Analytical method for epyrifenacil (S-3100; V-10456) and its seven degradates S-3100-CA, S-3100-DA, S-3100-CA-RD, S-3100-CA-UR, S-3100-DP, 4′′-OH-S-3100-CA, and S-3100-DA-RD in soil

Reports: ECM: MRID No. 51778713. Chen, T. 2021. V-10456: Validation of Valent Method RM-52S-4, "Determination of Residues of V-10456 and its Degradates in Soil". Laboratory Project ID: V-21-202220. Report prepared, sponsored, and submitted by Valent U.S.A., LLC, San Ramon, California (pp. 1, 3); 162 pages. Final report issued August 25, 2021; Amendment No. 1 issued October 14, 2021.

ILV: MRID No. 51778718. Vandaveer, W. and J. Shepard. 2021. Independent Laboratory Validation of Valent Analytical Method RM-52S-4A: "Determination of V-10456, S-3100-CA, S-3100-DA, S-3100-CA-RD, S-3100-CA-UR, S-3100-DP, 4′′-OH-S-3100-CA, and S-3100-DA-RD in Soil". Laboratory Project ID: V-21-202602. Report prepared by SynTech Research, Stilwell, Kansas; sponsored and submitted Valent U.S.A., LLC, San Ramon, California (pp. 3, 5); 282 pages. Final report issued December 28, 2021.

Document No.: MRIDs 51778713 & 51778718

Guideline: 850.6100

Statements: ECM: This study was conducted in accordance with USEPA FIFRA Good Laboratory Practices (40 CFR Part 160, 1989; p. 3 of MRID 51778713). Signed and dated No Data Confidentiality and Quality Assurance statements were provided (pp. 2-3, 5). A Statement of Authenticity was not included.

ILV: This study was conducted in accordance with USEPA FIFRA Good Laboratory Practices (40 CFR Part 160, 1989; p. 3 of MRID 51778718). Signed and dated No Data Confidentiality and Quality Assurance statements were provided (pp. 2-3, 5). A Statement of Authenticity was not included.

Classification: This analytical method is classified as **Supplemental**. Since the reported method LOQs were not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQs are the lowest levels of method validation (LLMVs) rather than LOQs. Valent Method RM-52S-4 and Valent Method RM-52S-4A are considered the same method since Valent Method RM-52S-4A was only issued to correct typographical errors in the original method. The ILV modification of the ECM method to use the same calibration range (0.050-25.0 ng/mL) for all analyses/analytes required that the LOD for all analytes should be 0.0001 mg/kg, based on the reported LOD calculation equation; however, the ILV study report listed the same LODs for the analytes as the ECM, and this typographical error should be corrected in the ILV study report. The ILV soil matrix was not characterized; its soil texture and source were not specified but could be inferred from the raw data. The soil texture for the ECM test soil and ILV test soil were the same. The ILV soil matrix (clay) did not cover the range of soils used in the

	one submitted epyrifenacil (S-3100; V-10456) terrestrial field dissipation (TFD) study with four sites (MRID 51781215) since only one ILV test soil was included; however, the reviewer noted that the ILV test soil provided a difficult sample condition. The number of ILV trials was not reported. It could not be determined if the ILV was conducted independently from the ECM due to lack of data. The reported/calculated LOD for epyrifenacil (S-3100; V-10456), S-3100-CA, S-3100-DA, and S-3100-DP in the ECM and ILV was 0.0001 mg/kg which was 60% of the LOQ, and only one calibration standard was present below the LOQ fortification level for these analytes.		
PC Code:	116100		
EFED Final Reviewer:	He Zhong, Ph.D. Biologist	Signature:	HE ZHONG Digitally signed by HE ZHONG Date: 2024.09.12 17:23:54 -04'00'
		Date:	09/12/2024
PB&A/CSS JV Reviewers:	Lisa Muto, M.S., Environmental Scientist	Signature:	Lisa Muto
		Date:	02/01/2023
	Summer Piantes, M.S., Environmental Scientist	Signature:	Summer Piantes
		Date:	02/06/2023

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, Valent Method RM-52S-4 (Valent Method RM-52S-4A), is designed for the quantitative determination of epyrifenacil (S-3100; V-10456) and its seven degradates: S-3100-CA, S-3100-DA, S-3100-CA-RD, S-3100-CA-UR, S-3100-DP, 4″-OH-S-3100-CA, and S-3100-DA-RD in soil using LC/MS/MS. Valent Method RM-52S-4 (Valent Method RM-52S-4A) reported a limit of quantification (LOQ) of 0.00015 mg/kg for epyrifenacil, S-3100-CA, S-3100-DA, and S-3100-DP; a LOQ of 0.001 mg/kg for S-3100-CA-RD, S-3100-DA-RD, and 4″-OH-S-3100-CA; and a LOQ of 0.005 mg/kg for S-3100-CA-UR. The epyrifenacil LOQ (0.00015 mg/kg) are equal to the lowest toxicological level of concern in soil (IC_{25}=0.0003 lb a.i./A or 0.00015 mg/kg[1]) for epyrifenacil and its seven degradates: S-3100-CA, S-3100-DA, S-3100-CA-RD, S-3100-CA-UR, S-3100-DP, 4″-OH-S-3100-CA, and S-3100-DA-RD. Valent Method RM-52S-4 and Valent Method RM-52S-4A are considered the same method, since Valent Method RM-52S-4A was only issued to correct typographical errors in the original method.

Since the reported method LOQs were not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQs are the lowest levels of method validation (LLMVs) rather than LOQs. Based on the performance data submitted by the ILV and ECM, the LLMVs

[1] The number is calculated by 0.0003 lb a.i./A × 4.53E05 mg/lb × 3.94 inches/dm × 2.47E-06 × [1/6 inches] × [1/1.5 kg/L] with an assumption of a 6-inch soil depth and a 1.5 kg/L soil density,

were equivalent to the respective ECM reported method LOQs for epyrifenacil (S-3100; V-10456) and its analytes in soil.
The ILV validated the method using uncharacterized clay soil matrix which was sourced from the terrestrial field dissipation study (Valent Study No. V-18-200320; MRID 51781215) and supplied by the Sponsor (Valent U.S.A. LLC). The ECM validated the method using characterized clay soil matrix which was sourced from the terrestrial field dissipation study (Valent Study No. V-18-200320; MRID 51781215). Since the ILV soil matrix was not characterized in the study report, it could not be determined if the ILV test soil matrix and ECM test soil matrix were the same samples, but the soil texture for the ECM test soil and ILV test soil were the same. It could not be determined if the ILV was conducted independently from the ECM due to lack of data.

The method, Valent Method RM-52S-4A (Valent Method RM-52S-4), was validated by the ILV for epyrifenacil (S-3100; V-10456) and its degradates at the following LOQ and 10×LOQ levels in soil:

- LOQ (0.00015 mg/kg) and 10×LOQ (0.0015 mg/kg) for epyrifenacil (S-3100; V-10456), S-3100-CA, S-3100-DA, and S-3100-DP.
- LOQ (0.001 mg/kg) and 10×LOQ (0.010 mg/kg) for S-3100-CA-RD, S-3100-DA-RD, and 4″-OH-S-3100-CA.
- LOQ (0.005 mg/kg) and 10×LOQ (0.050 mg/kg) for S-3100-CA-UR.

The method, Valent Method RM-52S-4A (Valent Method RM-52S-4), was validated by the ILV in soil with insignificant modifications to the analytical parameters and equipment, as well as the fact that recoveries were not corrected for residues quantified in the controls and the same calibration range (0.050-25.0 ng/mL) was used for all analyses/analytes. The ILV modification of the ECM method to use the same calibration range (0.050-25.0 ng/mL) for all analyses/analytes required that the LOD for all analytes should be 0.0001 mg/kg, based on the reported LOD calculation equation; however, the ILV study report listed the same LODs for the analytes as the ECM, and this typographical error should be corrected in the ILV study report. The number of ILV trials was not reported, but the reviewer assumed that the ILV validation occurred with the first trial based on the lack of method modifications.

