

Analytical method for Fluoxapiprolin (BCS-CS55621) and seven degradates BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 in soil and sediment

Reports: ECM 1: MRID 51820515. Li, Y. 2020. An Analytical Method for the Determination of Residues of BCS-CS55621, and Its Metabolites BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 in Soil and Sediment Using LC/MS/MS. Bayer Method No: TY-003-S20-01. Activity ID: RATY0178. Report prepared by Bayer Crop Science, Chesterfield, Missouri, and sponsored and submitted by Bayer Crop Science, St. Louis, Missouri; 50 pages. Final report issued March 19, 2020.

ECM 2: MRID 51820516. Li, Y. 2021. In House Laboratory Validation of Analytical Method for the Determination of Residues of BCS-CS55621, and Its Metabolites BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 in Soil and Sediment Using LC/MS/MS. Study and Activity ID: RATY0178. Report prepared by Bayer Crop Science, Chesterfield, Missouri, and sponsored and submitted by Bayer Crop Science, St. Louis, Missouri; 166 pages. Final report issued March 22, 2021.

ILV: MRID 51820519. Swaim, L. 2022. Independent Laboratory Validation of "An Analytical Method for the Determination of Residues of BCS-CS55621, and Its Metabolites BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 in Soil and Sediment Using LC/MS/MS". Bayer CropScience Study No.: RATY0250. Eurofins Study No.: 90854. eSM Study No.: S21-05694. Report prepared by Eurofins EAG Agrosience, LLC, Columbia, Missouri, and sponsored and submitted by Bayer CropScience, Chesterfield, Missouri; 218 pages. Final report issued February 4, 2022.

Document No.: MRIDs 51820515 & 51820516 & 51820519

Guideline: 850.6100

Statements: ECM 1: No claim of compliance with USEPA FIFRA Good Laboratory Practices (GLP) are made for the document since it was not a study as defined by 40 CFR Part 160 or current OECD GLP (p. 3 of MRID 51820515). Signed and dated No Data Confidentiality, GLP, and Authenticity statements were provided (pp. 2-4). A Quality Assurance statement was not included.

ECM 2: The study was conducted in accordance with USEPA FIFRA GLP standards (40 CFR Part 160; 1989; p. 3 of MRID 51820516). Signed and dated No Data Confidentiality, GLP, Quality Assurance, and Authenticity statements were provided (pp. 2-5).

ILV: The study was conducted in accordance with USEPA FIFRA GLP (40

CFR Part 160 (1989), which is compatible with OECD GLP [ENV/MC/CHEM (98) 17; p. 3 of MRID 51820519]. Signed and dated No Data Confidentiality, GLP, Quality Assurance, and Authenticity statements were provided (pp. 2-5). A statement of the authenticity was also included with the Quality Assurance statements. Applicant/Sponsor and Quality Assurance signatures were completed via an unidentified proxy (pp. 2-4).

Classification: This analytical method is classified as **unacceptable, but upgradeable**. ECM 1 MRID 51820515 contained the full method written in a step-wise manner, but no performance data; while ECM 2 MRID 51820516 contained performance data, but only a method summary. Since the reported method LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than LOQ. No sediment was included in the ILV; therefore, Bayer Method TY-003-S20-01 was not independently validated for sediment matrices.

An updated method Bayer Method TY-003-S20-01 should be submitted which corrects significant typographical errors, contains instruction to allow the samples to cool for *ca.* 15 minutes after microwave extract (before adding the internal standard and acetic acid), and provides alternative procedures for the LC parameters and microwave extraction technique when only standard/common analytical laboratory equipment is available; additionally, the method Bayer Method TY-003-S20-01 should be updated with designating the confirmation ion transition as an identification analysis only and not a quantification analysis.

Issues regarding repeatability, accuracy, precision, or specificity were noted for fluoxapiprolin (BCS-CS55621), BCS-CY96288, BCS-CU97237, and BCS-DH17585 based on ILV performance data. Extensive communication between the ILV study personnel and the Sponsor Monitor was necessary for the successful completion of the ILV validation. It could not be determined if the one ILV soil matrix covered the range of soil and sediments used in the terrestrial field dissipation (TFD) studies since no fluoxapiprolin (BCS-CS55621) TFD studies were available for review. ECM 2 recovery results were corrected for residues quantified in the controls.

PC Code: 110304

EFED Final Reviewer: Richard Shamblen
Biologist

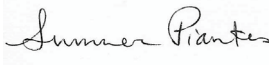
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This Data Evaluation Record may have been altered by the Environmental Fate and Effects Division subsequent to signing by PB&A/CSS Joint Venture personnel. The PB&A/CSS JV role does not include establishing Agency policies.

Executive Summary

This analytical method, Bayer Method TY-003-S20-01, is designed for the quantitative determination of fluoxapiprolin (BCS-CS55621) and seven degradates BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 at 0.5 ng/g in soil and sediment using LC/MS/MS. The LOQ is **less than** the lowest toxicological level of concern in soil and sediment for all analytes. Since the reported method LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ. Based on the performance data submitted by the ILV and ECM 2, the LLMV was equivalent to the ECM 2 and ILV reported method LOQ for all analytes in soil (0.5 ng/g). No sediment was included in the ILV; therefore, Bayer Method TY-003-S20-01 was not independently validated for sediment matrices. ECM 1 MRID 51820515 contained the full method written in a step-wise manner, but no performance data; while ECM 2 MRID 51820516 contained performance data, but only a method summary.

The ILV validated the method using one characterized soil matrix (sandy loam); the ECM 2 validated the method using two characterized soil matrices (loamy sand and silty clay loam) and one characterized sediment matrix (silty clay loam).

The ILV validated the method, Bayer Method TY-003-S20-01, with the first trial in one soil matrix, and the overall mean recovery (119%) of fluoxapiprolin (BCS-CS55621) was used to support the validation of the method for this analyte, even though the mean recovery at 10×LOQ (127%) was unacceptable. The ILV performed the ECM method, Bayer Method TY-003-S20-01, as written, except for the use of a N-evap instead of a TurboVap for evaporation of the extraction sample to aqueous, the addition of allowing the sample to cool for *ca.* 15 minutes after microwave extract (before adding the internal standard and acetic acid), insignificant changes of analytical equipment, and the use of the analytical parameters from Bayer Method TY-004-W21-01 [MRID 52029302 (water method)]. Based on the ILV validation of Bayer Method TY-003-S20-01, the ILV recommended that the ECM method Bayer Method TY-003-S20-01 be updated with the following:

- 1) corrected typographical errors in the listing of BCS-CY96288-IS in the mass transition tables and the IUPAC names and/or molecular formulas for BCS-CY96288, BCS-DA63612 and BCS-CU97237;
- 2) the inclusion of analytical parameters for the more common 2-pump LC system; and
- 3) the inclusion of any changes to the procedure for single-sample versus multi-sample microwave extractor use.

An updated method Bayer Method TY-003-S20-01 should be submitted which corrects significant typographical errors, contains instruction to allow the samples to cool for *ca.* 15 minutes after microwave extract (before adding the internal standard and acetic acid), and provides alternative procedures for the LC parameters and microwave extraction technique when only standard/common analytical laboratory equipment is available. ECM 1 MRID 51820515

and ECM 2 MRID 51820516 did not contain these updates or most of the ILV recommendations. The reviewer also noted that, since the ILV laboratory could not generate acceptable performance data for the confirmation ion transitions, the method Bayer Method TY-003-S20-01 should be updated with designating the confirmation ion transition as an identification analysis only and not a quantification analysis.

Although the ILV was conducted independently of the internal validation (ECM 1 and ECM 2), there was extensive communication between the ILV study personnel and the Sponsor Monitor which was necessary for the successful completion of the ILV validation since the laboratory personnel and equipment differed between the ILV laboratory and ECM 1 and ECM 2 laboratory

All ILV and ECM 2 data regarding repeatability, accuracy, precision, linearity, and specificity were satisfactory for fluoxapiprolin (BCS-CS55621), BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 at 0.5 ng/g and 5.0 ng/g in soil matrices, except for fluoxapiprolin (BCS-CS55621) at 5.0 ng/g, for which repeatability and reproducibility were not acceptable due to ILV performance data, and BCS-DH17585, for which the specificity of the method was not supported by ILV LOQ representative chromatograms. Additionally, ILV calculated LOQs exceeded the method LOQ (0.5 ng/g) for BCS-CY96288 (0.862 ng/g) and BCS-CU97237 (0.512 ng/g); ILV calculated LODs exceeded 30% of the method LOQ (0.15 ng/g) for BCS-CY96288, BCS-CU97237, and BCS-DH17585.

All ECM 2 data regarding repeatability, accuracy, precision, linearity, and specificity were satisfactory for fluoxapiprolin (BCS-CS55621), BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 at 0.5 ng/g and 5.0 ng/g in the sediment matrix; however, no representative chromatograms were provided for review.

Table 1. Analytical Method Summary

Analyte(s) by Pesticide	MRID		EPA Review	Matrix	Method Date (dd/mm/yyyy)	Registrant	Analysis	Limit of Quantitation (LOQ)
	Environmental Chemistry Method	Independent Laboratory Validation						
Fluoxapiprolin (BCS-CS55621)	51820515 ¹ & 51820516 ²	51820519 ^{3,4}		Soil and Sediment	19/03/2020 (ECM 1) 22/03/2021 (ECM 2)	Bayer Crop Science	LC/MS/MS	0.5 ng/g
BCS-CY96288								
BCS-CU97237								
BCS-DA63612								
BCS-CC26101								
BCS-CZ38260								
BCS-BP32808								
BCS-DH17585								

1 ECM 1 MRID 51820515 contained the full method written in a step-wise manner, but no performance data; while ECM 2 MRID 51820516 contained performance data, but only a method summary.

2 In the ECM 2 MRID 51820516, two soil matrices and one sediment matrix were included in the internal validation. The soil matrices were loamy sand soil [Sample ID: N19SD001-01-W-0001F-0002F-003; pH 6.9 (CaCl₂), 7.5 (aqueous solution); 81% sand, 15% silt, 4% clay, 0.50% organic matter, 0.29% organic carbon] obtained from a California terrestrial field dissipation study (Study METY0051) and silty clay loam soil [Sample ID: N19SD004-01-W-0001 2 3F; pH 7.0 (CaCl₂), 7.5 (aqueous solution); 8% sand, 58% silt, 34% clay, 3.5% organic matter, 2.0% organic carbon] obtained from an Iowa terrestrial field dissipation study (Study METY0057; p. 20 of MRID 51820516). The sediment matrix was silty clay loam sediment [Sample ID not reported; pH 4.3 (CaCl₂), 4.5 (aqueous solution); 8% sand, 64.5% silt, 27.5% clay, 13.3% organic matter, 7.9% organic carbon] obtained from Brandywine Creek at Chadds Ford, Pennsylvania (November 8, 2017). The laboratory which performed the matrix characterization (USDA texture classification) was not reported. The soil and sediment textures were verified by the reviewer using USDA-NRCS technical support tools. MRID numbers for the terrestrial field dissipation studies Study METY0051 and Study METY0057 were not reported in ECM 1 MRID 51820515 or ECM 2 MRID 51820516 and could not be determined by the reviewer (p. 33 of MRID 51820516).

3 In the ILV, one soil matrix was included in the independent validation: sandy loam soil [Sample ID: RMN-SL-PF (0-6" sample depth); pH 6.7 (1:1 soil:water ratio); 76% sand, 15% silt, 9% clay, 4.6% organic matter-Walkley Black; p. 25; Appendix 3, p. 192 of MRID 51820519]. The soil matrix was obtained from and characterized by Agvise Laboratories, Northwood, North Dakota (USDA texture classification). The soil texture was verified by the reviewer using USDA-NRCS technical support tools.

4 No sediment was included in the ILV.

I. Principle of the Method

Bayer Method TY-003-S20-01

Samples (5 ± 0.05 g) of homogenized soil or sediment in a 4-oz bottle with a magnetic stir bar were fortified with the appropriate amount of a 50 ng/mL mixed fortification solution (fluoxapiprolin, BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585), as necessary, then allowed to stand for 10

minutes (pp. 9-12 of MRID 51820515; p. 21 of MRID 51820516). The sample was extracted with 10 mL of acetonitrile:water (4:1, v:v) for 15 minutes in a microwave extractor with the following program: 400 W for 0-3 minutes (for ten samples; ambient temperature to *ca.* 70°C) then 110 W for 3-15 minutes (*ca.* 70°C). The internal standard (IS) mixture solution (200 µL of 100 ng/mL solution) and 300 µL of acetic acid were added, and the sample was allowed to sit for *ca.* 5 minutes. An aliquot (*ca.* 1.5 mL) of the supernatant was transferred to a microcentrifuge tube and centrifuged (*ca.* 13,000 rpm for 10 minutes). The supernatant was transferred to a glass tube or 96-well plate, and the organic solvent was evaporated via TurboVap at 40°C and 25 psi for *ca.* 20 minutes. The aqueous sample was diluted with 300 µL of acetonitrile:water (1:9, v:v) and mixed (centrifugation, as necessary). The sample was transferred to a HPLC vial or 96-well plate for LC/MS/MS analysis.

