number of replicates (n)].

The LOQ and LODs of DFA are summarized in the table below.

Matrix	Analyte	LOQ (mg/kg)	LOD (mg/kg)
Eggs	Difluoroacetic acid	0.010	0.0030*
Milk	Difluoroacetic acid	0.010	0.0013**
Muscle	Difluoroacetic acid	0.010	0.0031*
Kidney	Difluoroacetic acid	0.010	0.0017**
Liver	Difluoroacetic acid	0.010	0.0018*
Fat	Difluoroacetic acid	0.010	0.0033*

* refers to the range of calculated LOD calculated in study RARVN150 (2017; [M-611007-01-1](#))

** refers to the range of calculated LOD calculated in study RARVN149 (2017; [M-608471-01-1](#)).

For hen matrices the method was fully validated (two control samples and at least five repetitions at two fortification levels) by measuring the recoveries of the analyte untreated (control) eggs, liver, muscle, and fat samples fortified with difluoroacetic acid at the LOQ and at 10 times the LOQ (10X). Additional recoveries at higher fortification levels, for all commodities other than fat, validated the method for the highest residues observed in individual matrices. For the matrices egg whites and yolks, only a limited dataset of validation recoveries (one control sample and three repetitions at LOQ and 10X LOQ fortification levels) was conducted.

For cattle matrices the method was successfully fully validated by analysis of blank untreated control milk, mesenteric fat, perirenal fat, subcutaneous fat, liver, kidney, and muscle samples fortified with 0.010 mg/kg (LOQ) and 0.10 mg/kg (10X LOQ) of difluoroacetic acid. Additional recoveries at higher fortification levels validated the method for the highest residues observed in individual matrices. For the matrices cream and skim milk only a limited dataset of validation recoveries (one control sample and three repetitions at LOQ and 10X LOQ fortification levels) was conducted.

Mean recoveries for the individual matrices and/or fortification levels ranged between 81% and 106% for poultry matrices and between 82% and 109% for cattle matrices, which shows an acceptable accuracy of the method.

High precision was demonstrated by low relative standard deviations which ranged between 0.8% and 6.5% for poultry matrices and between 1.0% and 14.2% for cattle matrices.

Table A 68: Recovery results from method validation of difluoroacetic acid using the analytical method RV-006-A17-01

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
Hen eggs*	0.010	12	106	5.4	
	0.10	5	103	6.6	
	0.50	5	97	1.5	
Hen egg white	0.01	3	94	1.6	
	0.50	3	97	4.5	
Hen egg yolk	0.01	3	91	5.2	
	0.50	3	81	2.6	
Hen fat	0.010	5	97	3.0	
	0.10	5	99	2.0	
Hen liver	0.010	5	98	3.2	
	0.10	5	98	1.7	
	0.85	5	99	0.8	
Hen muscle	0.010	5	92	7.3	
	0.10	5	91	3.0	
	0.40	5	89	6.5	
Hen fat	0.010	5	97	3.0	
	0.10	5	99	2.0	
Cattle milk	0.010	17	82	14.7	
	0.10	5	108	1.4	
	0.50	5	108	1.8	
Cattle cream	0.01	3	95	4.6	
	0.50	3	106	1.4	
Cattle skim milk	0.01	3	86	2.0	
	0.50	3	106	1.4	
Cattle fat, mesenteric	0.010	5	91	7.4	
	0.10	5	107	1.4	
	1.4	7	95	1.8	
Cattle fat, perirenal	0.010	5	94	13.7	
	0.10	5	105	1.2	
	1.4	7	94	6.4	
Cattle fat, subcutaneous	0.010	5	101	4.5	
	0.10	5	104	4.1	
	1.4	7	93	6.6	

Matrix	Fortification level (mg/kg)	n	Mean recovery (%)	RSD (%)	Comments
Cattle, liver**	0.010	9	95	8.9	
	0.10	5	106	6.5	
	1.4	5	105	6.8	
Cattle, kidney*	0.010	8	104	10.8	
	0.10	5	107	4.7	
	1.4	5	109	6.5	
Cattle, muscle	0.010	9	94	3.3	
	0.10	5	102	4.1	
	1.4	5	106	7.2	

* Additional recoveries are available in the report ([M-611007-01-1](#)) at 0.020 and 0.050 mg/kg.