All ILV and ECM data regarding repeatability, accuracy, precision, linearity, and specificity were satisfactory for epyrifenacil (S-3100; V-10456), S-3100-CA, S-3100-DA, and S-3100-DP at 0.00015 mg/kg and 0.0015 mg/kg, for S-3100-CA-RD, S-3100-DA-RD, and 4″-OH-S-3100-CA at 0.001 mg/kg and 0.010 mg/kg, and for S-3100-CA-UR at 0.005 mg/kg and 0.050 mg/kg in soil. ILV and ECM representative chromatograms showed some matrix interferences (11% of the LOQ, based on peak area) and nearby contaminants for S-3100-DP, and ECM representative chromatograms also showed some matrix interferences (<24% of the LOQ, based on peak area) for epyrifenacil.

The reported/calculated LOD for epyrifenacil (S-3100; V-10456), S-3100-CA, S-3100-DA, and S-3100-DP in the ECM and ILV was 0.0001 mg/kg which was 60% of the LOQ, and only one calibration standard was present below the LOQ fortification level for these analytes.

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						
Epyrifenacil (S-3100; V-10456)	51778713[1,2]	51778718[3]		Soil	25/08/2021 (Original); 14/10/2021 (Amendment 1)	Valent U.S.A., LLC	LC/MS/MS	0.00015 mg/kg
S-3100-CA								
S-3100-DA								
S-3100-DP								
S-3100-CA-RD								0.001 mg/kg
S-3100-DA-RD								
4”-OH-S-3100-CA								
S-3100-CA-UR								0.005 mg/kg

1 ECM study report MRID 51778713 cited Valent Method RM-52S-4 as the analytical method which was validated by the performance data; however, both Valent Method RM-52S-4 and Valent Method RM-52S-4A were included in Appendix 2 of the ECM MRID 51778713. The only differences between Valent Method RM-52S-4 and Valent Method RM-52S-4A was the correction of typographical errors in Section 3 of Valent Method RM-52S-4 (Appendix 2, p. 103 of MRID 51778713).

2 In the ECM, the soil matrix was clay soil [Sample ID: V-18-200320-D-SC-(0-6); pH 7.8 (1:1 soil:water ratio); 15% sand, 32% silt, 53% clay; 3.5% organic matter (Walkley-Black)] obtained from the North Dakota site of the submitted epyrifenacil (S-3100; V-10456) terrestrial field dissipation (TFD) study (Valent Study No. V-18-200320; MRID 51781215) and characterized by Agvise Laboratories, Northwood, North Dakota (USDA texture classification; p. 14; Appendix 4, pp. 135-145 of MRID 51778713). The soil texture was verified by the reviewer using USDA-NRCS technical support tools. Soil characterization reports were provided for all soil depths for the untreated North Dakota soil sample (summarized in the table below); however, based on the organic matter data provided on p. 14 of MRID 51778713, the reviewer assumed that the soil matrix for the ECM study was from the 0-6 inch (0-15.24 cm) depth.

Sample ID	Soil Depth (cm)	Soil Texture	Sand %	Silt %	Clay %	Organic Matter (%)	pH (1:1 soil:water ratio)
V-18-200320-D-SC-(0-6)	0-15.24	Clay	15	32	53	3.5	7.8
V-18-200320-D-SC-(6-12)	15.24-30.48	Clay	11	30	59	1.8	7.9
V-18-200320-D-SC-(12-18)	30.48-45.72	Clay	15	26	59	1.6	8.1
V-18-200320-D-SC-(18-24)	45.72-60.96	Clay	19	20	61	1.4	8.3
V-18-200320-D-SC-(24-30)	60.96-76.2	Clay	23	20	57	1.2	8.3
V-18-200320-D-SC-(30-36)	76.2-91.44	Clay	21	18	61	1.3	8.2

Data obtained from Appendix 4, pp. 135-140 of MRID 51778713; USDA texture classification. The soil textures were verified by the reviewer using USDA-NRCS technical support tools.

3 In the ILV, the soil matrix was described only as untreated control samples of soil provided by the Sponsor and selected as the most difficult soil matrix (highest organic matter) from the terrestrial field dissipation study (p. 12 of MRID 51778718). No study number or citation was reported for the terrestrial field dissipation study, but the reviewer noted that the method validation sample identification numbers were "V-18-200320-NDSoil-x-n" (where x was UTC/LOQ/10XLOQ and n ranged 01 to 05) in the raw data spreadsheets and chromatograms (Appendix C, pp. 101-116; Appendix E, pp. 119-276). Therefore, the reviewer assumed that the ILV soil matrix was the soil from the North Dakota site of submitted epyrifenacil (S-3100; V-10456) terrestrial field dissipation (TFD) study (Valent Study No. V-18-200320; MRID 51781215). From this available data, the reviewer concluded that the ILV test soil texture was clay (USDA); however, the reviewer could not report soil characterization of the ILV test soil since the soil depth of the ILV test soil matrix was not reported.

4 ILV study report MRID 51778718 was submitted to validate Valent Method RM-52S-4A (pp. 9, 15 of MRID 51778718).

I. Principle of the Method

ECM (Valent Method RM-52S-4 and Valent Method RM-52S-4A)

Valent Method RM-52S-4 and Valent Method RM-52S-4A was included in Appendix 2 of ECM study report MRID 51778713. Soil samples (20.0 ± 0.1 g) were transferred to 50-mL polypropylene centrifuge tubes and fortified as necessary with: 0.3 mL of 0.010 or 0.100 µg/mL mixed fortification solutions of epyrifenacil (S-3100; V-10456), S-3100-CA, S-3100-DA, and S-3100-DP; 0.2 mL of 0.100 or 1.00 µg/mL mixed fortification solutions of S-3100-CA-RD, 4″-OH-S-3100-CA, and S-3100-DA-RD; or 0.1 mL of 10.0 or 100 µg/mL of S-3100-CA-UR (Appendix 2, pp. 89-90 of MRID 51778713). The samples were extracted three times with 25 mL of acetonitrile:0.1M hydrochloric acid (5:1, v:v), shaking on a reciprocating shaker for *ca.* 20 minutes. The extract was centrifuged at *ca*. 4000 rpm for *ca*. 5 minutes, and decanted. The extracts were combined, and the volume was adjusted to 100 mL with acetonitrile:0.1M hydrochloric acid (5:1, v:v). An aliquot (25.0 mL) of the combined extracts was mixed with 25.0 mL of HPLC-grade water in a 250-mL separatory funnel. The mixture was extracted three times with 50.0 mL of dichloromethane via shaking for 1 minute. The combined dichloromethane extract was concentrated to dryness using a rotary-evaporator and water bath set to 40°C. The residue was reconstituted in 5.0 mL of acetonitrile acidified with 0.1% formic acid and sonicated briefly, then 5.0 mL of HPLC-grade water acidified with 0.1% formic acid was added to the sample with sonication. An aliquot (*ca*. 1.5 mL) of the extract was filtered (PTFE 0.22 µm) into an autosampler vial and sonicated. The method noted that no more than four samples should be extracted at the same time during the partition step. Extracts were either analyzed immediately or stored refrigerated or frozen until analysis. The Analytical Scheme for Analysis was illustrated in Attachment 1, p. 102 of MRID 51778713.