Samples were analyzed for fluoxapiprolin (BCS-CS55621), BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 using an Applied Biosystems API 6500+ (identified in ILV communication log; Appendix 4, p. 196 of MRID 51820519) triple-quadrupole tandem mass spectrometer coupled with a Shimadzu LC-20ADXR HPLC equipped with an ESI interface, multiple reaction monitoring (MRM) mode (pp. 13-15 of MRID 51820515; pp. 21-23; Appendix 4, pp. 161-166 MRID 51820516). The following LC conditions were used: YMC-UltraHT Hydrosphere column (2.00 mm x 30 mm, 2.0 µm; column temperature 40°C), SecurityGuard ULTRA UHPLC C8 pre-column (optional; dimension not reported), mobile phase of (A) 0.5% acetic acid in water, (B) 0.5% acetic acid in acetonitrile, and (C) 0.1% formic acid in acetonitrile (binary flow rate, 0.80 mL/min.), MS temperature 600°C, and injection volume of 20 µL. The following LC gradient and flow rate parameters were reported in the ECM 1 and ECM 2 (p. 13 of MRID 51820515; p. 22; Appendix 3, pp. 146-147 of MRID 51820516).

Time (min.)	Module	Events	Parameters
0.0	Pumps	Pump C Flow	0
0.0	Pumps	Pump B Conc	5
0.10	Pumps	Pump B Conc	5
0.70	Pumps	Pump B Conc	90
1.20	Pumps	Total Flow	0.5
1.30	Pumps	Pump C Flow	0
1.40	Pumps	Pump C Flow	0.4
2.00	Pumps	Pump C Flow	0.4
2.10	Pumps	Total Flow	0.5
2.10	Pumps	Pump C Flow	0
2.20	Pumps	Total Flow	0.8
4.00	Pumps	Pump B Conc	90
4.10	Pumps	Pump B Conc	5
5.00	Controller	Stop	

Two ion pair transitions were monitored for fluoxapiprolin (BCS-CS55621), BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585. The following MS settings were reported in the ECM 1 and ECM 2.

Analyte	Primary	Confirmatory	Mode	Expected Retention Times (minutes)
Fluoxapiprolin (BCS-CS55621)	m/z 650→610.2	m/z 650→378	Positive	<i>ca.</i> 1.27
BCS-CS55621-($^{13}\text{C}_3$, $^{15}\text{N}_3$)-IS	m/z 656→616.2	--	Positive	<i>ca.</i> 1.27
BCS-CY96288	m/z 666→626.1	m/z 666→191	Positive	<i>ca.</i> 1.22
BCS-CY96288-($^{13}\text{C}_3$, $^{15}\text{N}_3$)-IS*	m/z 672→634.1	--	Positive	<i>ca.</i> 1.22
BCS-CU97237	m/z 442.2→332	m/z 442.2→208	Positive	<i>ca.</i> 0.86
BCS-CU97237-($^{13}\text{C}_6$)-IS	m/z 448→338	--	Positive	<i>ca.</i> 0.86
BCS-DA63612	m/z 456→345.2	m/z 456→222.1	Positive	<i>ca.</i> 1.06
BCS-DA63612-($^{13}\text{C}_6$)-IS	m/z 462→351	--	Positive	<i>ca.</i> 1.06
BCS-CC26101	m/z 225→161	m/z 225→141	Negative	<i>ca.</i> 1.13
BCS-CC26101-($^{13}\text{C}_2$)-IS	m/z 227→162	--	Negative	<i>ca.</i> 1.13
BCS-CZ38260	m/z 161→76	--	Negative	<i>ca.</i> 0.84
	--	m/z 163.1→125	Positive	
BCS-CZ38260-($^{15}\text{N}_2$)-IS	m/z 163→77	--	Negative	<i>ca.</i> 0.84
	--	m/z 165→127	Positive	
BCS-BP32808	m/z 169→101	m/z 169→149	Positive	<i>ca.</i> 1.00
BCS-BP32808-($^{15}\text{N}_2$)-IS	m/z 171→101	--	Positive	<i>ca.</i> 1.00
BCS-DH17585	m/z 403→169	m/z 403→157	Positive	<i>ca.</i> 1.90
BCS-DH17585-($^{13}\text{C}_6$)-IS	m/z 409→169	--	Positive	<i>ca.</i> 1.90

* Note: BCS-CY96288-IS was erroneously reported as BCS-CS55621-IS in ECM 1 and ECM 2. The reviewer made the assignment of BCS-CY96288-IS based on the molecular weight/primary ion transition, as well as supporting chromatograms and calibration plots (Table 8, pp. 14-15 of MRID 51820515; pp. 16, 23; Appendix 2, pp. 99-144; Appendix 3, pp. 146-147 of MRID 51820516). The ILV MRID 51820519 also noted this typographical error (p. 33 of MRID 51820519).

Calibration standards were prepared in water:acetonitrile (90:10, v:v) in the range of 0.25 ng/mL to 50 ng/mL with extra calibration standards at 80 ng/mL and 100 ng/mL for the analysis of high residue samples (p. 11 of MRID 51820515). Internal standard (IS) was added to each calibration standard (5 ng/mL concentration). The ratio of the analyte to the IS was used to generate calibration curves for quantifying analytes in test samples (Appendix 2, pp. 26-33 of MRID 51820515; Appendix 3, pp. 145-160 of MRID 51820516). The use of isotopically-labeled internal standards in quantification methods is a method which is used to negate any matrix effects which may be present.

ILV

The ILV was based on MRID 51820515 (Bayer Method TY-003-S20-01) without the inclusion of a sediment matrix (pp. 12, 24-28 of MRID 51820519). The ILV performed the ECM method, Bayer Method TY-003-S20-01, as written, except for the use of a N-evap instead of a TurboVap for evaporation of the extraction sample to aqueous, the addition of allowing the sample to cool for *ca.* 15 minutes after microwave extract (before adding the internal standard and acetic acid), insignificant changes of analytical equipment, and the use of the analytical parameters from Bayer Method TY-004-W21-01 [MRID 52029302 (water method); pp. 26-28; Appendix 4, pp. 193-202 of MRID 51820519]. Samples were analyzed for fluoxapiprolin (BCS-CS55621), BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 using an Applied Biosystems/Sciex API 6500 (Q-Trap mass spectrometer coupled with a Shimadzu HPLC (unspecified model) equipped with a Turbo Ion Spray (TIS)

interface, multiple reaction monitoring (MRM) mode. The LC/MS/MS parameters were as follows: Phenomenex Luna Omega C18 column (2.1 mm x 100 mm, 1.6 μ m; column temperature 40°C), no pre-column used, mobile phase of (A) 0.5% acetic acid in water, and (B) 0.5% acetic acid in acetonitrile (see below for LC mobile phase parameters), MS temperature 600°C, and injection volume of 20 μ L.

Time (min.)	Flow (mL/min.)	% A	% B
0.00	0.3	95	5
2.50	0.3	20	80
5.80	0.3	0	100
5.90	0.3	95	5
7.00	0.3	95	5

Mobile Phase (A) = 0.5% acetic acid in water.

Mobile Phase (B) = 0.5% acetic acid in acetonitrile

One ion pair transition was monitored for fluoxapiprolin (BCS-CS55621), BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585. The following MS settings were reported in the ILV.

Analyte	Primary	Mode	Expected Retention Times (minutes)
Period 1 Experiment 1			
Fluoxapiprolin (BCS-CS55621)	<i>m/z</i> 650.0→610.2	Positive	<i>ca.</i> 3.9
BCS-CS55621-(¹³ C ₃ , ¹⁵ N ₃)-IS	<i>m/z</i> 656.0→616.2	Positive	
BCS-CY96288	<i>m/z</i> 666.0→626.0	Positive	<i>ca.</i> 3.8
BCS-CY96288-(¹³ C ₃ , ¹⁵ N ₃)-IS*	<i>m/z</i> 672.0→634.0	Positive	
BCS-CU97237	<i>m/z</i> 442.0→332.0	Positive	<i>ca.</i> 2.9
BCS-CU97237-(¹³ C ₆)-IS	<i>m/z</i> 448.0→338.0	Positive	
BCS-DA63612	<i>m/z</i> 456.0→345.0	Positive	<i>ca.</i> 3.3
BCS-DA63612-(¹³ C ₆)-IS	<i>m/z</i> 462.0→351.0	Positive	
BCS-BP32808	<i>m/z</i> 169.0→101.0	Positive	<i>ca.</i> 3.3
BCS-BP32808-(¹⁵ N ₂)-IS	<i>m/z</i> 171.0→101.0	Positive	
BCS-DH17585	<i>m/z</i> 403.0→169.0	Positive	<i>ca.</i> 3.4
BCS-DH17585-(¹³ C ₆)-IS	<i>m/z</i> 409.0→169.0	Positive	
Period 1 Experiment 2			
BCS-CC26101	<i>m/z</i> 225.0→161.0	Negative	<i>ca.</i> 3.2
BCS-CC26101-(¹³ C ₂)-IS	<i>m/z</i> 227.0→162.0	Negative	
BCS-CZ38260	<i>m/z</i> 161.0→76.0	Negative	<i>ca.</i> 2.8
BCS-CZ38260-(¹⁵ N ₂)-IS	<i>m/z</i> 163.0→77.0	Negative	

The monitored quantitation/primary ion transitions of the ILV were similar to those of the ECM; however, no confirmation ion transition was monitored for the analytes. Based on the reported ILV communications, the omission of the confirmation ion transition was due to irregularities in the performance data (Appendix 4, pp. 201-202). Based on the reported ILV communications and the ILV method comments/changes section of the ILV study report, the instrumental conditions in Bayer Method TY-003-S20-01 which employ a 3-pump LC system were difficult to implement since the ILV laboratory only had a 2-pump LC system (which is the more common type of LC system for laboratories to have; p. 33; Appendix 4, pp. 193-202 of MRID

51820519). Initially, after discussion with the Sponsor, the ILV laboratory attempted to implement the LC mobile phase in Bayer Method TY-003-S20-01 by modifying with the use of two injections (see below for LC mobile phase parameters), one using 0.5% acetic acid in acetonitrile as phase B (for all analytes, except BCS-DH17585) and one using 0.5% formic acid in acetonitrile as phase B (for BCS-DH17585 only). However, these LC conditions did not provide satisfactory results for a majority of the analytes at an injection volume of 20 µL (method injection volume) or 10 µL (ILV modified injection volume).

Time (min.)	Flow (mL/min.)	% A	% B
0.0	0.8	95	5
0.1	0.8	95	5
0.7	0.8	10	90
1.2	0.8	10	90
4.0	0.8	10	90
4.1	0.8	95	5
5.0	0.8	95	5

Mobile Phase (A) = 0.5% acetic acid in water.

Mobile Phase (B) = 0.5% acetic acid in acetonitrile (all analytes but BCS-DH17585), or 0.1% formic acid in acetonitrile (BCS-DH17585).

After the unsuccessful implementation/modification of the 3-pump LC system instrumental conditions in Bayer Method TY-003-S20-01 to a 2-pump LC system, the ILV personnel asked for permission to use the analytical parameters from Bayer Method TY-004-W21-01 [MRID 52029302 (water method)], which employed a 2-pump LC system and had “been shown to work for soil also” (Appendix 4, p. 197 of MRID 51820519). After the Sponsor gave permission to use the analytical parameters from Bayer Method TY-004-W21-01, the ILV laboratory was able to achieve overall acceptable results for the method (for the quantitation ion transition only).

Based on the ILV validation of Bayer Method TY-003-S20-01, the ILV recommended that the ECM method Bayer Method TY-003-S20-01 be updated with the following (p. 33 of MRID 51820519):

- 1) corrected typographical errors in the listing of BCS-CY96288-IS in the mass transition tables and the IUPAC names and/or molecular formulas for BCS-CY96288, BCS-DA63612 and BCS-CU97237;
- 2) the inclusion of analytical parameters for the more common 2-pump LC system; and
- 3) the inclusion of any changes to the procedure for single-sample versus multi-sample microwave extractor use.

The ILV also noted that the extraction procedures, which are critical steps, should be added to the method to reflect a single sample microwave extractor, interspersing the calibration standards within the injection sequence should be considered, and that the units for the standards in the representative linearity curves (µg/L) do not match the units of the calibration standards (ng/mL; p. 33 of MRID 51820519). The reviewer noted that the ILV communications discussed a concern about the method use of a microwave with a stirrer (Appendix 4, p. 197 of MRID 51820519). The “retrofitting” of the ILV microwave with a magnetic stirrer required a cost of “*ca.* \$5,000” (which was approved by the Sponsor). The method requirement of a microwave with a stirrer appeared to create another issue in which the method (Bayer Method TY-003-S20-01) utilized equipment which was not commonly found in other analytical laboratories.