** An additional recovery is available in the report ([M-608471-01-1](#)) at 0.70 mg/kg.

Mean recoveries and RSD values were recalculated based on rounded values available in the report, therefore minor deviations may occur.

Table A 69: Characteristics for the analytical method used for validation of difluoroacetic acid residues in animal matrices (milk, cream, skim milk, fat, liver, muscle, kidney, eggs, egg whites and egg yolks)

	Difluoroacetic acid
Specificity	Mass spectra are provided Blank values < 30% LOQ
Calibration (type, number of data points)	Calibration line presented number of data points ≥ 5 R > 0.99
Calibration range	standards in solvent with internal standards at 0.015 µg/L. Cattle feeding study: 0.050 to 50 ng/mL corresponding calibration range in mass ratio units for the sample: 0.0015 mg/kg to 1.5 mg/kg Hen feeding study: 0.050 to 35 ng/mL corresponding calibration range in mass ratio units for the sample: 0.0015 mg/kg to 1.05 mg/kg
Assessment of matrix effects is presented	No. The use of stable isotopically labelled internal standards compensates for matrix effect.
Limit of determination/quantification	DFA: 0.01 mg/kg

Conclusion

The method RV-006-A17-01 allows determination of difluoroacetic acid (DFA) in animal matrices of hen (eggs, egg white, and egg yolk, liver, muscle and fat) and cattle (milk, cream and skim milk, mesenteric, perirenal and subcutaneous fat, liver, kidney and muscle) with a limit of quantification of 0.01 mg/kg. All the method validation results are in compliance with the European guideline requirements for data generation methods (SANCO/3029/99 rev. 4, 11/07/2000).

A 2.2.1.3 Description of analytical methods for the determination of residues in support to environmental fate studies (KCP 5.1)

No new or additional studies have been submitted

A 2.2.1.4 Description of analytical methods for the determination of residues in support to toxicological studies (KCP 5.1)

No new or additional studies have been submitted

A 2.2.1.5 Description of analytical methods for the determination of residues in support of

operator, worker, resident and bystander exposure studies (KCP 5.1)

No new or additional studies have been submitted

A 2.2.1.6 Description of analytical methods for the determination of residues in of ecotoxicology studies (KCP 5.1)

A 2.2.1.6.1 Analytical method 01182

Comments of zRMS:	<p>This method was developed for the determination of BYI 02960 in test water from aquatic toxicity tests.</p> <p>Aliquots of the water samples are directly injected into the HPLC instrument. Identification and quantitative determination are done by means of electrospray MS/MS-detection in the positive ionisation mode.</p> <p>For method validation test water samples were fortified with BYI 02960 at 0.05 µg/L and at 0.5 µg/L.</p> <p>The relative standard deviation for the peak areas of BYI 02960 was 1.8 % (0.05 µg/L) and 1.4 % (0.5 µg/L). The relative standard deviation for the retention time was ≤ 0.3 % (0.05 µg/L and 0.5 µg/L).</p> <p>BYI 02960 was not detected in test water control samples.</p> <p>The limit of quantitation was 0.05 µg/L. The limit of detection (LOD) for BYI 02960 was 0.02 µg/L.</p> <p>According to the SANCO/3029/99 rev.4:</p> <p><i>GLP: The development of a method is not subject to GLP, however where the method is used to generate data for safety purposes, for example residues data, data generation must be conducted to GLP.</i></p>
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Reference:	KCP 5.1.2.6/15
Title:	Method 01182 for the determination of BYI 02960 in test water from aquatic toxicity tests by HPLC-MS/MS
Report:	Krebber, R.; Sandau, C.; 2010; 01182; M-363959-01-1
Authority registration No:	
Guideline(s):	not specified
Deviations:	not specified
GLP/GEP:	no
Acceptability:	yes
Duplication (if vertebrate study):	

This method 01182 was developed for the determination of BYI 02960 in test water from aquatic toxicity tests via HPLC-MS/MS.