Samples were analyzed for epyrifenacil (S-3100; V-10456), S-3100-CA, S-3100-DA, S-3100-DP, S-3100-CA-RD, 4″-OH-S-3100-CA, S-3100-DA-RD, and S-3100-CA-UR using an Agilent 1290 Infinity II UPLC system equipped with Phenomenex Kinetex® Biphenyl column 100 Å (150 x 4.6 mm, 5 µm) and coupled to a Sciex Triple Quad 6500+ mass spectrometer (Series # not reported; Appendix 2, pp. 87-88, 90-95 of MRID 51778713). The following LC conditions were used for epyrifenacil (S-3100; V-10456), S-3100-CA, S-3100-DA, and S-3100-DA-RD: column temperature 30 ± 0.8°C, mobile phase of (A) 0.05% formic acid in water and (B) acetonitrile [mobile gradient phase of percent A:B (v:v) at 0.0-1.0 min. 77:23, 7.5-18.0 min. 10:90, 19.0-25.0 min. 77:23], MS temperature 700°C, positive TurboSpray® Ion Electrospray

with multiple reaction monitoring (MRM), and injection volume of 5 µL. The following LC conditions were used for S-3100-CA-RD, S-3100-CA-UR, and S-3100-DP: column temperature 30 ± 0.8°C, mobile phase of (A) 0.05% formic acid in water and (B) acetonitrile [mobile gradient phase of percent A:B (v:v) at 0.0-1.0 min. 85:15, 9.0-13.0 min. 5:95, 13.5-20.0 min. 85:15], MS temperature 600°C, negative TurboSpray® Ion Electrospray with multiple reaction monitoring (MRM), and injection volume of 15 µL. The following LC conditions were used for 4″-OH-S-3100-CA: column temperature 40 ± 0.8°C, mobile phase of (A) 0.05% formic acid in water and (B) 0.05% formic acid in methanol [mobile gradient phase of percent A:B (v:v) at 0.0-1.0 min. 60:40, 1.5-12.0 min. 10:90, 12.5-18.0 min. 60:40], MS temperature 600°C, positive TurboSpray® Ion Electrospray with multiple reaction monitoring (MRM), and injection volume of 15 µL.

Expected approximate retention times were 9.30, 7.15, 6.83, 8.17, 8.77, 7.68, 8.46, and 6.78 minutes for epyrifenacil (S-3100; V-10456), S-3100-DA, S-3100-DA-RD, S-3100-CA, S-3100-CA-RD, S-3100-CA-UR, S-3100-DP, and 4″-OH-S-3100-CA, respectively (Appendix 2, pp. 90-95 of MRID 51778713). Two ion pair transitions were monitored (primary and confirmatory, respectively): *m/z* 518.0→293.0 and *m/z* 518.0→250.0 for epyrifenacil (S-3100; V-10456), *m/z* 432.0→281.0 and *m/z* 432.0→82.0 for S-3100-DA, *m/z* 434.1→281.1 and *m/z* 434.1→323.0 for S-3100-DA-RD, *m/z* 490.0→250.0 and *m/z* 490.0→293.0 for S-3100-CA, *m/z* 490.0→376.0 and *m/z* 490.0→319.0 for S-3100-CA-RD, *m/z* 368.0→293.0 and *m/z* 368.0→337.0 for S-3100-CA-UR, *m/z* 337.0→186.0 and *m/z* 337.0→150.0 for S-3100-DP, and *m/z* 508.1→385.0 and *m/z* 508.1→489.9 for 4″-OH-S-3100-CA. Solvent-based calibration standards were used (Appendix 2, pp. 85-86).

ILV

The ILV performed the ECM method, Valent Method RM-52S-4 and Valent Method RM-52S-4A, as written, except for the insignificant modifications to the analytical parameters and equipment, as well as the fact that recoveries were not corrected for residues quantified in the controls and the same calibration range (0.050-25.0 ng/mL) was used for all analyses/analytes (pp. 9, 15-16; Appendix A, pp. 35-37; Appendix A, Appendix 1, pp. 40-91; Appendix C, pp. 101-116; Appendix D, p. 117, Appendix F, pp. 277-282 of MRID 51778718).

Samples were analyzed for epyrifenacil (S-3100; V-10456), S-3100-CA, S-3100-DA, S-3100-DP, S-3100-CA-RD, 4″-OH-S-3100-CA, S-3100-DA-RD, and S-3100-CA-UR using an **ExionLC AC Pump (Serial #ABDXR5671011 and Serial #ABDXR5671012)** equipped with Phenomenex Kinetex Biphenyl column (150 x 4.6 mm, 5 µm) and coupled to a Sciex Triple Quad 6500+ mass spectrometer (**Serial # CG23321704**; Appendix F, pp. 277-282 of MRID 51778718). The following LC conditions were used for epyrifenacil (S-3100; V-10456), S-3100-CA, S-3100-DA, and S-3100-DA-RD: column temperature 30°C, mobile phase of (A) 0.05% formic acid in water and (B) acetonitrile [mobile gradient phase of percent A:B (v:v) at 0.00-1.00 min. 77:23, 7.50-18.0 min. 10:90, 19.0-25.0 min. 77:23], MS temperature **600°C**, positive TurboSpray® Ion Electrospray with multiple reaction monitoring (MRM), and injection volume of 5 µL. The following LC conditions were used for S-3100-CA-RD, S-3100-CA-UR, and S-3100-DP: column temperature 30°C, mobile phase of (A) 0.05% formic acid in water and (B) acetonitrile [mobile gradient phase of percent A:B (v:v) at 0.00-1.00 min. 85:15, 9.00-13.0 min.

5:95, 13.5-20.0 min. 85:15], MS temperature 600°C, negative TurboSpray® Ion Electrospray with multiple reaction monitoring (MRM), and injection volume of 15 µL. The following LC conditions were used for 4″-OH-S-3100-CA: column temperature 40°C, mobile phase of (A) 0.05% formic acid in water and (B) 0.05% formic acid in methanol [mobile gradient phase of percent A:B (v:v) at 0.00-1.00 min. 60:40, 1.50-12.0 min. 10:90, 12.5-18.0 min. 60:40], MS temperature 600°C, positive TurboSpray® Ion Electrospray with multiple reaction monitoring (MRM), and injection volume of 15 µL. The differences between the ILV analytical method and the ECM analytical method were **bolded** for clarity.

Expected retention times were not reported in the study; however, based on provided representative chromatograms, the reviewer observed the following approximate retention times: 9.18-9.20, 6.97-6.99, 6.63-6.65, 7.99-8.01, 8.56-8.60, 7.49-7.55, 8.25-8.30, and 6.62-6.64 minutes for epyrifenacil (S-3100; V-10456), S-3100-DA, S-3100-DA-RD, S-3100-CA, S-3100-CA-RD, S-3100-CA-UR, S-3100-DP, and 4″-OH-S-3100-CA, respectively (Appendix E, pp. 119-276 of MRID 51778718). Two ion pair transitions were monitored (primary and confirmatory, respectively): *m/z* 518.0→293.0 and *m/z* 518.0→250.0 for epyrifenacil (S-3100; V-10456), *m/z* 432.0→281.0 and *m/z* 432.0→82.0 for S-3100-DA, *m/z* 434.1→281.1 and *m/z* 434.1→323.0 for S-3100-DA-RD, *m/z* 490.0→250.0 and *m/z* 490.0→293.0 for S-3100-CA, *m/z* 490.0→376.0 and *m/z* 490.0→319.0 for S-3100-CA-RD, *m/z* 368.0→293.0 and *m/z* 368.0→337.0 for S-3100-CA-UR, *m/z* 337.0→186.0 and *m/z* 337.0→150.0 for S-3100-DP, and *m/z* 508.1→385.0 and *m/z* 508.1→489.9 for 4″-OH-S-3100-CA (p. 13; Appendix F, pp. 277-282). The monitored ion transitions of the ILV were the same as those of the ECM. Solvent-based calibration standards were used (Appendix A, p. 35; Appendix A, Appendix 1, pp. 44-45).

LOD/LOQ

In the ECM and ILV, Valent Method RM-52S-4 and Valent Method RM-52S-4A reported a limit of detection (LOD) of 0.0001 mg/kg and a limit of quantification (LOQ) of 0.00015 mg/kg for V-10456, S-3100-CA, S-3100-DA, and S-3100-DP, a LOD of 0.0002 mg/kg and a LOQ of 0.001 mg/kg for S-3100-CA-RD, S-3100-DA-RD, and 4″-OH-S-3100-CA, and a LOD of 0.0010 mg/kg and a LOQ of 0.005 mg/kg for S-3100-CA-UR (see Reviewer's Comments; pp. 13, 15; Appendix 2, pp. 81, 98 of MRID 51778713; p. 15; Appendix A, p. 35; Appendix A, Appendix 1, pp. 40, 57 of MRID 51778718).