An updated method Bayer Method TY-003-S20-01 should be submitted which corrects significant typographical errors, contains instruction to allow the samples to cool for *ca.* 15 minutes after microwave extract (before adding the internal standard and acetic acid), and provides alternative procedures for the LC parameters and microwave extraction technique when only standard/common analytical laboratory equipment is available. The reviewer noted that ECM 2 MRID 51820516 contained the corrected IUPAC names and/or molecular formulas for BCS-CY96288, BCS-DA63612 and BCS-CU97237, but typographical errors of the IUPAC names and/or molecular formulas for BCS-CY96288, BCS-DA63612 and BCS-CU97237 were found in ECM 1 MRID 51820515; neither ECM 1 MRID 51820515 or ECM 2 MRID 51820516 contained the corrected listing of BCS-CY96288-IS in the mass transition tables (Appendix 1, pp. 18-19 of MRID 51820515; pp. 14-15 of 51820516). The reviewer also noted that, since the ILV laboratory could not generate acceptable performance data for the confirmation ion transitions, the method Bayer Method TY-003-S20-01 should be updated with designating the confirmation ion transition as an identification analysis only and not a quantification analysis.

LOD/LOQ

The Limit of Quantification (LOQ) in soil and sediment was reported as 0.5 ng/g for fluoxapiprolin (BCS-CS55621), BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 in the ECM 1 and ECM 2 (p. 6 of MRID 51820515; pp. 10-11, 26 of MRID 51820516). The ILV reported the nominal LOQ of 0.5 ng/g for these analytes in soil; however, the LOQ was not applied to sediment (pp. 12, 32 of MRID 51820519). In the ILV, the LOQ was calculated for each analyte in soil based on the standard deviation at the 0.5 ng/g fortification ($n = 5$; quantitation ion transition only) and was reported as 0.141-0.454 ng/g for all analytes, except BCS-CY96288 (0.862 ng/g) and BCS-CU97237 (0.512 ng/g; Table 3, pp. 42-43 of MRID 51820519). These exceptions were above the method LOQ of 0.5 ng/g. The Limit of Detection (LOD) was not reported in ECM 1. In ECM 2, the LOD was calculated for each analyte based on the standard deviation at the 0.5 ng/g fortification ($n = 14$ for soil; $n = 7$ for sediment) and was reported as 0.043-0.111 ng/g for all analytes in soil and as 0.037-0.189 ng/g for all analytes in sediment (p. 30; Tables 17-18, pp. 39-40 of MRID 51820516). In the ILV, the LOD was calculated for each analyte in soil based on the standard deviation at the 0.5 ng/g fortification ($n = 5$; quantitation ion transition only) and was reported as 0.0469-0.287 ng/g for all analytes (Table 3, pp. 42-43 of MRID 51820519). Since the LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ.

II. Recovery Findings

ECM 1 (MRID 51820515): MRID 51820515 was a method only study report. No performance data was submitted in this study.

ECM 2 (MRID 51820516): Mean recoveries and relative standard deviations (RSDs) met requirements (mean 70-120%; $RSD \leq 20\%$) for analysis of fluoxapiprolin (BCS-CS55621), BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 in two soil matrices and one sediment matrix at the LOQ (0.5 ng/g; $n = 7$) and

10×LOQ (5.0 ng/g; n = 5; pp. 27-29; Tables 1-16, pp. 34-38; Appendix 1, pp. 47-98 of MRID 51820516). Recovery results of the quantitative and confirmatory ion transitions were comparable for all analytes/matrices, except for BCS-CZ38260 recoveries at the LOQ in the Iowa soil and Pennsylvania sediment where mean recoveries were 15-20% lower in the quantitative ion transition result versus the confirmatory ion transition result. Recovery results were corrected for residues quantified in the controls (pp. 15-16 of MRID 51820515; pp. 24-25; Appendix 1, pp. 47-98 of MRID 51820516). Two soil matrices and one sediment matrix were included in the internal validation. The soil matrices were loamy sand soil [Sample ID: N19SD001-01-W-0001F-0002F-003; pH 6.9 (CaCl₂) 7.5 (aqueous solution); 81% sand, 15% silt, 4% clay, 0.50% organic matter, 0.29% organic carbon] obtained from a California terrestrial field dissipation study (Study METY0051) and silty clay loam soil [Sample ID: N19SD004-01-W-0001 2 3F; pH 7.0 (CaCl₂) 7.5 (aqueous solution); 8% sand, 58% silt, 34% clay, 3.5% organic matter, 2.0% organic carbon] obtained from an Iowa terrestrial field dissipation study (Study METY0057; p. 20 of MRID 51820516). The sediment matrix was silty clay loam sediment [Sample ID - not reported; pH 4.3 (CaCl₂) 4.5 (aqueous solution); 8% sand, 64.5% silt, 27.5% clay, 13.3% organic matter, 7.9% organic carbon] obtained from Brandywine Creek at Chadds Ford, Pennsylvania (November 8, 2017). The laboratory which performed the matrix characterization (USDA texture classification) was not reported. The soil and sediment textures were verified by the reviewer using USDA-NRCS technical support tools. MRID numbers for the terrestrial field dissipation studies Study METY0051 and Study METY0057 were not reported in ECM 1 MRID 51820515 or ECM 2 MRID 51820516 and could not be determined by the reviewer (p. 33 of MRID 51820516).

ILV (MRID 51820519): Mean recoveries and RSDs met requirements for analysis of fluoxapiprolin (BCS-CS55621), BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 in one soil matrix at the LOQ (0.5 ng/g; n = 5) and 10×LOQ (5.0 ng/g; n = 5), except for fluoxapiprolin (BCS-CS55621) at 10×LOQ (mean 127%; Table 1, pp. 37-40; Appendix 5, pp. 203-218 of MRID 51820519). One soil matrix was included in the independent validation: sandy loam soil [Sample ID: RMN-SL-PF (0-6" sample depth); pH 6.7 (1:1 soil:water ratio); 76% sand, 15% silt, 9% clay, 4.6% organic matter-Walkley Black; p. 25; Appendix 3, p. 192 of MRID 51820519]. The soil matrix was obtained from and characterized by Agvise Laboratories, Northwood, North Dakota (USDA texture classification). The soil texture was verified by the reviewer using USDA-NRCS technical support tools.

The method, Bayer Method TY-003-S20-01, was validated by the ILV with the first trial in one soil matrix, and the overall mean recovery (119%) of fluoxapiprolin (BCS-CS55621) was used to support the validation of the method for this analyte, even though the mean recovery at 10×LOQ (127%) was unacceptable (pp. 33-34 of MRID 51820519). The ILV performed the ECM method, Bayer Method TY-003-S20-01, as written, except for the use of a N-evap instead of a TurboVap for evaporation of the extraction sample to aqueous, the addition of allowing the sample to cool for *ca.* 15 minutes after microwave extract (before adding the internal standard and acetic acid), insignificant changes of analytical equipment, and the use of the analytical parameters from Bayer Method TY-004-W21-01 [MRID 52029302 (water method); pp. 26-28; Appendix 4, pp. 193-202]. Based on the ILV validation of Bayer Method TY-003-S20-01, the ILV recommended

that the ECM method Bayer Method TY-003-S20-01 be updated with the following (p. 33 of MRID 51820519):

- 1) corrected typographical errors in the listing of BCS-CY96288-IS in the mass transition tables and the IUPAC names and/or molecular formulas for BCS-CY96288, BCS-DA63612 and BCS-CU97237;
- 2) the inclusion of analytical parameters for the more common 2-pump LC system; and
- 3) the inclusion of any changes to the procedure for single-sample versus multi-sample microwave extractor use.

The ILV also noted that the extraction procedures, which are critical steps, should be added to the method to reflect a single sample microwave extractor, interspersing the calibration standards within the injection sequence should be considered, and that the units for the standards in the representative linearity curves ($\mu\text{g/L}$) do not match the units of the calibration standards (ng/mL ; p. 33 of MRID 51820519). The reviewer noted that the ILV communications discussed a concern about the method use of a microwave with a stirrer (Appendix 4, p. 197). Note: even though two ILV trials were performed, the results of the first trial were used to validate the ECM method Bayer Method TY-003-S20-01 (see Reviewer's Comment #12 for more details).

An updated method Bayer Method TY-003-S20-01 should be submitted which corrects significant typographical errors, contains instruction to allow the samples to cool for *ca.* 15 minutes after microwave extract (before adding the internal standard and acetic acid), and provides alternative procedures for the LC parameters and microwave extraction technique when only standard/common analytical laboratory equipment is available. The reviewer noted that ECM 2 MRID 51820516 contained the corrected IUPAC names and/or molecular formulas for BCS-CY96288, BCS-DA63612 and BCS-CU97237, but typographical errors of the IUPAC names and/or molecular formulas for BCS-CY96288, BCS-DA63612 and BCS-CU97237 were found in ECM 1 MRID 51820515, IUPAC names obtained from DER Attachment 1; neither ECM 1 MRID 51820515 or ECM 2 MRID 51820516 contained the corrected listing of BCS-CY96288-IS in the mass transition tables (Appendix 1, pp. 18-19 of MRID 51820515; pp. 14-15 of 51820516). The reviewer also noted that, since the ILV laboratory could not generate acceptable performance data for the confirmation ion transitions, the method Bayer Method TY-003-S20-01 should be updated with designating the confirmation ion transition as an identification analysis only and not a quantification analysis.

No sediment was included in the ILV; therefore, Bayer Method TY-003-S20-01 was not independently validated for sediment matrices.

Table 2. Initial Validation Method Recoveries for Fluoxapiprolin (BCS-CS55621), BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 in Soil and Sediment^{1,2,3}

Analyte	Fortification Level (ng/g)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
California Loamy Sand Soil						
Quantitation ion transition						
Fluoxapiprolin (BCS-CS55621)	0.5 (LOQ)	7	94-114	102	6.9	6.7
	5.0	5	94-105	100	4.8	4.8
BCS-CY96288	0.5 (LOQ)	7	76-108	96	10.9	11.3
	5.0	5	81-110	97	10.2	10.6
BCS-CU97237	0.5 (LOQ)	7	74-92	86	6.8	7.9
	5.0	5	59-87	76	10.5	13.8
BCS-DA63612	0.5 (LOQ)	7	91-101	97	3.8	3.9
	5.0	5	91-105	101	5.4	5.3
BCS-CC26101	0.5 (LOQ)	7	90-100	97	3.5	3.6
	5.0	5	89-104	99	5.6	5.7
BCS-CZ38260	0.5 (LOQ)	7	90-101	97	4.3	4.4
	5.0	5	87-105	98	6.6	6.7
BCS-BP32808	0.5 (LOQ)	7	81-102	94	7.1	7.6
	5.0	5	74-107	94	13.5	14.4
BCS-DH17585	0.5 (LOQ)	7	92-102	96	4.0	4.2
	5.0	5	90-105	100	6.2	6.2
Confirmation ion transition						
Fluoxapiprolin (BCS-CS55621)	0.5 (LOQ)	7	88-108	97	9.1	9.4
	5.0	5	96-112	104	6.0	5.7
BCS-CY96288	0.5 (LOQ)	7	89-113	101	7.9	7.9
	5.0	5	91-113	99	8.8	8.8
BCS-CU97237	0.5 (LOQ)	7	80-92	88	4.3	4.9
	5.0	5	62-86	79	9.6	12.2
BCS-DA63612	0.5 (LOQ)	7	91-101	96	4.3	4.5
	5.0	5	93-105	100	4.6	4.7
BCS-CC26101	0.5 (LOQ)	7	93-107	98	4.8	4.9
	5.0	5	89-106	101	6.8	6.7
BCS-CZ38260	0.5 (LOQ)	7	89-114	100	9.1	9.1
	5.0	5	89-108	100	6.8	6.8
BCS-BP32808	0.5 (LOQ)	7	79-104	94	8.9	9.5
	5.0	5	70-106	92	14.3	15.7
BCS-DH17585	0.5 (LOQ)	7	91-102	96	4.1	4.3
	5.0	5	92-106	101	5.6	5.5
Iowa Silty Clay Loam Soil						
Quantitation ion transition						
Fluoxapiprolin (BCS-CS55621)	0.5 (LOQ)	7	91-110	97	7.0	7.2
	5.0	5	95-99	96	1.7	1.8
BCS-CY96288	0.5 (LOQ)	7	86-102	96	5.8	6.1
	5.0	5	90-99	93	4.0	4.3
BCS-CU97237	0.5 (LOQ)	7	80-87	83	2.6	3.1
	5.0	5	74-87	82	5.3	6.4