Materials and methods

Aliquots of the water samples are directly injected into the HPLC instrument. Identification and quantitative determination are done by means of electrospray MS/MS-detection in the positive ionisation mode. For quantitation a MRM transition was monitored for BYI 02960 (m/z 289 → m/z 126).

Results and discussions

The results of the method validation are summarized in the tables below.

Table A 70: Characteristics for the analytical method used for validation of BYI 02960 residues in water

	BYI 02960
Specificity	No residues of BYI 02960 were detected in the test water control sample
Calibration	For test water the mass spectrometric detector showed linear response in the concentration range of 0.05 µg/L to 11 µg/L for the quantification ion with a correlation coefficient of 0.9993 (1/x weighted).
Recovery and precision	Because of the direct measurement of fortified samples without separate extraction and clean-up steps it is not possible to determine recovery rates and an estimate of the accuracy of the analytical technique was made by an assessment of the linearity of calibration and by determination of the reproducibility of sample analysis. For method validation test water samples were fortified with BYI 02960 at 0.05 µg/L and at 0.5 µg/L. These test solutions were injected ten times each into the HPLC-MS/MS instrument. The relative standard deviation for the peak areas of BYI 02960 was 1.8 % (0.05 µg/L) and 1.4 % (0.5 µg/L). The relative standard deviation for the retention time was ≤ 0.3 % (0.05 µg/L and 0.5 µg/L).
Recovery of validation samples	For an additional demonstration of the reliability of the method, the validation samples were evaluated like recovery rates. The mean recoveries were 93 ± 2.1% at 0.05 µg/L and 106 ± 1.3 at 0.5 µg/L fortification level.
Limit of determination/quantification	The limit of quantitation (LOQ) for BYI 02960 is 0.05 µg/L. The limit of detection (LOD) for BYI 02960 is 0.02 µg/L.

Conclusion

In conclusion, the results summarized in the tables above show that the method presented here is satisfactory for the determination of BYI 02960 in test water from aquatic toxicity tests via HPLC-MS/MS.

A 2.2.1.6.2 Analytical method 01206/M001

Comments of zRMS:	<p>This modification M001 of the analytical method 1206 describes the determination of the residues of BYI 02960 and Difluoroethylaminofuranone (DFEAF) in/on bees, pollen, honey/nectar, green material and flowers/blossoms.</p> <p>Determination of recoveries for BYI 02960 and DFEAF with fortification levels of 0.001 mg/kg (=LOQ) and 0.01 mg/kg (=10xLOQ) have been performed for bees, pollen, honey/nectar, green material and flowers/blossoms.</p> <p>The detection limits (LOD) were from 0.1 to 0.2 µg/kg.</p> <p>Blank values in untreated control samples were below 30% of the LOQ.</p> <p>The mean recovery was between 70 and 110% with a relative standard deviation of ≤ 20%.</p> <p>The results of the method validation were confirmed using a second MRM transition for confirmation.</p> <p>All method validation data are in compliance with the guideline requirements for residue data generation and enforcement.</p> <p>Accepted.</p>
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Reference:	KCP 5.1.2.6/16
Title:	Modification M001 of the analytical method 01206 for the determination of residues of BYI 02960 and Difluoroethylaminofuranone by HPLC with electrospray and MS/MS - detection
Report:	Schoening, R.; Koester, P.; 2011; 01206/M001; M-404877-01-1
Authority registration No:	
Guideline(s):	91/414/EEC, 96/68/EC, 91/414, SANCO/3029/99
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

This modification M001 of the analytical method 01206 describes the determination of the residues of BYI 02960 and Difluoroethylaminofuranone (DFEAF) in/on bees, pollen, honey/nectar, green material and flowers/blossoms.

Materials and methods

Residues of BYI 02960 and Difluoroethylaminofuranone (DFEAF) were extracted from the sample materials using a mixture of acetonitrile/water (4/1, v/v). After filtration an aliquot of the extract was evaporated to the aqueous remainder and cleaned-up on a Chromabond® XTR cartridge. After elution of the residues with dichloromethane the extract was evaporated to dryness and re-dissolved in an internal standard solution of $^{13}\text{C}_5$ - ^{15}N -BYI 02960 (BYI 02960-ISTD) and $^{13}\text{C}_2$ - Difluoroethylaminofuranone (DFEAF-ISTD). The residues were quantified by reversed phase HPLC with electrospray and MS/MS-detection.