Since the LOQs were not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQs are the lowest levels of method validation (LLMVs) rather than LOQs.

II. Recovery Findings

ECM (MRID 51778713): Mean recoveries and relative standard deviations (RSDs) met requirements (mean 70-120%; RSD ≤20%) in one soil matrix for analysis of epyrifenacil (S-3100; V-10456), S-3100-CA, S-3100-DA, and S-3100-DP at the LOQ (0.00015 mg/kg) and 10×LOQ (0.0015 mg/kg); analysis of S-3100-CA-RD, S-3100-DA-RD, and 4″-OH-S-3100-CA at the LOQ (0.001 mg/kg) and 10×LOQ (0.010 mg/kg); and analysis of S-3100-CA-UR at the LOQ (0.005 mg/kg) and 10×LOQ (0.050 mg/kg; Tables 1-14, pp. 16-31; Appendix 5, pp. 147-162 of MRID 51778713). Recovery results of the quantitative and confirmatory ion transitions

were comparable. According to the analytical method (Valent Method RM-52S-4 and Valent Method RM-52S-4A), recovery results were corrected for residues quantified in the controls (p. 15 Appendix 2, pp. 95-98). While peaks at the retention time of the analyte were integrated for epyrifenacil (S-3100; V-10456) and S-3100-DP in the untreated control soils, the "concentration found" for these residues in the controls was set to 0.0000 mg/kg (Appendix 5, pp. 147-162). Therefore, it was determined that no correction of the recoveries was performed in the study.

The soil matrix was clay soil [Sample ID: V-18-200320-D-SC-(0-6); pH 7.8 (1:1 soil:water ratio); 15% sand, 32% silt, 53% clay; 3.5% organic matter (Walkley-Black)] obtained from the North Dakota site of the submitted epyrifenacil terrestrial field dissipation (TFD) study (Valent Study No. V-18-200320; MRID 51781215) and characterized by Agvise Laboratories, Northwood, North Dakota (USDA texture classification; p. 14; Appendix 4, pp. 135-145 of MRID 51778713). The soil texture was verified by the reviewer using USDA-NRCS technical support tools. Soil characterization reports were provided for all soil depths for the untreated North Dakota soil sample (summarized in the table below). The ECM reported that the soil was a composite of the North Dakota untreated control soil; however, based on the organic matter data provided on p. 14 of MRID 51778713, the reviewer assumed that the soil matrix for the ECM study was from the 0-6 inch (0-15.24 cm) depth.

Sample ID	Soil Depth (cm)	Soil Texture	Sand %	Silt %	Clay %	Organic Matter (%)	pH (1:1 soil:water ratio)
V-18-200320-D-SC-(0-6)	0-15.24	Clay	15	32	53	3.5	7.8
V-18-200320-D-SC-(6-12)	15.24-30.48	Clay	11	30	59	1.8	7.9
V-18-200320-D-SC-(12-18)	30.48-45.72	Clay	15	26	59	1.6	8.1
V-18-200320-D-SC-(18-24)	45.72-60.96	Clay	19	20	61	1.4	8.3
V-18-200320-D-SC-(24-30)	60.96-76.2	Clay	23	20	57	1.2	8.3
V-18-200320-D-SC-(30-36)	76.2-91.44	Clay	21	18	61	1.3	8.2

Data obtained from Appendix 4, pp. 135-140 of MRID 51778713; USDA texture classification. The soil textures were verified by the reviewer using USDA-NRCS technical support tools.

ILV (MRID 51778718): Mean recoveries and RSDs met requirements in one soil matrix for analysis of epyrifenacil (S-3100; V-10456), S-3100-CA, S-3100-DA, and S-3100-DP at the LOQ (0.00015 mg/kg) and 10×LOQ (0.0015 mg/kg); analysis of S-3100-CA-RD, S-3100-DA-RD, and 4″-OH-S-3100-CA at the LOQ (0.001 mg/kg) and 10×LOQ (0.010 mg/kg); and analysis of S-3100-CA-UR at the LOQ (0.005 mg/kg) and 10×LOQ (0.050 mg/kg; Tables 1-8, pp. 17-24; Appendix C, pp. 101-116 of MRID 51778718). Recovery results of the quantitative and confirmatory ion transitions were comparable.

The soil matrix was described only as untreated control samples of soil provided by the Sponsor and selected as the most difficult soil matrix (highest organic matter) from the terrestrial field dissipation study (p. 12 of MRID 51778718). No study number or citation was reported for the terrestrial field dissipation study, but the reviewer noted that the method validation sample

identification numbers were "V-18-200320-NDSoil-x-n" (where x was UTC/LOQ/10XLOQ and n ranged 01 to 05) in the raw data spreadsheets and chromatograms (Appendix C, pp. 101-116; Appendix E, pp. 119-276). Therefore, the reviewer assumed that the ILV soil matrix was the soil from the North Dakota site of submitted epyrifenacil terrestrial field dissipation (TFD) study (Valent Study No. V-18-200320; MRID 51781215). From this available data, the reviewer concluded that the ILV test soil texture was clay (USDA); however, the reviewer could not report soil characterization of the ILV test soil since the soil depth of the ILV test soil matrix was not reported.

The method, Valent Method RM-52S-4A (Valent Method RM-52S-4), was validated by the ILV for epyrifenacil (S-3100; V-10456) and its degradates at the following LOQ and 10×LOQ levels in soil:

- LOQ (0.00015 mg/kg) and 10×LOQ (0.0015 mg/kg) for epyrifenacil (S-3100; V-10456), S-3100-CA, S-3100-DA, and S-3100-DP.
- LOQ (0.001 mg/kg) and 10×LOQ (0.010 mg/kg) for S-3100-CA-RD, S-3100-DA-RD, and 4″-OH-S-3100-CA.
- LOQ (0.005 mg/kg) and 10×LOQ (0.050 mg/kg) for S-3100-CA-UR.

The method, Valent Method RM-52S-4A (Valent Method RM-52S-4), was validated by the ILV in soil with insignificant modifications to the analytical parameters and equipment, as well as the fact that recoveries were not corrected for residues quantified in the controls and the same calibration range (0.050-25.0 ng/mL) was used for all analyses/analytes (pp. 9, 15-16; Appendix A, pp. 35-37; Appendix A, Appendix 1, pp. 40-91; Appendix C, pp. 101-116; Appendix D, p. 117, Appendix F, pp. 277-282 of MRID 51778718). The ILV modification of the ECM method to use the same calibration range (0.050-25.0 ng/mL) for all analyses/analytes required that the LOD for all analytes should be 0.0001 mg/kg, based on the reported LOD calculation equation; however, the ILV study report listed the same LODs for the analytes as the ECM, and this typographical error should be corrected in the ILV study report.

The number of ILV trials was not reported, but the reviewer assumed that the ILV validation occurred with the first trial based on the lack of method modifications. Communications between the ILV and method developers was neither reported nor summarized, but the ILV Protocol stated that all contact with the Sponsor regarding the method would be documented in the raw data and reported (Appendix A, pp. 34 of MRID 51778718). The ILV Protocol also stated that the ILV laboratory was unfamiliar with the method (Appendix A, pp. 30). In response to EPA's inquiry, the registrant provided the following response on May 31, 2024 "*The ILV was successfully and independently validated on the first attempt. There was no contact between SynTech and the Valent method developer during the method setup and validation, so no amended report is needed. The study's raw data includes communication before the ILV method setup and validation. These communications were clerical and did not compromise the ILV; therefore, we did not include them in the report*".