Analyte	Fortification Level (ng/g)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
BCS-DA63612	0.5 (LOQ)	7	92-104	98	5.2	5.3
	5.0	5	95-102	98	2.7	2.7
BCS-CC26101	0.5 (LOQ)	7	89-95	94	2.1	2.2
	5.0	5	95-101	98	2.1	2.2
BCS-CZ38260	0.5 (LOQ)	7	83-98	87	5.2	5.9
	5.0	5	88-95	92	2.5	2.7
BCS-BP32808	0.5 (LOQ)	7	88-96	93	3.0	3.2
	5.0	5	89-102	97	4.9	5.1
BCS-DH17585	0.5 (LOQ)	7	82-92	86	3.8	4.5
	5.0	5	89-96	92	2.6	2.8
Confirmation ion transition						
Fluoxapiprolin (BCS-CS55621)	0.5 (LOQ)	7	93-110	100	7.2	7.2
	5.0	5	95-106	102	4.6	4.5
BCS-CY96288	0.5 (LOQ)	7	88-104	96	5.9	6.1
	5.0	5	91-97	94	2.3	2.5
BCS-CU97237	0.5 (LOQ)	7	75-97	84	8.2	9.7
	5.0	5	74-91	85	6.5	7.7
BCS-DA63612	0.5 (LOQ)	7	89-100	96	3.5	3.7
	5.0	5	92-106	97	5.3	5.5
BCS-CC26101	0.5 (LOQ)	7	93-102	97	3.3	3.3
	5.0	5	99-102	100	1.4	1.4
BCS-CZ38260	0.5 (LOQ)	7	91-118	108	9.7	9.0
	5.0	5	82-105	93	9.0	9.7
BCS-BP32808	0.5 (LOQ)	7	84-101	92	7.4	8.0
	5.0	5	90-98	95	3.6	3.8
BCS-DH17585	0.5 (LOQ)	7	75-88	82	4.9	6.0
	5.0	5	89-96	93	2.9	3.1
Pennsylvania Silty Clay Loam Sediment						
Quantitation ion transition						
Fluoxapiprolin (BCS-CS55621)	0.5 (LOQ)	7	85-104	93	6.0	6.5
	5.0	5	98-106	101	3.1	3.1
BCS-CY96288	0.5 (LOQ)	7	78-107	97	12.0	12.4
	5.0	5	90-106	98	5.7	5.8
BCS-CU97237	0.5 (LOQ)	7	77-86	82	3.3	4.0
	5.0	5	76-82	79	2.5	3.1
BCS-DA63612	0.5 (LOQ)	7	92-100	96	2.7	2.8
	5.0	5	96-102	98	2.3	2.4
BCS-CC26101	0.5 (LOQ)	7	91-99	95	2.4	2.5
	5.0	5	99-104	101	2.0	2.0
BCS-CZ38260	0.5 (LOQ)	7	81-88	84	2.9	3.4
	5.0	5	89-93	92	1.8	1.9
BCS-BP32808	0.5 (LOQ)	7	96-108	103	4.1	3.9
	5.0	5	99-110	103	4.5	4.4
BCS-DH17585	0.5 (LOQ)	7	90-108	95	6.0	6.2
	5.0	5	100-103	101	0.9	0.9
Confirmation ion transition						

Analyte	Fortification Level (ng/g)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
Fluoxapiprolin (BCS-CS55621)	0.5 (LOQ)	7	95-119	110	8.6	7.9
	5.0	5	99-112	104	4.8	4.6
BCS-CY96288	0.5 (LOQ)	7	89-112	101	7.9	7.9
	5.0	5	92-110	101	8.9	8.9
BCS-CU97237	0.5 (LOQ)	7	82-92	88	3.8	4.3
	5.0	5	78-85	81	2.7	3.4
BCS-DA63612	0.5 (LOQ)	7	93-102	96	3.5	3.6
	5.0	5	99-105	102	2.2	2.2
BCS-CC26101	0.5 (LOQ)	7	100-106	103	2.3	2.2
	5.0	5	100-109	104	3.6	3.5
BCS-CZ38260	0.5 (LOQ)	7	93-113	100	7.3	7.3
	5.0	5	88-98	92	4.3	4.7
BCS-BP32808	0.5 (LOQ)	7	89-107	100	5.7	5.7
	5.0	5	100-108	104	3.2	3.1
BCS-DH17585	0.5 (LOQ)	7	90-96	93	2.1	2.3
	5.0	5	99-105	102	2.4	2.4

Data (recovery results were corrected for residues quantified in the controls, pp. 15-16 of MRID 51820515; pp. 24-25; Appendix 1, pp. 47-98 of MRID 51820516) were obtained from pp. 27-29, Tables 1-16, pp. 34-38 of MRID 51820516. Since the LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ.

1 ECM 1 MRID 51820515 contained the full method written in a step-wise manner, but no performance data; while ECM 2 MRID 51820516 contained performance data, but only a method summary.

2 In the ECM 2 MRID 51820516 (Internal Validation), two soil matrices and one sediment matrix were included in the internal validation. The soil matrices were loamy sand soil [Sample ID: N19SD001-01-W-0001F-0002F-003; pH 6.9 (CaCl₂) 7.5 (aqueous solution); 81% sand, 15% silt, 4% clay, 0.50% organic matter, 0.29% organic carbon] obtained from a California terrestrial field dissipation study (Study METY0051) and silty clay loam soil [Sample ID: N19SD004-01-W-0001 2 3F; pH 7.0 (CaCl₂) 7.5 (aqueous solution); 8% sand, 58% silt, 34% clay, 3.5% organic matter, 2.0% organic carbon] obtained from an Iowa terrestrial field dissipation study (Study METY0057; p. 20 of MRID 51820516). The sediment matrix was silty clay loam sediment [Sample ID - not reported; pH 4.3 (CaCl₂) 4.5 (aqueous solution); 8% sand, 64.5% silt, 27.5% clay, 13.3% organic matter, 7.9% organic carbon] obtained from Brandywine Creek at Chadds Ford, Pennsylvania (November 8, 2017). The laboratory which performed the matrix characterization (USDA texture classification) was not reported. The soil and sediment textures were verified by the reviewer using USDA-NRCS technical support tools. MRID numbers for the terrestrial field dissipation studies, Study METY0051 and Study METY0057, were not reported in ECM 1 MRID 51820515 or ECM 2 MRID 51820516 and could not be determined by the reviewer (p. 33 of MRID 51820516).

3 Two ion pair transitions were monitored (primary and confirmatory, respectively): m/z 650→610.2 and m/z 650→378 for fluoxapiprolin (BCS-CS55621), m/z 666→626.1 and m/z 666→191 for BCS-CY96288, m/z 442.2→332 and m/z 442.2→208 for BCS-CU97237, m/z 456→345.2 and m/z 456→222.1 for BCS-DA63612, m/z 225→161 and m/z 225→141 for BCS-CC26101, m/z 161→76 and m/z 163.1→125 for BCS-CZ38260, m/z 169→101 and m/z 169→149 for BCS-BP32808, and m/z 403→169 and m/z 403→157 for BCS-DH17585.

Table 3. Independent Validation Method Recoveries for Fluoxapiprolin (BCS-CS55621), BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 in Soil^{1,2,3}

Analyte	Fortification Level (ng/g)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
Sandy Loam Soil						
Quantitation ion transition						
Fluoxapiprolin (BCS-CS55621)	0.5 (LOQ)	5	104-118	110	5.3	4.8
	5.0	5	122-132	127	3.9	3.1
BCS-CY96288	0.5 (LOQ)	5	73-111	96	15.3	16.0
	5.0	5	108-115	112	3.0	2.7
BCS-CU97237	0.5 (LOQ)	5	68-91	76	9.2	12.1
	5.0	5	79-107	89	11.5	13.0
BCS-DA63612	0.5 (LOQ)	5	80-97	87	6.9	7.9
	5.0	5	109-124	115	5.6	4.9
BCS-CC26101	0.5 (LOQ)	5	96-103	99	2.6	2.6
	5.0	5	112-121	116	3.8	3.3
BCS-CZ38260	0.5 (LOQ)	5	90-105	98	5.9	6.0
	5.0	5	115-121	117	2.5	2.1
BCS-BP32808	0.5 (LOQ)	5	87-104	94	6.2	6.6
	5.0	5	109-121	114	4.7	4.1
BCS-DH17585	0.5 (LOQ)	5	72-90	82	8.3	10.1
	5.0	5	92-108	99	7.5	7.6

Data (uncorrected results, pp. 29-31; Appendix 5, pp. 203-218) were obtained from Table 1, pp. 37-40 of MRID 51820519. Since the LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ.

1 In the ILV, one soil matrix was included in the independent validation: sandy loam soil [Sample ID: RMN-SL-PF (0-6" sample depth); pH 6.7 (1:1 soil:water ratio); 76% sand, 15% silt, 9% clay, 4.6% organic matter-Walkley Black; p. 25; Appendix 3, p. 192 of MRID 51820519]. The soil matrix was obtained from and characterized by Agvise Laboratories, Northwood, North Dakota (USDA texture classification). The soil texture was verified by the reviewer using USDA-NRCS technical support tools.

2 No sediment was included in the ILV.

3 One ion pair transition was monitored for each analyte: m/z 650.0→610.2 for fluoxapiprolin (BCS-CS55621), m/z 666.0→626.0 for BCS-CY96288, m/z 442.0→332.0 for BCS-CU97237, m/z 456.0→345.0 for BCS-DA63612, m/z 225.0→161.0 for BCS-CC26101, m/z 161.0→76.0 for BCS-CZ38260, m/z 169.0→101.0 for BCS-BP32808, and m/z 403.0→169.0 for BCS-DH17585; the monitored quantitation/primary ion transitions of the ILV were similar to those of the ECM; however, no confirmation ion transition was monitored for the analytes.

III. Method Characteristics

The LOQ in soil and sediment was reported as 0.5 ng/g for fluoxapiprolin (BCS-CS55621), BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 in the ECM 1 and ECM 2 (p. 6 of MRID 51820515; pp. 10-11, 26 of MRID 51820516). No justification or calculation for LOQ was reported in ECM 1. In ECM 2, the LOQ was defined as the lowest fortification level in which the method was validated where mean recovery was 70-110% and relative standard deviation was $\leq 20\%$, as well as blank values were below 30% at this level. The LOD was not reported in ECM 1. In ECM 2, the LOD was calculated for each analyte the standard deviation at the 0.5 ng/g fortification ($n = 14$ for soil; $n = 7$ for sediment) using the following equation (p. 30 of MRID 51820516):

$$\text{LOD} = (t_{0.99} \times \text{SD})$$

Where, $t_{0.99}$ is the one-tailed t statistic for $n = 14$ (2.650; soil) or $n = 7$ (3.143; sediment) and SD is the standard deviation of the analyte recovery measurements at the target LOQ.

In ECM 2, the LOQs were calculated as 0.043-0.111 ng/g for all analytes in soil and as 0.037-0.189 ng/g for all analytes in sediment (p. 30; Tables 17-18, pp. 39-40 of MRID 51820516). No further justification for LOD was reported in ECM 2.

The ILV reported the nominal LOQ of 0.5 ng/g for fluoxapiprolin (BCS-CS55621), BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 in soil; however, the LOQ was not applied to sediment (pp. 12, 32 of MRID 51820519). In the ILV, the LOQ and LOD were calculated for each analyte in soil based on the standard deviation at the 0.5 ng/g fortification ($n = 5$; quantitation ion transition only) using the following equations (Table 3, pp. 42-43):

$$\text{LOD} = (t_{0.99} \times \text{SD})$$

Where, $t_{0.99}$ is the one-tailed t statistic for $n = 5$ (3.747) and SD is the standard deviation of the analyte recovery measurements at the target LOQ.

$$\text{LOQ} = 3 \times (\text{Calculated LOD})$$

In the ILV, the LOQs were calculated as 0.141-0.454 ng/g for all analytes, except BCS-CY96288 (0.862 ng/g) and BCS-CU97237 (0.512 ng/g; Table 3, pp. 42-43 of MRID 51820519). These exceptions were above the method LOQ of 0.5 ng/g. The LODs were calculated as 0.0469-0.287 ng/g for all analytes (Table 3, pp. 42-43 of MRID 51820519). No justifications for the LOQ or LOD were reported in the ILV.

Since the LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ.