Results and discussions

The results of the method validation are summarized in the tables below.

Table A 71: **Characteristics for the analytical method used for validation of BYI 02960 and DFEAF residues in ~~water~~ bees, pollen, honey/nectar, green material and flowers/blossoms**

	BYI 02960	DFEAF																												
Specificity	Up to three untreated control samples were examined. The determined residues for BYI 02960 and DFEAF were well below 30% of the LOQ level.	Up to three untreated control samples were examined. The determined residues for BYI 02960 and DFEAF were well below 30% of the LOQ level.																												
Calibration	<table><tr><td>Parameter</td><td>BYI 02960</td></tr><tr><td>Linear range [µg/L]</td><td>0.05 – 5.0</td></tr><tr><td>IS ¹³C₅-¹⁵N-BYI 02960 [µg/L]</td><td>1.0</td></tr><tr><td>No. of concentrations</td><td>5</td></tr><tr><td>No. of injections</td><td>1</td></tr><tr><td>Model</td><td>1/x weighted linear regression</td></tr><tr><td>Correlation coefficient R</td><td>0.9993 – 0.9999</td></tr></table>	Parameter	BYI 02960	Linear range [µg/L]	0.05 – 5.0	IS ¹³ C ₅ - ¹⁵ N-BYI 02960 [µg/L]	1.0	No. of concentrations	5	No. of injections	1	Model	1/x weighted linear regression	Correlation coefficient R	0.9993 – 0.9999	<table><tr><td>Parameter</td><td>DFEAF</td></tr><tr><td>Linear range [µg/L]</td><td>0.05 – 5.0</td></tr><tr><td>IS DFEAF [µg/L]</td><td>1.0</td></tr><tr><td>No. of concentrations</td><td>5</td></tr><tr><td>No. of injections</td><td>1</td></tr><tr><td>Model</td><td>1/x weighted linear regression</td></tr><tr><td>Correlation coefficient R</td><td>0.9998 – 1.000</td></tr></table>	Parameter	DFEAF	Linear range [µg/L]	0.05 – 5.0	IS DFEAF [µg/L]	1.0	No. of concentrations	5	No. of injections	1	Model	1/x weighted linear regression	Correlation coefficient R	0.9998 – 1.000
	Parameter	BYI 02960																												
	Linear range [µg/L]	0.05 – 5.0																												
	IS ¹³ C ₅ - ¹⁵ N-BYI 02960 [µg/L]	1.0																												
	No. of concentrations	5																												
	No. of injections	1																												
	Model	1/x weighted linear regression																												
Correlation coefficient R	0.9993 – 0.9999																													
Parameter	DFEAF																													
Linear range [µg/L]	0.05 – 5.0																													
IS DFEAF [µg/L]	1.0																													
No. of concentrations	5																													
No. of injections	1																													
Model	1/x weighted linear regression																													
Correlation coefficient R	0.9998 – 1.000																													
Recovery and precision	Determination of recoveries for BYI 02960 and DFEAF with fortification levels of 0.001 mg/kg (= LOQ) and 0.01 mg/kg (= 10 x LOQ) have been performed for bees, pollen, honey/nectar, green material and flowers/blossoms. The overall mean recovery was 91% with an RSD of 4.0%.	Determination of recoveries for BYI 02960 and DFEAF with fortification levels of 0.001 mg/kg (= LOQ) and 0.01 mg/kg (= 10 x LOQ) have been performed for bees, pollen, honey/nectar, green material and flowers/blossoms. The overall mean recovery was 96% with an RSD of 8.0%.																												
Assessment of matrix effects	The internal standard procedure, using stable isotopically labelled internal standards, compensates for matrix effects.	The internal standard procedure, using stable isotopically labelled internal standards, compensates for matrix effects.																												
Limit of determination/quantification	LOQ = 0.001 mg/kg for all matrices. LOD = 0.1 to 0.2 µg/kg for all matrices.	LOQ = 0.001 mg/kg for all matrices. LOD = 0.1 to 0.2 µg/kg for all matrices.																												