Table 2. Initial Validation Method Recoveries for Epyrifenacil (S-3100; V-10456) and Its Metabolites S-3100-CA, S-3100-DA, S-3100-CA-RD, S-3100-CA-UR, S-3100-DP, 4′′-OH-S-3100-CA, and S-3100-DA-RD in Soil[1,2]

Analyte	Fortification Level (mg/kg)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
Clay Soil						
Quantitation ion transition						
Epyrifenacil (S-3100; V-10456)	0.00015 (LOQ)	5	76.5-83.5	80.6	2.6	3.2
	0.0015	5	82.7-86.4	84.7	1.9	2.2
S-3100-CA	0.00015 (LOQ)	5	84.5-96.7	89.3	4.6	5.1
	0.0015	5	96.4-103	99.8	2.6	2.6
S-3100-DA	0.00015 (LOQ)	5	92.5-99.0	95.0	2.8	3.0
	0.0015	5	98.8-104	101	2.0	2.0
S-3100-CA-UR	0.005 (LOQ)	5	84.8-91.1	87.9	2.3	2.6
	0.050	5	104-110	106	2.5	2.3
S-3100-CA-RD	0.001 (LOQ)	5	68.3-78.6	75.3	4.1	5.4
	0.010	5	89.2-91.4	90.0	0.9	1.0
S-3100-DP	0.00015 (LOQ)	5	68.8-71.4	70.1	1.2	1.7
	0.0015	5	79.1-80.6	79.9	0.6	0.8
4′′-OH-S-3100-CA	0.001 (LOQ)	5	79.8-85.8	82.5	2.5	3.0
	0.010	5	82.9-92.0	88.1	3.7	4.3
S-3100-DA-RD	0.001 (LOQ)	5	108-111	110	1.4	1.3
	0.010	5	105-111	109	2.4	2.2
Confirmation ion transition						
Epyrifenacil (S-3100; V-10456)	0.00015 (LOQ)	5	75.3-81.3	79.5	2.5	3.1
	0.0015	5	81.5-85.8	83.8	1.8	2.1
S-3100-CA	0.00015 (LOQ)	5	87.4-96.9	90.0	3.9	4.3
	0.0015	5	98.8-106	102	2.7	2.6
S-3100-DA	0.00015 (LOQ)	5	87.4-103	98.3	6.2	6.3
	0.0015	5	97.1-102	100	2.2	2.2
S-3100-CA-UR	0.005 (LOQ)	5	83.1-90.4	87.7	2.7	3.1
	0.050	5	100-106	102	2.8	2.7
S-3100-CA-RD	0.001 (LOQ)	5	70.1-77.3	74.6	3.0	4.0
	0.010	5	89.6-92.0	91.0	1.0	1.1
S-3100-DP	0.00015 (LOQ)	5	68.3-73.6	71.0	2.4	3.3
	0.0015	5	77.1-81.1	79.7	1.7	2.1
4′′-OH-S-3100-CA	0.001 (LOQ)	5	68.6-74.8	72.2	2.3	3.2
	0.010	5	82.8-92.8	88.1	4.2	4.8
S-3100-DA-RD	0.001 (LOQ)	5	107-115	111	3.7	3.3
	0.010	5	109-115	112	2.3	2.0

Data (uncorrected recovery results, Appendix 2, pp. 95-98; Appendix 5, pp. 147-162) were obtained from Tables 1-14, pp. 16-31; Appendix 5, pp. 147-162 of MRID 51778713. Since the LOQs were not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQs are the lowest levels of method validation (LLMVs) rather than LOQs.

1 In the ECM, the soil matrix was clay soil [Sample ID: V-18-200320-D-SC-(0-6); pH 7.8 (1:1 soil:water ratio); 15% sand, 32% silt, 53% clay; 3.5% organic matter (Walkley-Black)] obtained from the North Dakota site of the submitted epyrifenacil (S-3100; V-10456) terrestrial field dissipation (TFD) study (Valent Study No. V-18-200320; MRID 51781215) and characterized by Agvise Laboratories, Northwood, North Dakota (USDA texture classification; p. 14; Appendix 4, pp. 135-145 of MRID 51778713). The soil texture was verified by the reviewer using USDA-NRCS technical support tools. Soil characterization reported were provided for all soil depths for the untreated North Dakota soil sample (summarized in the table below); however, based on the organic matter data provided on p. 14 of MRID 51778713, the reviewer assumed that the soil matrix for the ECM study was from the 0-6 inch (0-15.24 cm) depth.

Sample ID	Soil Depth (cm)	Soil Texture	Sand %	Silt %	Clay %	Organic Matter (%)	pH (1:1 soil:water ratio)
V-18-200320-D-SC-(0-6)	0-15.24	Clay	15	32	53	3.5	7.8
V-18-200320-D-SC-(6-12)	15.24-30.48	Clay	11	30	59	1.8	7.9
V-18-200320-D-SC-(12-18)	30.48-45.72	Clay	15	26	59	1.6	8.1
V-18-200320-D-SC-(18-24)	45.72-60.96	Clay	19	20	61	1.4	8.3
V-18-200320-D-SC-(24-30)	60.96-76.2	Clay	23	20	57	1.2	8.3
V-18-200320-D-SC-(30-36)	76.2-91.44	Clay	21	18	61	1.3	8.2

Data obtained from Appendix 4, pp. 135-140 of MRID 51778713; USDA texture classification. The soil textures were verified by the reviewer using USDA-NRCS technical support tools.

2 Two ion pair transitions were monitored (primary and confirmatory, respectively): *m/z* 518.0→293.0 and *m/z* 518.0→250.0 for epyrifenacil (S-3100; V-10456); *m/z* 432.0→281.0 and *m/z* 432.0→82.0 for S-3100-DA: *m/z* 434.1→281.1 and *m/z* 434.1→323.0 for S-3100-DA-RD; *m/z* 490.0→250.0 and *m/z* 490.0→293.0 for S-3100-CA; *m/z* 490.0→376.0 and *m/z* 490.0→319.0 for S-3100-CA-RD; *m/z* 368.0→293.0 and *m/z* 368.0→337.0 for S-3100-CA-UR; *m/z* 337.0→186.0 and *m/z* 337.0→150.0 for S-3100-DP; and *m/z* 508.1→385.0 and *m/z* 508.1→489.9 for 4″-OH-S-3100-CA (Appendix 2, pp. 90-95 of MRID 51778713).

Table 3. Independent Validation Method Recoveries for Epyrifenacil (S-3100; V-10456) and Its Metabolites S-3100-CA, S-3100-DA, S-3100-CA-RD, S-3100-CA-UR, S-3100-DP, 4″-OH-S-3100-CA, and S-3100-DA-RD in Soil[1,2,3]