Table 4a. Method Characteristics

			Fluoxapiprolin (BCS-CS55621)	BCS-CY96288	BCS-CU97237	BCS-DA63612
Limit of Quantitation (LOQ)*	ECM 1 ¹		0.5 ng/g (noted that it can be adjusted, as required)			
	ECM 2 ²		0.5 ng/g			
	ILV	Nominal	0.5 ng/g			
		Calculated	0.286 ng/g	0.862 ng/g ³	0.512 ng/g ³	0.387 ng/g
Limit of Detection (LOD)	ECM 1		Not reported			
	ECM 2 (calculated)		0.097 ng/g (soil) 0.095 ng/g (sediment)	0.111 ng/g (soil) 0.189 ng/g (sediment)	0.067 ng/g (soil) 0.051 ng/g (sediment)	0.060 ng/g (soil) 0.043 ng/g (sediment)
	ILV (calculated)		0.0953 ng/g	0.287 ng/g ⁴	0.171 ng/g ⁴	0.129 ng/g
Linearity (calibration curve r and concentration range)	ECM 1 (unspecified matrix)		r = 0.9990 (Q)	r = 0.9989 (Q)	r = 0.9997 (Q)	r = 0.9996 (Q)
			0.25-100 µg/L			
	ECM 2 ⁵		r = 0.9990 (Q, soil) r = 0.9987 (C, soil) r = 0.9988 (Q, sediment) r = 0.9981 (C, sediment)	r = 0.9991 (Q, soil) r = 0.9993 (C, soil) r = 0.9983 (Q, sediment) r = 0.9978 (C, sediment)	r = 0.9994 (Q, soil) r = 0.9993 (C, soil) r = 0.9997 (Q, sediment) r = 0.9995 (C, sediment)	r = 0.9988 (Q, soil) r = 0.9992 (C, soil) r = 0.9997 (Q, sediment) r = 0.9991 (C, sediment)
			0.250-50.0 ng/mL			
			ILV ⁶		r = 0.99840846 (Q)	r = 0.99851185 (Q)
	0.250-50.0 ng/mL (equivalent to 0.200-40.0 ng/g)					
Repeatable	ECM 1		No performance data submitted			
	ECM 2 ⁷		Yes for LOQ (0.5 ng/g) and 10×LOQ (5.0 ng/g) in two characterized soil matrices (loamy sand and silty clay loam) and one characterized sediment matrix (silty clay loam)			
	ILV ^{8,9}		Yes for LOQ (0.5 ng/g) in one characterized soil matrix (sandy loam); No for 10×LOQ (5.0 ng/g; mean 127%) No sediment was included	Yes for LOQ (0.5 ng/g) and 10×LOQ (5.0 ng/g) in one characterized soil matrix (sandy loam) No sediment was included		
Reproducible ^{10,11}			Yes for 0.5 ng/g (LLMV)* in soil matrices. No for 5.0 ng/g in soil matrices.	Yes for 0.5 ng/g (LLMV)* and 5.0 ng/g in soil matrices.		

			Fluoxapiprolin (BCS-CS55621)	BCS-CY96288	BCS-CU97237	BCS-DA63612
			Could not be determined for sediment matrices; only one set of performance data was submitted.			
Specific	ECM 1 - Soil (unspecified matrix)		Yes, no baseline interferences were observed near the LOQ analyte peak.	Yes, only minor baseline interferences were observed near the LOQ analyte peak.	Yes, only minor baseline interferences were observed near the LOQ analyte peak, but baseline was elevated at RT of analyte.	Yes, only minor baseline interferences were observed near the LOQ analyte peak.
			Only representative LOQ chromatograms were provided. No untreated control representative chromatograms were provided to assess matrix interferences at the RT of the analyte.			
	ECM 2	Soil	Yes, no matrix interferences were observed (based on quantified residues). Minor baseline noise was observed near the analyte (C only).	Yes, no matrix interferences were observed (based on quantified residues), but notable baseline noise surrounding LOQ analyte peak (Q & C).	Yes, matrix interferences were <3% of the LOQ (based on quantified residues). Some baseline noise was observed near the analyte (more notable in silty clay loam soil).	Yes, matrix interferences were <5% of the LOQ (based on quantified residues). Minor baseline noise was observed near the analyte.
		Sediment	Yes, no matrix interferences were observed (based on quantified residues).	Yes, matrix interferences were <4% of the LOQ (based on quantified residues).	Yes, matrix interferences were 2.4-16.4% (Q) ¹² and <6% (C) of the LOQ (based on quantified residues).	Yes, matrix interferences were <6% of the LOQ (based on quantified residues).
			No representative chromatograms were provided.			
	ILV - Soil		Yes, no matrix interferences were observed.	Yes, no matrix interferences were observed.	Yes, no matrix interferences were observed. Minor baseline noise was observed near the analyte.	Yes, no matrix interferences were observed. Minor baseline noise was observed near the analyte.
			Only representative chromatograms from the quantitation ion transition were provided.			

Data were obtained from p. 6 (LOQ/LOD); Appendix 2, pp. 26-33 (linearity coefficients & calibration curves); Appendix 3, pp. 34-41 (chromatograms) of MRID 51820515; pp. 10-11, 26, 30; Tables 17-18, pp. 39-40 (LOQ/LOD); pp. 27-29; Tables 1-16, pp. 34-38; Appendix 1, pp. 47-94 (recovery data); Appendix 1, pp. 47-98; Appendix 3, pp. 145-160 (linearity coefficients & calibration curves); Appendix 2, pp. 99-144 (chromatograms) of MRID 51820516; Table 3, pp. 42-43 (LOQ/LOD); Table 1, pp. 37-40; Appendix 5, pp. 203-218 (recovery data); p. 29; Appendix 5, pp. 203-218 (linearity coefficients); Figure 2, pp. 61-68 (calibration curves); Figures 3-9, pp. 69-124 (chromatograms) of MRID 51820519; DER Excel Attachment. Q = quantitative ion transition; C = confirmatory ion transition.

- * Since the LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ. The lowest concentration tested with sufficiently accurate and precise recoveries is the LLMV.
- 1 ECM 1 MRID 51820515 contained the full method written in a step-wise manner, but no performance data.
 - 2 ECM 2 MRID 51820516 (Internal validation) contained the method summary and performance data.
 - 3 Calculated LOQ > method LOQ (0.5 ng/g).
 - 4 Calculated LOD >30% of method LOQ (0.15 ng/g).
 - 5 Reported r values were reviewer-calculated from r^2 values reported in the study report (Appendix 1, pp. 47-94 of MRID 51820516; DER Excel Attachment). Values were reported to four significant figures.
 - 6 In the ILV, no confirmation ion transition was monitored for the analytes.
 - 7 In the ECM 2 MRID 51820516 (Internal Validation), two soil matrices and one sediment matrix were included in the internal validation. The soil matrices were loamy sand soil [Sample ID: N19SD001-01-W-0001F-0002F-003; pH 6.9 (CaCl₂) 7.5 (aqueous solution); 81% sand, 15% silt, 4% clay, 0.50% organic matter, 0.29% organic carbon] obtained from a California terrestrial field dissipation study (Study METY0051) and silty clay loam soil [Sample ID: N19SD004-01-W-0001 2 3F; pH 7.0 (CaCl₂) 7.5 (aqueous solution); 8% sand, 58% silt, 34% clay, 3.5% organic matter, 2.0% organic carbon] obtained from an Iowa terrestrial field dissipation study (Study METY0057; p. 20 of MRID 51820516). The sediment matrix was silty clay loam sediment [Sample ID - not reported; pH 4.3 (CaCl₂) 4.5 (aqueous solution); 8% sand, 64.5% silt, 27.5% clay, 13.3% organic matter, 7.9% organic carbon] obtained from Brandywine Creek at Chadds Ford, Pennsylvania (November 8, 2017). The laboratory which performed the matrix characterization (USDA texture classification) was not reported. The soil and sediment textures were verified by the reviewer using USDA-NRCS technical support tools. MRID numbers for the terrestrial field dissipation studies Study METY0051 and Study METY0057 were not reported in ECM 1 MRID 51820515 or ECM 2 MRID 51820516 and could not be determined by the reviewer (p. 33 of MRID 51820516).
 - 8 In the ILV, one soil matrix was included in the independent validation: sandy loam soil [Sample ID: RMN-SL-PF (0-6" sample depth); pH 6.7 (1:1 soil:water ratio); 76% sand, 15% silt, 9% clay, 4.6% organic matter-Walkley Black; p. 25; Appendix 3, p. 192 of MRID 51820519]. The soil matrix was obtained from and characterized by Agvise Laboratories, Northwood, North Dakota (USDA texture classification). The soil texture was verified by the reviewer using USDA-NRCS technical support tools.
 - 9 The ILV validated the method, BAYER METHOD TY-003-S20-01, with the first trial in one soil matrix, and the overall mean recovery (119%) of fluoxapiprolin (BCS-CS55621) was used to support the validation of the method for this analyte, even though the mean recovery at 10×LOQ (127%) was unacceptable (pp. 33-34 of MRID 51820519). The ILV performed the ECM method, Bayer Method TY-003-S20-01, as written, except for the use of a N-evap instead of a TurboVap for evaporation of the extraction sample to aqueous, the addition of allowing the sample to cool for *ca.* 15 minutes after microwave extract (before adding the internal standard and acetic acid), insignificant changes of analytical equipment, and the use of the analytical parameters from Bayer Method TY-004-W21-01 [MRID 52029302 (water method); pp. 26-28; Appendix 4, pp. 193-202]. Based on the ILV validation of Bayer Method TY-003-S20-01, the ILV recommended that the ECM method Bayer Method TY-003-S20-01 be updated with the following (p. 33):
 - 1) corrected typographical errors in the listing of BCS-CY96288-IS in the mass transition tables and the IUPAC names and/or molecular formulas for BCS-CY96288, BCS-DA63612 and BCS-CU97237;
 - 2) the inclusion of analytical parameters for the more common 2-pump LC system; and
 - 3) the inclusion of any changes to the procedure for single-sample versus multi-sample microwave extractor use.The ILV also noted that the extraction procedures are the critical steps, interspersing the calibration standards within the injection sequence should be considered, and that the units for the standards in the representative linearity curves (µg/L) do not match the units of the calibration standards (ng/mL; p. 33 of MRID 51820519). The reviewer noted that the ILV communications discussed a concern about the method use of a microwave with a stirrer (Appendix 4, p. 197).
 - 10 An updated method Bayer Method TY-003-S20-01 should be submitted which corrects significant typographical errors, contains instruction to allow the samples to cool for *ca.* 15 minutes after microwave extract (before adding the internal standard and acetic acid), and provides alternative procedures for the LC

parameters and microwave extraction technique when only standard/common analytical laboratory equipment is available. The reviewer noted that ECM 2 MRID 51820516 contained the corrected IUPAC names and/or molecular formulas for BCS-CY96288, BCS-DA63612 and BCS-CU97237, but typographical errors of the IUPAC names and/or molecular formulas for BCS-CY96288, BCS-DA63612 and BCS-CU97237 were found in ECM 1 MRID 51820515; neither ECM 1 MRID 51820515 or ECM 2 MRID 51820516 contained the corrected listing of BCS-CY96288-IS in the mass transition tables (Appendix 1, pp. 18-19 of MRID 51820515; pp. 14-15 of 51820516). The reviewer also noted that, since the ILV laboratory could not generate acceptable performance data for the confirmation ion transitions, the method Bayer Method TY-003-S20-01 should be updated with designating the confirmation ion transition as an identification analysis only and not a quantification analysis.

11 No sediment was included in the ILV; therefore, Bayer Method TY-003-S20-01 was not independently validated for sediment matrices.

12 Data obtained from Appendix 1, p. 83 of MRID 51820516. The reviewer noted that interferences of 16.4% (0.082 ng/g) would be >50% of the typical nominal LOD of 30% of the LOD.

Table 4b. Method Characteristics (con't)

		BCS-CC26101	BCS-CZ38260	BCS-BP32808	BCS-DH17585
Limit of Quantitation (LOQ)*	ECM 1 ¹	0.5 ng/g (noted that it can be adjusted, as required)			
	ECM 2 ²	0.5 ng/g			
	ILV	Nominal	0.5 ng/g		
		Calculated	0.141 ng/g	0.322 ng/g	0.347 ng/g
Limit of Detection (LOD)	ECM 1	Not reported			
	ECM 2 (calculated)	0.043 ng/g (soil) 0.037 ng/g (sediment)	0.090 ng/g (soil) 0.045 ng/g (sediment)	0.069 ng/g (soil) 0.064 ng/g (sediment)	0.083 ng/g (soil) 0.094 ng/g (sediment)
	ILV (calculated)	0.0469 ng/g	0.107 ng/g	0.116 ng/g	0.151 ng/g³
Linearity (calibration curve r and concentration range)	ECM 1 (unspecified matrix)	r = 0.9999 (Q)	r = 0.9999 (Q)	r = 0.9996 (Q)	r = 0.9998 (Q)
	ECM 2 ⁴	0.25-100 µg/L			
		r = 0.9998 (Q, soil) r = 0.9999 (C, soil) r = 0.9999 (Q, sediment) r = 0.9998 (C, sediment)	r = 0.9997 (Q, soil) r = 0.9987 (C, soil) r = 0.9996 (Q, sediment) r = 0.9988 (C, sediment)	r = 0.9998 (Q, soil) r = 0.9997 (C, soil) r = 0.9993 (Q, sediment) r = 0.9994 (C, sediment)	r = 0.9997 (Q, soil) r = 0.9997 (C, soil) r = 0.9998 (Q, sediment) r = 0.9997 (C, sediment)
		0.250-50.0 ng/mL			
	ILV ⁵	r = 0.99933409 (Q)	r = 0.99888524 (Q)	r = 0.99844947 (Q)	r = 0.99897208 (Q)
		0.250-50.0 ng/mL (equivalent to 0.200-40.0 ng/g)			
Repeatable	ECM 1	No performance data submitted			
	ECM 2 ⁶	Yes for LOQ (0.5 ng/g) and 10×LOQ (5.0 ng/g) in two characterized soil matrices (loamy sand and silty clay loam) and one characterized sediment matrix (silty clay loam)			
	ILV ^{7,8}	Yes for LOQ (0.5 ng/g) and 10×LOQ (5.0 ng/g) in one characterized soil matrix (sandy loam) No sediment was included			
Reproducible ^{9,10}		Yes for 0.5 ng/g (LLMV)* and 5.0 ng/g in soil matrices.			
		Could not be determined for sediment matrices; only one set of performance data was submitted.			