The results of the method validation were confirmed using a second MRM transition for confirmation.

Table A 72: Characteristics for the confirmatory method used for validation of BYI 02960 and DFEAF residues in water

	BYI 02960	DFEAF
Recovery and precision	Determination of recoveries for BYI 02960 and DFEAF with fortification levels of 0.001 mg/kg (= LOQ) and 0.01 mg/kg (= 10 x LOQ) have been performed for bees, pollen, honey/nectar, green material and flowers/blossoms. The overall mean recovery was 89% with an RSD of 11.4%.	Determination of recoveries for BYI 02960 and DFEAF with fortification levels of 0.001 mg/kg (= LOQ) and 0.01 mg/kg (= 10 x LOQ) have been performed for bees, pollen, honey/nectar, green material and flowers/blossoms. The overall mean recovery was 97% with an RSD of 6.9%.

Conclusion

In conclusion, the results summarized in the tables above show that the method presented here is satisfactory for the determination of the residues of BYI 02960 and Difluoroethylaminofuranone (DFEAF) in/on bees, pollen, honey/nectar, green material and flowers/blossoms.

A 2.2.1.7 Description of analytical methods for the determination of residues in support of physical and chemical properties tests (KCP 5.1)

Analytical methods used for the generation of pre-authorization data are the same as the ones described in part B section 5.

A 2.2.2 Methods for post-authorization control and monitoring purposes (KCP 5.2)

A 2.2.2.1 Description of analytical methods for the determination of residues in plant matrices (KCP 5.2)

No new or additional studies have been submitted

A 2.2.2.2 Description of analytical methods for the determination of residues in animal matrices (KCP 5.2)

No new or additional studies have been submitted

A 2.2.2.3 Description of Methods for the Analysis of Body Fluids and Tissues (KCP 5.2)

A 2.2.2.3.1 Analytical method 1 (Method 01495)

A 2.2.2.3.1.1 Method validation

Comments of zRMS:	<p>The method 01495 was validated for the determination of residues of flupyradifurone in blood plasma by HPLC-MS/MS with electrospray ionization and Multiple Reaction Monitoring (MRM).</p> <p>The limit of quantitation (LOQ) for flupyradifurone in plasma is 0.05 mg/L.</p> <p>The limit of detection (LOD) is 0.015 mg/L.</p> <p>Fortification experiments were performed at the limit of quantitation (LOQ) and 10x limit of quantitation. Mean recoveries for each fortification level and the overall mean recoveries were within the 70% - 110% range for flupyradifurone for both MRM transitions. Relative standard deviations were below 20% for flupyradifurone for both MRM transitions.</p> <p>Two MRM transitions were successfully validated for plasma. Therefore, an additional confirmatory method is not necessary.</p> <p>All method validation data are in compliance with the guideline requirements according to the SANCO/825/00 rev. 8.1 and SANCO/3029/99 rev. 4.</p> <p>Accepted.</p>
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Reference:	KCP 5.2.3/02
Title:	Analytical method 01495 for the determination of various pesticides and selected pesticide metabolites in blood plasma by HPLC-MS/MS
Report:	Kaussmann, M.; 2016; 01495; M-570324-01-1
Authority registration No:	
Guideline(s):	<p>Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market</p> <p>Guidance Document on Residue Analytical Methods, SANCO/825/00 rev. 8.1 of November 16, 2010</p> <p>European Commission Guidance Document for Generating and Reporting Methods of Analysis in Support of Pre-Registration data Requirements for Annex II (part A, section 4) and Annex III (part A, section 5) of directive 91/414, SANCO/3029/99 rev. 4, July 11, 2000</p>
Deviations:	none
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Method 01495 is a multi-residue method for the determination of several active substances of plant protection products - including flupyradifurone - and/or their metabolites in plasma of blood by HPLC-MS/MS. Only the results relevant to flupyradifurone are reported here.