Analyte	Fortification Level (mg/kg)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
Clay Soil						
Quantitation ion transition						
Epyrifenacil (S-3100; V-10456)	0.00015 (LOQ)	5	87.3-107.9	102	8.5	8.3
	0.0015	5	99.1-104.8	101	2.7	2.7
S-3100-CA	0.00015 (LOQ)	5	72.2-94.1	87	8.9	10.2
	0.0015	5	95.1-98.5	96	1.3	1.4
S-3100-DA	0.00015 (LOQ)	5	86.5-105.8	100	7.7	7.7
	0.0015	5	100.2-103.9	102	1.4	1.4
S-3100-CA-RD	0.001 (LOQ)	5	89.6-956.3	93	3.4	3.6
	0.010	5	88.2-95.7	92	2.7	3.0
S-3100-CA-UR	0.005 (LOQ)	5	83.8-96.0	88	4.8	5.4
	0.050	5	89.0-96.7	92	3.4	3.7
S-3100-DP	0.00015 (LOQ)	5	85.7-102.3	95	6.0	6.3
	0.0015	5	93.0-96.3	95	1.2	1.3
4″-OH-S-3100-CA	0.001 (LOQ)	5	86.8-95.9	92	3.5	3.9
	0.010	5	92.1-94.4	93	1.0	1.1
S-3100-DA-RD	0.001 (LOQ)	5	78.7-96.5	92	7.4	8.1
	0.010	5	96.0-100.5	97	1.9	2.0
Confirmation ion transition						
Epyrifenacil (S-3100; V-10456)	0.00015 (LOQ)	5	82.4-104.1	99	9.2	9.3
	0.0015	5	99.4-106.0	102	2.5	2.4
S-3100-CA	0.00015 (LOQ)	5	70.7-95.8	86	9.6	11.1
	0.0015	5	93.8-99.2	96	1.9	2.0
S-3100-DA	0.00015 (LOQ)	5	83.3-99.7	92	6.3	6.8
	0.0015	5	95.3-102.8	99	2.7	2.8
S-3100-CA-RD	0.001 (LOQ)	5	90.9-100.8	95	3.8	4.0
	0.010	5	89.4-97.1	93	2.9	3.1
S-3100-CA-UR	0.005 (LOQ)	5	81.8-93.9	89	4.4	5.0
	0.050	5	83.0-98.2	89	6.5	7.3
S-3100-DP	0.00015 (LOQ)	5	91.9-101.7	96	3.7	3.8
	0.0015	5	91.8-95.5	94	1.5	1.6
4″-OH-S-3100-CA	0.001 (LOQ)	5	81.6-90.7	86	3.7	4.3
	0.010	5	91.6-94.9	94	1.3	1.4
S-3100-DA-RD	0.001 (LOQ)	5	92.7-98.8	92	7.7	8.3
	0.010	5	97.4-100.5	98	1.5	1.5

Data (uncorrected results, Appendix D, p. 117) were obtained from p. 12; Tables 1-8, pp. 17-24; Appendix C, pp. 101-116 of MRID 51778718. Since the LOQs were not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQs are the lowest levels of method validation (LLMVs) rather than LOQs.

1 Reported recovery ranges were obtained from data in Appendix C, pp. 101-116 of MRID 51778718, while reported means, standard deviations, and relative standard deviations were obtained from Tables 1-8, pp. 17-24 of MRID 51778718. Recovery ranges in Tables 1-8, pp. 17-24 of MRID 51778718 were rounded, but the means, standard deviations, and relative standard deviations in Tables 1-8, pp. 17-24 of MRID 51778718 were based on unrounded recovery values.

2 In the ILV, the soil matrix was described only as untreated control samples of soil provided by the Sponsor and selected as the most difficult soil matrix (highest organic matter) from the terrestrial field dissipation study (p. 12 of MRID 51778718). No study number or citation was reported for the terrestrial field dissipation study, but the reviewer noted that the method validation sample identification numbers were "V-18-200320-NDSoil-x-n" (where x was UTC/LOQ/10XLOQ and n ranged 01 to 05) in the raw data spreadsheets and chromatograms (Appendix C, pp. 101-116; Appendix E, pp. 119-276). Therefore, the reviewer assumed that the ILV soil matrix was the soil from the North Dakota site of submitted epyrifenacil (S-3100; V-10456) terrestrial field dissipation (TFD) study (Valent Study No. V-18-200320; MRID 51781215). From this available data, the reviewer concluded that the ILV test soil texture was clay (USDA);however, the reviewer could not report soil characterization of the ILV test soil from the available data since the soil depth of the ILV test soil matrix was not reported.

3 Two ion pair transitions were monitored (primary and confirmatory, respectively): *m/z* 518.0→293.0 and *m/z* 518.0→250.0 for epyrifenacil (S-3100; V-10456);*m/z* 432.0→281.0 and *m/z* 432.0→82.0 for S-3100-DA; *m/z* 434.1→281.1 and *m/z* 434.1→323.0 for S-3100-DA-RD; *m/z* 490.0→250.0 and *m/z* 490.0→293.0 for S-3100-CA; *m/z* 490.0→376.0 and *m/z* 490.0→319.0 for S-3100-CA-RD; *m/z* 368.0→293.0 and *m/z* 368.0→337.0 for S-3100-CA-UR; *m/z* 337.0→186.0 and *m/z* 337.0→150.0 for S-3100-DP; and *m/z* 508.1→385.0 and *m/z* 508.1→489.9 for 4″-OH-S-3100-CA (p. 13; Appendix F, pp. 277-282 of MRID 51778718). The monitored ion transitions of the ILV were the same as those of the ECM.

III. Method Characteristics

In the ECM and ILV, Valent Method RM-52S-4 and Valent Method RM-52S-4A reported a limit of detection (LOD) of 0.0001 mg/kg and a limit of quantification (LOQ) of 0.00015 mg/kg for epyrifenacil (S-3100;V-10456), S-3100-CA, S-3100-DA, and S-3100-DP; a LOD of 0.0002 mg/kg and a LOQ of 0.001 mg/kg for S-3100-CA-RD, S-3100-DA-RD, and 4″-OH-S-3100-CA; and a LOD of 0.0010 mg/kg and a LOQ of 0.005 mg/kg for S-3100-CA-UR (pp. 13, 15; Appendix 2, pp. 81, 98 of MRID 51778713; p. 15; Appendix A, p. 35; Appendix A, Appendix 1, pp. 40, 57 of MRID 51778718).

In the ILV, the LOQ was defined as the lowest concentration of an analyte tested at which an unambiguous identification of the analyte can be proven and at which an acceptable mean recovery with an acceptable relative standard deviation is obtained (p. 15 of MRID 51778718). No justifications or calculations for the LOQ were reported in the ECM; no calculations for the LOQ were reported in the ILV. In the ECM and ILV, the LOD was calculated by dividing the lowest calibration standard concentration by the effective matrix concentration in the sample extracts (Appendix 2, pp. 81, 98 of MRID 51778713; p. 15; Appendix A, Appendix 1, p. 57 of MRID 51778718). The reviewer noted that an ILV modification of the ECM method (Valent Method RM-52S-4 and Valent Method RM-52S-4A) was the use of the same calibration range (0.050-25.0 ng/mL) for all analyses/analytes; therefore, using the reported LOD calculation equation, the LOD for all analytes should be 0.0001 mg/kg since the lowest calibration standard was 0.05 ng/mL for all analytes (see Reviewer's Comments).

Since the LOQs were not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQs are the lowest levels of method validation (LLMVs) rather than LOQs.

Table 4a. Method Characteristics

		Epyrifenacil (S-3100; V-10456)	S-3100-CA	S-3100-DA	S-3100-DP
Limit of Quantitation (LOQ)*	ECM	0.00015 mg/kg			
	ILV				
Limit of Detection (LOD)	ECM	0.0001 mg/kg (reported) 0.0001 mg/kg (reviewer-calculated based on LOD calculation equation)[1]			
	ILV				
Linearity (calibration curve r and concentration range)[2]	ECM	r = 0.9999 (Q) r = 1.0000 (C)	r = 1.0000 (Q & C)	r = 1.0000 (Q) r = 0.9997 (C)	r = 1.0000 (Q & C)
		0.05-5.00 ng/mL			
	ILV	r = 1.0000 (Q & C)	r = 1.0000 (Q & C)	r = 1.0000 (Q & C)	r = 1.0000 (Q & C)
		0.0500-25.00 ng/mL			
Repeatable	ECM[3,4]	Yes for LOQ (0.00015 mg/kg) and 10×LOQ (0.0015 mg/kg) in one characterized soil matrix (clay).			
	ILV[5,6,7]	Yes for LOQ (0.00015 mg/kg) and 10×LOQ (0.0015 mg/kg) in one uncharacterized soil matrix (clay).			
Reproducible		Yes for 0.00015 mg/kg (LLMV)* and 0.0015 mg/kg in tested soil matrix.			
Specific	ECM	Yes, matrix interferences were <22% (Q) and <24% (C) of the LOQ (based on peak areas) at the RT of epyrifenacil (S-3100; V-10456).[8]	Yes, no matrix interferences were observed at the RT of S-3100-CA.	Yes, no matrix interferences were observed at the RT of S-3100-DA, but a nearby peak (RT 6.88-6.95 min.; peak height *ca*. <5% of Q LOQ peak height and *ca*. 50% of C LOQ peak height) was observed.[9]	Yes, matrix interferences were <11% of the LOQ (based on peak areas) at the RT of S-3100-DP, but a nearby peak (RT 8.64-8.66 min.; peak height *ca*. <10% of LOQ peak height) was observed which interfered with analyte peak attenuation and integration.[10]
	ILV	Yes, matrix interferences were <6% of the LOQ (based on peak areas) at the RT of epyrifenacil (S-3100; V-10456).[11]	Yes, no matrix interferences were observed at the RT of S-3100-CA. Minor baseline noise was observed at the LOQ.	Yes, matrix interferences were <5% (Q & C) of the LOQ (based on peak areas) at the RT of S-3100-DA.[12]	Yes, matrix interferences were <8% of the LOQ (based on peak areas) at the RT of S-3100-DP, but nearby peaks (RT 8.48 and 8.64-8.66 min.; peak height *ca*. <15% of LOQ peak height) were observed which interfered with analyte peak attenuation and integration.[13]