		BCS-CC26101	BCS-CZ38260	BCS-BP32808	BCS-DH17585	
Specific	ECM 1 - Soil (unspecified matrix)		Yes, only minor baseline interferences were observed near the LOQ analyte peak. A notable contaminant (<i>ca.</i> 50% of LOQ peak area, based on visual comparison) was located at <i>ca.</i> 2.75 min.	Yes, no baseline interferences were observed near the LOQ analyte peak.	Yes, only minor baseline interferences were observed near the LOQ analyte peak.	
	Only representative LOQ chromatograms were provided. No untreated control representative chromatograms were provided to assess matrix interferences at the RT of the analyte.					
	ECM 2	Soil	Yes, matrix interferences were <2% of the LOQ (based on quantified residues). A notable contaminant (<i>ca.</i> 40% of LOQ peak area, based on visual comparison) was located at <i>ca.</i> 1 min.	Yes for Q ion, no matrix interferences were observed (based on quantified residues). Yes for C ion, matrix interferences were <10% of the LOQ (based on quantified residues). Notable baseline noise surrounding LOQ analyte peak.	Yes, matrix interferences were <1% of the LOQ (based on quantified residues). Minor baseline noise was observed near the analyte	Yes, no matrix interferences were observed (based on quantified residues). A major nearby contaminant (RT <i>ca.</i> 1.75 min) was noted in the C ion. ¹¹
		Sediment	Yes, matrix interferences were <1% of the LOQ (based on quantified residues).	Yes, no matrix interferences were observed (based on quantified residues).	Yes, matrix interferences were <1% of the LOQ (based on quantified residues).	Yes, no matrix interferences were observed (based on quantified residues).
			No representative chromatograms were provided.			
ILV - Soil		Yes, no matrix interferences were observed (based on quantified residues). Elevated baseline noise was observed near the analyte.	Yes, matrix interferences were <4% of the LOQ (based on quantified residues).	Yes, matrix interferences were <10% of the LOQ (based on quantified residues in reagent blank only). A notable contaminant region (<i>ca.</i> 50% of LOQ peak area/height, based on visual comparison) was located at <i>ca.</i> 2.5-2.7 min. ¹²	No, LOQ peak height was the same as nearby contaminants (RT <i>ca.</i> 2.5-2.6 min) and baseline was elevated around the analyte peak. ¹³ No matrix interferences were observed (based on quantified residues).	

		BCS-CC26101	BCS-CZ38260	BCS-BP32808	BCS-DH17585
		Only representative chromatograms from the quantitation ion transition were provided.			

Data were obtained from p. 6 (LOQ/LOD); Appendix 2, pp. 26-33 (linearity coefficients & calibration curves); Appendix 3, pp. 34-41 (chromatograms) of MRID 51820515; pp. 10-11, 26, 30; Tables 17-18, pp. 39-40 (LOQ/LOD); pp. 27-29; Tables 1-16, pp. 34-38; Appendix 1, pp. 47-94 (recovery data); Appendix 1, pp. 47-98; Appendix 3, pp. 145-160 (linearity coefficients & calibration curves); Appendix 2, pp. 99-144 (chromatograms) of MRID 51820516; Table 3, pp. 42-43 (LOQ/LOD); Table 1, pp. 37-40; Appendix 5, pp. 203-218 (recovery data); p. 29; Appendix 5, pp. 203-218 (linearity coefficients); Figure 2, pp. 61-68 (calibration curves); Figures 3-9, pp. 69-124 (chromatograms) of MRID 51820519; DER Excel Attachment. Q = quantitative ion transition; C = confirmatory ion transition; LS = Loamy sand soil; SCL = Silty clay loam soil; SCLS = Silty clay loam sediment; SL = Sandy loam soil.

* Since the LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ. The lowest concentration tested with sufficiently accurate and precise recoveries is the LLMV.

1 ECM 1 MRID 51820515 contained the full method written in a step-wise manner, but no performance data.

2 ECM 2 MRID 51820516 (Internal validation) contained the method summary and performance data.

3 Calculated LOD > 30% of method LOQ (0.15 ng/g).

4 Reported r values were reviewer-calculated from r² values reported in the study report (Appendix 1, pp. 47-94 of MRID 51820516; DER Excel Attachment). Values were reported to four significant figures.

5 In the ILV, no confirmation ion transition was monitored for the analytes.

6 In the ECM 2 MRID 51820516 (Internal Validation), two soil matrices and one sediment matrix were included in the internal validation. The soil matrices were loamy sand soil [Sample ID: N19SD001-01-W-0001F-0002F-003; pH 6.9 (CaCl₂) 7.5 (aqueous solution); 81% sand, 15% silt, 4% clay, 0.50% organic matter, 0.29% organic carbon] obtained from a California terrestrial field dissipation study (Study METY0051) and silty clay loam soil [Sample ID: N19SD004-01-W-0001 2 3F; pH 7.0 (CaCl₂) 7.5 (aqueous solution); 8% sand, 58% silt, 34% clay, 3.5% organic matter, 2.0% organic carbon] obtained from an Iowa terrestrial field dissipation study (Study METY0057; p. 20 of MRID 51820516). The sediment matrix was silty clay loam sediment [Sample ID - not reported; pH 4.3 (CaCl₂) 4.5 (aqueous solution); 8% sand, 64.5% silt, 27.5% clay, 13.3% organic matter, 7.9% organic carbon] obtained from Brandywine Creek at Chadds Ford, Pennsylvania (November 8, 2017). The laboratory which performed the matrix characterization (USDA texture classification) was not reported. The soil and sediment textures were verified by the reviewer using USDA-NRCS technical support tools. MRID numbers for the terrestrial field dissipation studies Study METY0051 and Study METY0057 were not reported in ECM 1 MRID 51820515 or ECM 2 MRID 51820516 and could not be determined by the reviewer (p. 33 of MRID 51820516).

7 In the ILV, one soil matrix was included in the independent validation: sandy loam soil [Sample ID: RMN-SL-PF (0-6" sample depth); pH 6.7 (1:1 soil:water ratio); 76% sand, 15% silt, 9% clay, 4.6% organic matter-Walkley Black; p. 25; Appendix 3, p. 192 of MRID 51820519]. The soil matrix was obtained from and characterized by Agvise Laboratories, Northwood, North Dakota (USDA texture classification). The soil texture was verified by the reviewer using USDA-NRCS technical support tools.

8 The ILV validated the method, BAYER METHOD TY-003-S20-01, with the first trial in one soil matrix, and the overall mean recovery (119%) of fluoxapiprolin (BCS-CS55621) was used to support the validation of the method for this analyte, even though the mean recovery at 10×LOQ (127%) was unacceptable (pp. 33-34 of MRID 51820519). The ILV performed the ECM method, Bayer Method TY-003-S20-01, as written, except for the use of a N-evap instead of a TurboVap for evaporation of the extraction sample to aqueous, the addition of allowing the sample to cool for *ca.* 15 minutes after microwave extract (before adding the internal standard and acetic acid), insignificant changes of analytical equipment, and the use of the analytical parameters from Bayer Method TY-004-W21-01 [MRID 52029302 (water method); pp. 26-28; Appendix 4, pp. 193-202]. Based on the ILV validation of Bayer Method TY-003-S20-01, the ILV recommended that the ECM method Bayer Method TY-003-S20-01 be updated with the following (p. 33):

- 1) corrected typographical errors in the listing of BCS-CY96288-IS in the mass transition tables and the IUPAC names and/or molecular formulas for BCS-CY96288, BCS-DA63612 and BCS-CU97237;
- 2) the inclusion of analytical parameters for the more common 2-pump LC system; and
- 3) the inclusion of any changes to the procedure for single-sample versus multi-sample microwave extractor use.

The ILV also noted that the extraction procedures are the critical steps, interspersing the calibration standards within the injection sequence should be considered, and that the units for the standards in the representative linearity curves ($\mu\text{g/L}$) do not match the units of the calibration standards (ng/mL ; p. 33 of MRID 51820519). The reviewer noted that the ILV communications discussed a concern about the method use of a microwave with a stirrer (Appendix 4, p. 197).

- 9 An updated method Bayer Method TY-003-S20-01 should be submitted which corrects significant typographical errors, contains instruction to allow the samples to cool for *ca.* 15 minutes after microwave extract (before adding the internal standard and acetic acid), and provides alternative procedures for the LC parameters and microwave extraction technique when only standard/common analytical laboratory equipment is available. The reviewer noted that ECM 2 MRID 51820516 contained the corrected IUPAC names and/or molecular formulas for BCS-CY96288, BCS-DA63612 and BCS-CU97237, but typographical errors of the IUPAC names and/or molecular formulas for BCS-CY96288, BCS-DA63612 and BCS-CU97237 were found in ECM 1 MRID 51820515; neither ECM 1 MRID 51820515 or ECM 2 MRID 51820516 contained the corrected listing of BCS-CY96288-IS in the mass transition tables (Appendix 1, pp. 18-19 of MRID 51820515; pp. 14-15 of 51820516). The reviewer also noted that, since the ILV laboratory could not generate acceptable performance data for the confirmation ion transitions, the method Bayer Method TY-003-S20-01 should be updated with designating the confirmation ion transition as an identification analysis only and not a quantification analysis.
- 10 No sediment was included in the ILV; therefore, Bayer Method TY-003-S20-01 was not independently validated for sediment matrices.
- 11 Data obtained in Appendix 2, pp. 123, 137, 142 of MRID 51820516.
- 12 Data obtained in Figure 8, p. 115 of MRID 51820519.
- 13 Data obtained in Figure 8, p. 116 of MRID 51820519.

IV. Method Deficiencies and Reviewer's Comments

1. This DER was prepared with two MRIDs as the internal laboratory validations (ECMs): MRID 51820515 & MRID 51820516. ECM 1 = MRID 51820515 (Bayer Method TY-003-S20-01). ECM 2 = MRID 51820516 (Internal validation). ECM 2 MRID 51820516 contained only a method summary, while ECM 1 MRID 51820515 contained the full method written in a step-wise manner (pp. 11-12 of MRID 51820515; pp. 20-21 of MRID 51820516). In OCSPP guideline 850.6100 states that "The ECM should be clearly written with complete analytical methods that describe the exact procedure, materials, and equipment in sufficient detail to be used by laboratory chemists to review the ECM and its associated ILV results".

OCSPP guideline 850.6100 could not have been satisfied using only ECM 2 MRID 51820516 since the ECM method (Bayer Method No. TY-003-S20-01) was not completely reproduced in ECM 2 MRID 51820516. Method details such as volume of extraction solvent, microwave extraction procedure, volume of mixed internal standard solution to add to samples, and calibration standard preparation were not included in ECM 2 MRID 51820516. These details were found in ECM 1 MRID 51820515.

2. Since the reported method LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ (p. 6 of MRID 51820515; pp. 10-11, 26, 30; Tables 17-18, pp. 39-40 of MRID 51820516; pp. 12, 32; Table 3, pp. 42-43 of MRID 51820519). The lowest concentration tested with sufficiently accurate and precise recoveries is the LLMV. Based on the performance data submitted by the ILV and ECM 2, the LLMV was equivalent to the ECM 2 and ILV reported method LOQ for all analytes in soil (0.5 ng/g).
3. No sediment was included in the ILV; therefore, Bayer Method TY-003-S20-01 was not independently validated for sediment matrices.
4. Bayer Method TY-003-S20-01 could not be validated by the ILV as written, since Bayer Method TY-003-S20-01 contained significant typographical errors, employed laboratory equipment which is not commonly found in laboratories, and lacked important method details. Most importantly, the ILV could not validate the analytical method portion of Bayer Method TY-003-S20-01. The ILV attempted to adapt the 3-pump LC system instrumental conditions in Bayer Method TY-003-S20-01 to the available 2-pump LC system, but these efforts were unsuccessful. The ILV personnel asked for permission to use the analytical parameters from Bayer Method TY-004-W21-01 [MRID 52029302 (water method)], which employed a 2-pump LC system and had "been shown to work for soil also" (Appendix 4, p. 197 of MRID 51820519). After the Sponsor gave permission to use the analytical parameters from Bayer Method TY-004-W21-01, the ILV laboratory was able to achieve overall acceptable results for the method (for the quantitation ion transition only).