Materials and methods

In a first step, the plasma samples were denaturated by mixing with a solution of acetonitrile/water (6/1, v/v) containing 56 mg/L ammonium acetate and 0.14 mL/L formic acid. The sample was subjected to centrifugation to separate sediment and supernatant. An aliquot of the supernatant was subjected to HPLC-MS/MS analysis and the residues were quantified using matrix matched standards. All compounds (including flupyradifurone) were measured in positive ion mode.

The quantification of flupyradifurone was done using the following mass transitions:

- primary method (for quantification): m/z 289 \rightarrow 126

- confirmatory method: m/z 289 \rightarrow 90

Results and discussions

Specificity

Apparent residues in control samples were below 0.3 x LOQ. Two MRM transitions were monitored for each analyte. Therefore, the HPLC-MS/MS method is highly specific and an additional confirmatory method is not necessary.

Linearity

At least five calibration points were used. The correlation between the injected amount of flupyradifurone and the detector response was linear (1/x weighted) for matrix matched standard solutions ranging from 0.0015 to 0.075 $\mu\text{g/mL}$ (corresponding to 1.5 $\mu\text{g/L}$ to 75 $\mu\text{g/L}$ in plasma).

The correlation coefficients were ≥ 0.99 .

Accuracy

Fortification experiments were performed at the limit of quantitation (LOQ) and 10 x limit of quantitation. Mean recoveries for each fortification level were within the 70 - 110% range for both MRM transitions (Table A 73).

Precision

For both mass transitions monitored, relative standard deviations (RSD) per fortification level were below 20% (Table A 73).

Stability of Analytes

The analytes were stable in plasma for at least 3 days when stored in a freezer at ≤ -18 °C. In addition the stability of the analytes in extracts was demonstrated for a period of at least 3 days when stored in a refrigerator at $\leq +6$ °C under dark conditions.

Table A 73: Recovery results from method validation of flupyradifurone using the analytical method 01495

Matrix	Fortification level (mg/L)	n	Mean recovery (%)	RSD (%)	Comments
Flupyradifurone (MRM: m/z 289 \rightarrow 126, quantification)					
Plasma	0.05	5	105	2.8	
	0.5	5	104	3.5	
Flupyradifurone (MRM: m/z 289 \rightarrow 90, confirmation)					
Plasma	0.05	5	106	2.1	
	0.5	5	104	3.6	

Table A 74: Characteristics for the analytical method used for validation of flupyradifurone residues in plasma

	Flupyradifurone
Specificity	Blank value < 30% LOQ. Two mass transitions were used for quantification for both mass transitions. Quantification: m/z 289 → 126 Confirmation: m/z 289 → 90 Therefore, this LC/MS-MS method can be considered as highly specific and the development of additional confirmatory detection techniques are not necessary. Mass spectra are provided in the original report.
Calibration (type, number of data points)	1/x weighted linear regression Using matrix-matched standards, for both MRM transitions, the correlation coefficients (r) were above 0.99 Number of data points: 7
Calibration range	In matrix matched standard (quantitative and confirmatory MRM): Plasma – Concentration range 1.5 to 75 µg/L
Assessment of matrix effects is presented	Matrix matched standards were used for the evaluation of all analytes which compensate for matrix effects.
Limit of determination/quantification (LOD/LOQ)	LOD: 0.015 mg/L LOQ: 0.05 mg/L

Conclusion

The method meets the guideline criteria (SANCO/825/00 rev. 8.1) to determine residues of flupyradifurone in plasma (body fluids) with at a limit of quantitation (LOQ) of 0.05 mg/L and is therefore suitable as monitoring method.

A 2.2.2.4 Description of Methods for the Analysis of Soil (KCP 5.2)

No new or additional studies have been submitted.

A 2.2.2.5 Description of Methods for the Analysis of Water (KCP 5.2)

No new or additional studies have been submitted.

A 2.2.2.6 Description of Methods for the Analysis of Air (KCP 5.2)

No new or additional studies have been submitted.

A 2.2.2.7 A.2.A.9 Other Studies/ Information

No new or additional studies have been submitted.