Data were obtained from p. 13 (LOQ/LOD); Tables 1-14, pp. 16-31 (recovery data); Appendix 2, pp. 85-86; Appendix 5, pp. 147-162 (calibration curves); Figures 1-40, pp. 32-71 (chromatograms) of MRID 51778713; p. 15 (LOQ/LOD); Tables 1-8, pp. 17-24 (recovery data); Appendix A, p. 35; Appendix A, Appendix 1, pp. 44-45; Appendix C, pp. 101-116 (calibration curves); Appendix E, pp. 119-276 (chromatograms) of MRID 51778718; DER Excel Attachment.
Q = quantitative ion transition; C = confirmatory ion transition.

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

1 In the ECM and ILV, the LOD was calculated by dividing the lowest calibration standard concentration by the effective matrix concentration in the sample extracts (Appendix 2, pp. 81, 98 of MRID 51778713; p. 15; Appendix A, Appendix 1, p. 57 of MRID 51778718). The reviewer calculated the LOD for each sample set based on this reported equation (see Reviewer's Comments).

2 In the ECM and ILV, calibration curves were based on a second-order polynomial fit (relative weight, 1/concentration), $y = ax^2 + bx + c$ (Appendix 5, pp. 147-162 of MRID 51778713; Appendix C, pp. 101-116 of MRID 51778718). Correlation coefficients were reported as r^2. The reviewer converted reported r^2 values to r (see DER Excel Attachment). The reviewer reported r values to four decimal places, even though the study reported r^2 to five decimal places. Solvent-based calibration standards were used in the ECM and ILV.

3 ECM study report MRID 51778713 cited Valent Method RM-52S-4 as the analytical method which was validated by the performance data; however, both Valent Method RM-52S-4 and Valent Method RM-52S-4A were included in Appendix 2 of the ECM MRID 51778713. The only differences between Valent Method RM-52S-4 and Valent Method RM-52S-4A was the correction of typographical errors in Section 3 of Valent Method RM-52S-4 (Appendix 2, p. 103 of MRID 51778713).

4 In the ECM, the soil matrix was clay soil [Sample ID: V-18-200320-D-SC-(0-6); pH 7.8 (1:1 soil:water ratio); 15% sand, 32% silt, 53% clay; 3.5% organic matter (Walkley-Black)] obtained from the North Dakota site of the submitted epyrifenacil (S-3100; V-10456) terrestrial field dissipation (TFD) study (Valent Study No. V-18-200320; MRID 51781215) and characterized by Agvise Laboratories, Northwood, North Dakota (USDA texture classification; p. 14; Appendix 4, pp. 135-145 of MRID 51778713). The soil texture was verified by the reviewer using USDA-NRCS technical support tools. Soil characterization reported were provided for all soil depths for the untreated North Dakota soil sample (summarized in the table below); however, based on the organic matter data provided on p. 14 of MRID 51778713, the reviewer assumed that the soil matrix for the ECM study was from the 0-6 inch (0-15.24 cm) depth.

Sample ID	Soil Depth (cm)	Soil Texture	Sand %	Silt %	Clay %	Organic Matter (%)	pH (1:1 soil:water ratio)
V-18-200320-D-SC-(0-6)	0-15.24	Clay	15	32	53	3.5	7.8
V-18-200320-D-SC-(6-12)	15.24-30.48	Clay	11	30	59	1.8	7.9
V-18-200320-D-SC-(12-18)	30.48-45.72	Clay	15	26	59	1.6	8.1
V-18-200320-D-SC-(18-24)	45.72-60.96	Clay	19	20	61	1.4	8.3
V-18-200320-D-SC-(24-30)	60.96-76.2	Clay	23	20	57	1.2	8.3
V-18-200320-D-SC-(30-36)	76.2-91.44	Clay	21	18	61	1.3	8.2

Data obtained from Appendix 4, pp. 135-140 of MRID 51778713; USDA texture classification. The soil textures were verified by the reviewer using USDA-NRCS technical support tools.

5 In the ILV, the soil matrix was described only as untreated control samples of soil provided by the Sponsor and selected as the most difficult soil matrix (highest organic matter) from the terrestrial field dissipation study (p. 12 of MRID 51778718). No study number or citation was reported for the terrestrial field dissipation study, but the reviewer noted that the method validation sample identification numbers were "V-18-200320-NDSoil-x-n" (where x was UTC/LOQ/10XLOQ and n ranged 01 to 05) in the raw data spreadsheets and chromatograms (Appendix C, pp. 101-116; Appendix E, pp. 119-276). Therefore, the reviewer assumed that the ILV soil matrix was the soil from the North Dakota site of submitted epyrifenacil (S-3100; V-10456) terrestrial field dissipation

(TFD) study (Valent Study No. V-18-200320; MRID 51781215). From this available data, the reviewer concluded that the ILV test soil texture was clay (USDA); however, the reviewer could not report soil characterization for the ILV test soil since the soil depth of the ILV test soil matrix was not reported.

6 ILV study report MRID 51778718 was submitted to validate Valent Method RM-52S-4A (pp. 9, 15 of MRID 51778718).

7 The ILV validated the method, Valent Method RM-52S-4A, for epyrifenacil (S-3100; V-10456) and its degradates in soil at their respective LOQs and 10×LOQs with insignificant modifications to the analytical parameters and equipment, as well as the fact that recoveries were not corrected for residues quantified in the controls and the same calibration range (0.050-25.0 ng/mL) was used for all analyses/analytes (pp. 9, 15-16; Appendix A, pp. 35-37; Appendix A, Appendix 1, pp. 40-91; Appendix C, pp. 101-116; Appendix D, p. 117, Appendix F, pp. 277-282 of MRID 51778718). The number of ILV trials was not reported, but the reviewer assumed that the ILV validation occurred with the first trial based on the lack of method modifications and reported communications of method issues.