An updated method Bayer Method TY-003-S20-01 should be submitted which corrects significant typographical errors, contains instruction to allow the samples to cool for *ca.* 15 minutes after microwave extract (before adding the internal standard and acetic acid), and provides alternative procedures for the LC parameters and microwave extraction technique when only standard/common analytical laboratory equipment is available. The reviewer noted that ECM 2 MRID 51820516 contained the corrected IUPAC names and/or molecular formulas for BCS-CY96288, BCS-DA63612 and BCS-CU97237, but typographical errors of the IUPAC names and/or molecular formulas for BCS-CY96288, BCS-DA63612 and BCS-CU97237 were found in ECM 1 MRID 51820515, IUPAC names obtained from DER Attachment 1; neither ECM 1 MRID 51820515 nor ECM 2 MRID 51820516 contained the corrected listing of BCS-CY96288-IS in the mass transition tables (Appendix 1, pp. 18-19 of MRID 51820515; pp. 14-15 of 51820516). The reviewer also noted that, since the ILV laboratory could not generate acceptable performance data for the confirmation ion transitions, the method Bayer Method TY-003-S20-01 should be updated with designating the confirmation ion transition as an identification analysis only and not a quantification analysis.

5. Issues regarding repeatability, accuracy, precision, or specificity were noted for several analytes based on ILV performance data.

Recovery of fluoxapiprolin (BCS-CS55621) at the 5.0 ng/g fortification level (mean 127%) did not meet OSCPP guideline requirements (mean 70-120%; RSD $\leq$ 20%; Table 1, pp. 37-40; Appendix 5, pp. 203-218 of MRID 51820519).

The specificity of the method was not supported by ILV LOQ representative chromatograms of BCS-DH17585 since LOQ peak height was the same as nearby contaminants (RT *ca.* 2.5-2.6 min) and baseline was elevated around the analyte peak (Figure 8, p. 116 of MRID 51820519). The reviewer noted that no matrix interferences were observed (based on quantified residues; Appendix 5, pp. 203-218).

ILV calculated LOQs exceeded the method LOQ (0.5 ng/g) for BCS-CY96288 (0.862 ng/g) and BCS-CU97237 (0.512 ng/g); ILV calculated LODs exceeded 30% of the method LOQ (0.15 ng/g) for BCS-CY96288, BCS-CU97237, and BCS-DH17585 (Table 3, pp. 42-43 of MRID 51820519).

6. Although the ILV was conducted independently of the internal validation (ECM 1 and ECM 2) since the laboratory personnel and equipment differed between the ILV laboratory and ECM 1 and ECM 2 laboratory, there was extensive communication between the ILV study personnel and the Sponsor Monitor (Leah Riter, Bayer Crop Science) which was necessary for the successful completion of the ILV validation (pp. 7, 33; Appendix 4, pp. 193-202 of MRID 51820519). OCSPP guidelines specify that the ILV must be conducted independently of the internal validation without collusion between the laboratory personnel or equipment. The communications between the ILV Study Director/Author (Lisa Swaim, Eurofins EAG Agrosience, LLC), ILV personnel (Emily Vogel and Erin Martin, Eurofins EAG Agrosience, LLC), Study Sponsor (Leah Riter, Bayer Crop Science), and other unspecified personnel (Suman Shrestha) was listed

in detail. Communications (emails and teleconference) involved protocol and report template issue, method clarifications, extensive communication regarding the LC method, microwave method and instrument, ILV trial results, and guideline discussion.

Communications occurred pre- and post- trial 1 and pre- and post- trial 2. Note: even though two ILV trials were performed, the results of the first trial were used to validate the ECM method Bayer Method TY-003-S20-01 (see Reviewer's Comment #12 for more details).

7. It could not be determined if the one ILV soil matrix [sandy loam (Sample ID: RMN-SL-PF (0-6" sample depth); pH 6.7 (1:1 soil:water ratio); 76% sand, 15% silt, 9% clay, 4.6% organic matter-Walkley Black; p. 25; Appendix 3, p. 192 of MRID 51820519] covered the range of soil and sediments used in the terrestrial field dissipation (TFD) studies since no fluoxapiprolin (BCS-CS55621) TFD studies were available for review by PB&A/CSS Joint Venture personnel. Even though a certain number of soil matrices is not specified in the OCSPP guidelines, more than one soil/soil matrix would need to be included in an ILV in order to cover the range of soils used in the terrestrial field dissipation studies.

OCSPP 850.6100 guidance suggests for a given sample matrix, the registrant should select the most difficult analytical sample condition from the study (*e.g.*, high organic content versus low organic content in a soil and sediment matrix) to analyze from the study to demonstrate how well the method performs. The ILV soil matrix contained a high organic content but low clay content.

8. Based on the method (Bayer Method TY-003-S20-01), ECM 2 recovery results were corrected for residues quantified in the controls (pp. 15-16 of MRID 51820515; pp. 24-25; Appendix 1, pp. 47-98 of MRID 51820516). OCSPP 850.6100 guidance states that "for an acceptable ECM, reported sample values should not be corrected for recoveries".
9. The determinations of the LOD and LOQ in the ECM 1, ECM 2, and ILV were not based on scientifically acceptable procedures as defined in 40 CFR Part 136 (p. 6 of MRID 51820515; pp. 10-11, 26, 30; Tables 17-18, pp. 39-40 of MRID 51820516; pp. 12, 32; Table 3, pp. 42-43 of MRID 51820519). No justification or calculation for LOQ was reported in ECM 1. In ECM 2, the LOQ was defined as the lowest fortification level in which the method was validated where mean recovery was 70-110% and relative standard deviation was $\leq 20\%$, as well as blank values were below 30% at this level. The LOD was not reported in ECM 1. In ECM 2, the LOD was calculated for each analyte based on the standard deviation at the 0.5 ng/g fortification level ($n = 14$ for soil; $n = 7$ for sediment) using the following equation: $LOD = (t_{0.99} \times SD)$, where, $t_{0.99}$ is the one-tailed t statistic for $n = 14$ (2.650; soil) or $n = 7$ (3.143; sediment) and SD is the standard deviation of the analyte recovery measurements at the target LOQ. In the ILV, the LOQ and LOD were calculated for each analyte in soil based on the standard deviation at the 0.5 ng/g fortification ($n = 5$; quantitation ion transition only) using the following equations: $LOD = (t_{0.99} \times SD)$ and $LOQ = 3 \times (\text{Calculated LOD})$, where, $t_{0.99}$ is the one-tailed t statistic for $n = 5$ (3.747) and SD is the standard deviation of the analyte recovery measurements at the target LOQ. Calculated LOQs exceeded the method LOQ for BCS-CY96288 (0.862 ng/g) and BCS-CU97237 (0.512 ng/g).

Detection limits should not be based on the arbitrarily selected lowest concentration in the spiked samples.

Since the LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ.

The reviewer noted that the LOD calculation provided in ECM 1 and ECM 2 corresponded to the MDL calculation detailed in USEPA Definition and Procedure for the Determination of the Method Detection Limit, Revision 2; 2016.

10. The reviewer noted that additional performance data was presented in ECM 2 for BCS-BP32808, and BCS-DH17585 at 5.0 ng/g where the soil and sediment matrices were assessed together with one calibration standard set (quantitation ion transition only; Appendix 1, pp. 95-98 of MRID 51820516). This data was not reported in the results of the study report.
11. No reagent blank was present in the ECM 2 performance data.
12. The ILV conducted two trials. These are the overall acceptability results of the trials (Appendix 4, p. 201 of MRID 51820519):

Trial 1: 1) 10×LOQ recovery was >120% for both transitions of BCS-CS55621, so the average recovery was >120%, which did not pass ILV criteria. 2) The %RSD for the confirmatory transition was >20% for BCS-CZ38260, which did not pass ILV criteria.

Trial 2: 1) The %RSD for BCS-CS55621 for both transitions at the LOQ level was >20%, the average for the 10×LOQ confirmatory transition was >120%, and the overall %RSD was >20% which does not pass ILV criteria. 2) For BCS-CC26101, the mean 10×LOQ was 120% for the confirmatory transition, which is right at the ILV criteria. 3) For BCS-CZ38260, the mean 10×LOQ for both transitions is >120%, which does not pass ILV criteria. 4) For BCS-DH17585, the mean recovery at each fortification level, as well as the overall mean for the quantitation transition >120%, which does not pass ILV criteria. 5) Although the method does not state correlation coefficient criteria, SOP states that they should be ≥0.995. For the second trial, there are two analytes that do not pass that criteria, so we will have an SOP deviation for those, as noted in the ILV.

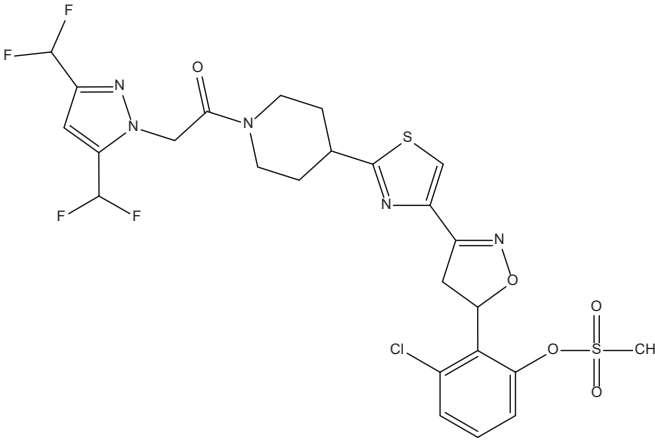
Based on the ILV check of OCSPP guidelines, the ILV determined that the confirmation ion transition data was not necessary to satisfy the requirements of the OCSPP guidelines (Appendix 4, pp. 201-202 of MRID 51820519). Additionally, due to that determination, the ILV decided to use the results of Trial 1, and the overall mean recovery (119%) of fluoxapiprolin (BCS-CS55621) was used to support the validation of the method for this analyte, even though the mean recovery at 10×LOQ (127%) was unacceptable (pp. 31-34 of MRID 51820519).

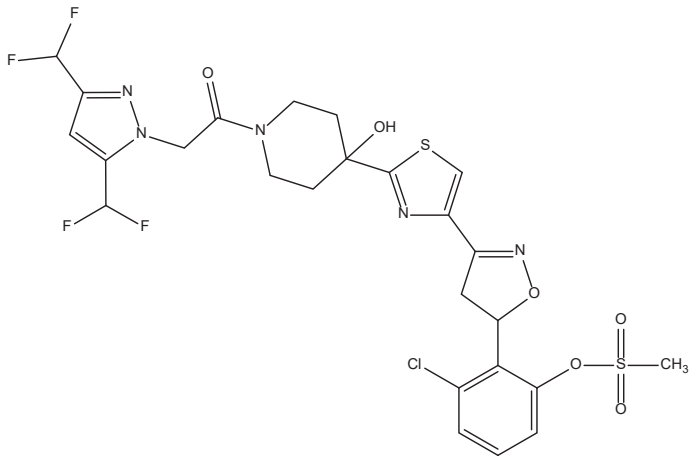
13. In ECM 2, the stability of the final sample extract was determined to be up to 10 days under refrigerated (mean temperature 3.5°C) storage (stability defined as $\pm 15\%$; p. 31; Table 19, p. 41 of MRID 51820516). The stability of the standard solutions [in acetonitrile:water (4:1, v:v)] was determined to be up to 122 days under refrigerated ($\leq 10^\circ\text{C}$) storage (stability defined as $\pm 15\%$; p. 31; Table 20, pp. 42-45).
14. Matrix effects were determined in the ILV to be significant ($> \pm 20\%$) in the test soil; however, the ILV noted that the use of isotopically-labeled internal standards compensated for the matrix effects since acceptable recovery results were generated using solvent-based calibration standards (p. 32; Table 2, p. 41 of MRID 51820519).
15. The time requirement for the method was reported in the ILV as *ca.* 9 hours (one extended workday) for a set of 13 samples, if standards, solutions, and reagents are prepared in advance, with LC/MS/MS analysis performed overnight (p. 33 of MRID 51820519). Standard preparation required two analysts *ca.* 22 hours (two workdays); preparation of solutions and reagents required *ca.* 2.5 hours. In the ECM 2, the time requirement for the method was reported as 2-3 hours for a batch of 15 samples, with HPLC/MS/MS analysis performed overnight (p. 31 of MRID 51820516). No time requirement was reported in ECM 1.

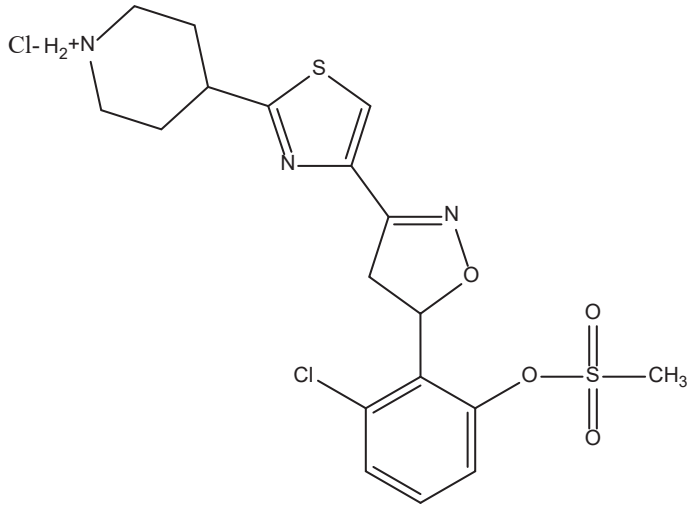
V. References

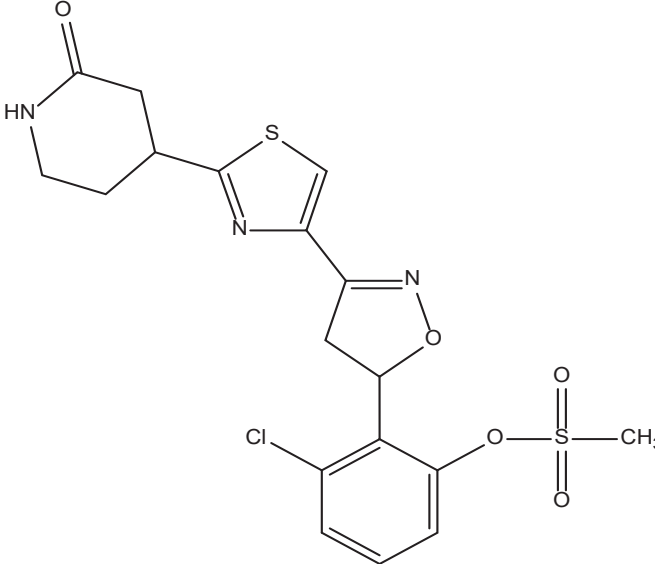
- U.S. Environmental Protection Agency. 2012. Ecological Effects Test Guidelines, OCSPP 850.6100, Environmental Chemistry Methods and Associated Independent Laboratory Validation. Office of Chemical Safety and Pollution Prevention, Washington, DC. EPA 712-C-001.
- USEPA. 2012. *Environmental Chemistry Method Guidance*. Memorandum From D. Brady to Environmental Fate and Effects Division. December 20, 2012. Environmental Fate and Effects Division. Office of Pesticide Programs. Office of Chemical Safety and Pollution Prevention. U.S. Environmental Protection Agency. Available at: <https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/environmental-chemistry-methods-guidance-pesticides>.
- 40 CFR Part 136. Appendix B. Definition and Procedure for the Determination of the Method Detection Limit-Revision 1.11, pp. 344-347, and Revision 2; 2015 and 2016.

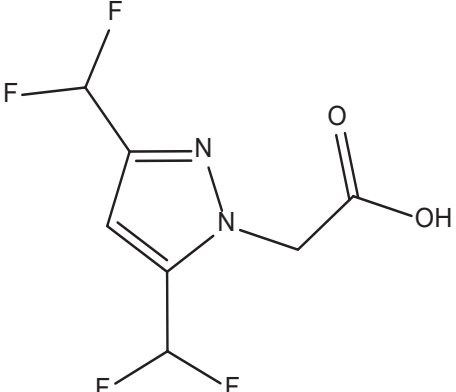
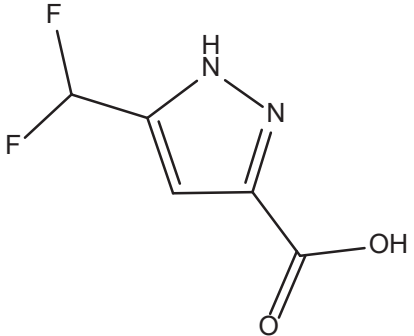
DER ATTACHMENT 1. Fluoxapiprolin and Its Environmental Transformation Products. ^A

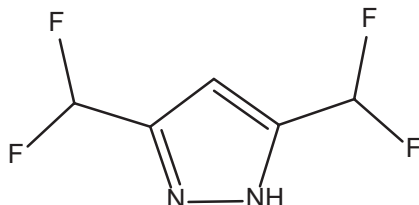
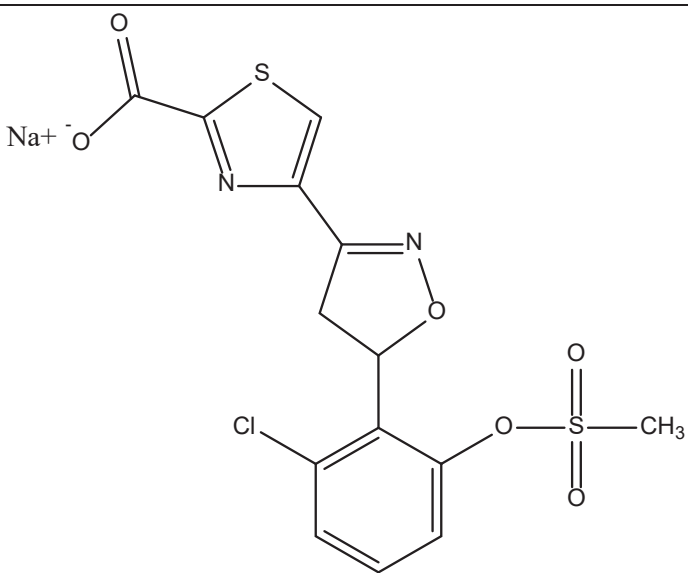
Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)	Final %AR (study length)
PARENT						
Fluoxapiprolin (BCS-CS55621)	IUPAC: 2-[(5RS)-3-[2-(1-{[3,5-bis(difluoromethyl)-1H-pyrazol-1-yl]acetyl}-4-piperidyl)thiazol-4-yl]-4,5-dihydroisoxazol-5-yl]-3-chlorophenyl methanesulfonate CAS: 2-[3,5-bis(difluoromethyl)-1H-pyrazol-1-yl]-1-[4-[4-[5-[2-chloro-6-[(methylsulfonyl)oxy]phenyl]-4,5-dihydro-3-isoxazolyl]-2-thiazolyl]-1-piperidinyl]ethanone CAS No.: 1360819-11-9 Formula: C ₂₅ H ₂₄ ClF ₄ N ₅ O ₅ S ₂ MW: 650.1g/mol SMILES: FC(F)C1=NN(CC(N2CCCC(C3=NC(C4=NOC(C5=C(Cl)C=C(C=C5OS(C)(=O)=O)C4)=CS3)CC2)=O)C(C(F)F)=C1		850.6100 ECM Soil	51820515 51820516	PRT	PRT
			850.6100 ILV Soil	51820519		
			850.6100 ECM Water	51820517 52029302		
			850.6100 ILV Water	51820518		

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)	Final %AR (study length)
BCS-CY96288	IUPAC: 2-(3-(2-(1-(2-(3,5-bis(difluoromethyl)-1H-pyrazol-1-yl)acetyl)-4-hydroxypiperidin-4-yl)thiazol-4-yl)-4,5-dihydroisoxazol-5-yl)-3-chlorophenyl methanesulfonate Formula: C ₂₅ H ₂₄ ClF ₄ N ₅ O ₆ S ₂ MW: 666.1 g/mol SMILES: <chem>FC(F)C1=NN(CC(N2CCCC(C3=NC(C4=NOC(C5=C(Cl)C=C(C=C5OS(C)(=O)=O)C4)=CS3)(O)CC2)=O)C(C(F)F)=C1</chem>		850.6100 ECM Soil	51820515 51820516	PRT	PRT
			850.6100 ILV Soil	51820519		
			850.6100 ECM Water	51820517 52029302		
			850.6100 ILV Water	51820518		

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)	Final %AR (study length)
BCS-CU97237	IUPAC: 4-(4-(5-(2-Chloro-6-((methylsulfonyl)oxy)phenyl)-4,5-dihydroisoxazol-3-yl)thiazol-2-yl)piperidin-1-ium chloride Formula: C ₁₈ H ₂₁ ClN ₃ O ₄ S ₂ Cl MW: 478.4 g/mol SMILES: <chem>CS(OC1=CC=CC(Cl)=C1C2C(C(C3=CSC(C4CC[NH2]CC4)=N3)=NO2)(=O)=O.[Cl-])</chem>		850.6100 ECM Soil	51820515 51820516	PRT	PRT
			850.6100 ILV Soil	51820519		
			850.6100 ECM Water	51820517 52029302		
			850.6100 ILV Water	51820518		

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)	Final %AR (study length)
BCS-DA63612	IUPAC: 3-Chloro-2-(3-(2-(2-oxopiperidin-4-yl)thiazol-4-yl)-4,5-dihydroisoxazol-5-yl)phenyl methanesulfonate Formula: C ₁₈ H ₁₈ ClN ₃ O ₅ S ₂ MW: 455.94 g/mol SMILES: <chem>CS(OC1=CC=CC(Cl)=C1C2C(C(C3=CSC(C(C4)CCNC4=O)=N3)=NO2)(=O)=O</chem>		850.6100 ECM Soil	51820515 51820516	PRT	PRT
			850.6100 ILV Soil	51820519		
			850.6100 ECM Water	51820517 52029302		
			850.6100 ILV Water	51820518		
BCS-CC26101	IUPAC: 2-(3,5-bis(difluoromethyl)-1H-pyrazol-1-yl)acetic acid Formula: C ₇ H ₆ F ₄ N ₂ O ₂ MW: 226.13 g/mol SMILES: <chem>FC(F)C1=NN(CC(O)=O)C(C(F)F)=C1</chem>		850.6100 ECM Soil	51820515 51820516	PRT	PRT
			850.6100 ILV Soil	51820519		
			850.6100 ECM Water	51820517 52029302		

			850.6100 ILV Water	51820518		
BCS-CZ38260	IUPAC: 5-(Difluoromethyl)-1H-pyrazole-3-carboxylic acid Formula: C ₅ H ₄ F ₂ N ₂ O ₂ MW: 162.1 g/mol SMILES: <chem>O=C(O)C1=NNC(C(F)F)=C1</chem>		850.6100 ECM Soil	51820515 51820516	PRT	PRT
			850.6100 ILV Soil	51820519		
			850.6100 ECM Water	51820517 52029302		
			850.6100 ILV Water	51820518		

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)	Final %AR (study length)
BCS-BP32808	IUPAC: 3,5-bis(difluoromethyl)-1H-pyrazole Formula: C ₅ H ₄ F ₄ N ₂ MW: 168.1 g/mol SMILES: FC(F)C1=NNC(C(F)F)=C1		850.6100 ECM Soil	51820515 51820516	PRT	PRT
			850.6100 ILV Soil	51820519		
			850.6100 ECM Water	51820517 52029302		
			850.6100 ILV Water	51820518		
BCS-DH17585	IUPAC: Sodium 4-(5-(2-chloro-6-((methylsulfonyl)oxy)phenyl)-4,5-dihydroisoxazol-3-yl)thiazole-2-carboxylate Formula: C ₁₄ H ₁₀ ClN ₂ O ₆ S ₂ Na MW: 424.8 g/mol SMILES: [O-]]C(C1=NC(C2=NOC(C3=C(Cl))C=CC=C3OS(C)(=O)=O)C2) =CS1)=O.[Na+]		850.6100 ECM Soil	51820515 51820516	PRT	PRT
			850.6100 ILV Soil	51820519		
			850.6100 ECM Water	51820517 52029302		
			850.6100 ILV Water	51820518		
MAJOR (>10%) TRANSFORMATION PRODUCTS						
No major transformation products were identified.						
MINOR (<10%) TRANSFORMATION PRODUCTS						

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)	Final %AR (study length)
No minor transformation products were identified.						
REFERENCE COMPOUNDS NOT IDENTIFIED						
All compounds used as reference compounds were identified.						

^A AR means "applied radioactivity". MW means "molecular weight". PRT means "parent". ECM means "environmental chemical methods". ILV means "independent laboratory validation".