8 Based on Figures 3-4, pp. 34-35, of MRID 51778713.

9 Based on Figure 14, p. 45, of MRID 51778713.

10 Based on Figures 28-30, pp. 59-61, of MRID 51778713.

11 Based on Appendix E, pp. 126-132, of MRID 51778718.

12 Based on Appendix E, pp. 166-172, of MRID 51778718.

13 Based on Appendix E, pp. 226-237, of MRID 51778718.

Table 4b. Method Characteristics (con't)

		S-3100-CA-RD	4″-OH-S-3100-CA	S-3100-DA-RD	S-3100-CA-UR
Limit of Quantitation (LOQ)*	ECM	0.001 mg/kg			0.005 mg/kg
	ILV				
Limit of Detection (LOD)	ECM	0.0002 mg/kg (reported) 0.0002 mg/kg (reviewer-calculated based on LOD calculation equation)[1]			0.0010 mg/kg (reported) 0.0010 mg/kg (reviewer-calculated based on LOD calculation equation)[1]
	ILV	0.0002 mg/kg (reported) 0.0001 mg/kg (reviewer-calculated based on LOD calculation equation)[1]			0.0010 mg/kg (reported) 0.0001 mg/kg (reviewer-calculated based on LOD calculation equation)[1]
Linearity (calibration curve r and concentration range)[2]	ECM	r = 0.9999 (Q) r = 1.0000 (C)	r = 1.0000 (Q & C)	r = 1.0000 (Q) r = 0.9999 (C)	r = 1.0000 (Q & C)
		0.10-25.0 ng/mL			0.50-50.00 ng/mL
	ILV	r = 1.0000 (Q & C)	r = 1.0000 (Q & C)	r = 1.0000 (Q & C)	r = 1.0000 (Q) r = 0.9999 (C)
		0.0500-25.00 ng/mL			
Repeatable	ECM[3,4]	Yes for LOQ (0.001 mg/kg) and 10×LOQ (0.010 mg/kg) in one characterized soil matrix (clay)			Yes for LOQ (0.005 mg/kg) and 10×LOQ (0.050 mg/kg) in one characterized soil matrix (clay)
	ILV[5,6,7]	Yes for LOQ (0.001 mg/kg) and 10×LOQ (0.010 mg/kg) in one uncharacterized soil matrix (clay)			Yes for LOQ (0.005 mg/kg) and 10×LOQ (0.050 mg/kg) in one characterized soil matrix (clay)
Reproducible		Yes for 0.001 mg/kg (LLMV)* and 0.010 mg/kg in tested soil matrix.			Yes for 0.005 mg/kg (LLMV)* and 0.050 mg/kg in tested soil matrix.
Specific	ECM	Yes, no matrix interferences were observed at the RT of S-3100-CA-RD. Minor baseline noise was noted.	Yes, no matrix interferences were observed at the RT of 4″-OH-S-3100-CA. Elevated baseline was noted in C chromatograms.	Yes, no matrix interferences were observed at the RT of S-3100-DA-RD.	Yes, no matrix interferences were observed at the RT of S-3100-CA-UR, but a nearby peak (RT 7.54 min.; peak height *ca.* <10% of LOQ peak height) was observed which interfered with analyte peak attenuation and integration in the C ion.[8]

	ILV	Yes, matrix interferences were <3% of the LOQ (based on peak areas) at the RT of S-3100-CA-RD. [9]	Yes, matrix interferences were <6% of the LOQ (based on peak areas) at the RT of 4″-OH-S-3100-CA. Elevated baseline was noted in C chromatograms. [10]	Yes, no matrix interferences were observed at the RT of S-3100-DA-RD	Yes, no matrix interferences were observed at the RT of S-3100-CA-UR, but a nearby peak (RT 7.46 min.; peak height *ca.* <5% of LOQ peak height) was observed which interfered with analyte peak attenuation and integration in the C ion.[11]

Data were obtained from p. 13 (LOQ/LOD); Tables 1-14, pp. 16-31 (recovery data); Appendix 2, pp. 85-86; Appendix 5, pp. 147-162 (calibration curves); Figures 1-40, pp. 32-71 (chromatograms) of MRID 51778713; p. 15 (LOQ/LOD); Tables 1-8, pp. 17-24 (recovery data); Appendix A, p. 35; Appendix A, Appendix 1, pp. 44-45; Appendix C, pp. 101-116 (calibration curves); Appendix E, pp. 119-276 (chromatograms) of MRID 51778718; DER Excel Attachment.
Q = quantitative ion transition; C = confirmatory ion transition.

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

1 In the ECM and ILV, the LOD was calculated by dividing the lowest calibration standard concentration by the effective matrix concentration in the sample extracts (Appendix 2, pp. 81, 98 of MRID 51778713; p. 15; Appendix A, Appendix 1, p. 57 of MRID 51778718). The reviewer calculated the LOD for each sample set based on this reported equation (see Reviewer's Comments).

2 In the ECM and ILV, calibration curves were based on a second-order polynomial fit (relative weight, 1/concentration), $y = ax^2 + bx + c$ (Appendix 5, pp. 147-162 of MRID 51778713; Appendix C, pp. 101-116 of MRID 51778718). Correlation coefficients were reported as r^2. The reviewer converted reported r^2 values to r (see DER Excel Attachment). The reviewer reported r values to four decimal places, even though the study reported r^2 to five decimal places. Solvent-based calibration standards were used in the ECM and ILV.

3 ECM study report MRID 51778713 cited Valent Method RM-52S-4 as the analytical method which was validated by the performance data; however, both Valent Method RM-52S-4 and Valent Method RM-52S-4A were included in Appendix 2 of the ECM MRID 51778713. The only differences between Valent Method RM-52S-4 and Valent Method RM-52S-4A was the correction of typographical errors in Section 3 of Valent Method RM-52S-4 (Appendix 2, p. 103 of MRID 51778713).

4 In the ECM, the soil matrix was clay soil [Sample ID: V-18-200320-D-SC-(0-6); pH 7.8 (1:1 soil:water ratio); 15% sand, 32% silt, 53% clay; 3.5% organic matter (Walkley-Black)] obtained from the North Dakota site of the submitted epyrifenacil (S-3100; V-10456) terrestrial field dissipation (TFD) study (Valent Study No. V-18-200320; MRID 51781215) and characterized by Agvise Laboratories, Northwood, North Dakota (USDA texture classification; p. 14; Appendix 4, pp. 135-145 of MRID 51778713). The soil texture was verified by the reviewer using USDA-NRCS technical support tools. Soil characterization reported were provided for all soil depths for the untreated North Dakota soil sample (summarized in the table below); however, based on the organic matter data provided on p. 14 of MRID 51778713, the reviewer assumed that the soil matrix for the ECM study was from the 0-6 inch (0-15.24 cm) depth.

Sample ID	**Soil Depth (cm)**	**Soil Texture**	**Sand %**	**Silt %**	**Clay %**	**Organic Matter (%)**	**pH (1:1 soil:water ratio)**
V-18-200320-D-SC-(0-6)	0-15.24	Clay	15	32	53	3.5	7.8
V-18-200320-D-SC-(6-12)	15.24-30.48	Clay	11	30	59	1.8	7.9
V-18-200320-D-SC-(12-18)	30.48-45.72	Clay	15	26	59	1.6	8.1
V-18-200320-D-SC-(18-24)	45.72-60.96	Clay	19	20	61	1.4	8.3
V-18-200320-D-SC-(24-30)	60.96-76.2	Clay	23	20	57	1.2	8.3
V-18-200320-D-SC-(30-36)	76.2-91.44	Clay	21	18	61	1.3	8.2

Data obtained from Appendix 4, pp. 135-140 of MRID 51778713; USDA texture classification. The soil textures were verified by the reviewer using USDA-NRCS technical support tools.

5 In the ILV, the soil matrix was described only as untreated control samples of soil provided by the Sponsor and selected as the most difficult soil matrix (highest organic matter) from the terrestrial field dissipation study (p. 12 of MRID 51778718). No study number or citation was reported for the terrestrial field dissipation study, but the reviewer noted that the method validation sample identification numbers were "V-18-200320-NDSoil-x-n" (where x was UTC/LOQ/10XLOQ and n ranged 01 to 05) in the raw data spreadsheets and chromatograms (Appendix C, pp. 101-116; Appendix E, pp. 119-276). Therefore, the reviewer assumed that the ILV soil matrix was the soil from the North Dakota site of submitted epyrifenacil (S-3100; V-10456) terrestrial field dissipation (TFD) study (Valent Study No. V-18-200320; MRID 51781215). From this available data, the reviewer concluded that the ILV test soil texture was clay (USDA); however, the reviewer could not report soil characterization of the ILV test soil. since the soil depth of the ILV test soil matrix was not reported.

6 ILV study report MRID 51778718 was submitted to validate Valent Method RM-52S-4A (pp. 9, 15 of MRID 51778718).

7 The ILV validated the method, Valent Method RM-52S-4A, for epyrifenacil (S-3100; V-10456) and its degradates in soil at their respective LOQs and 10×LOQs with insignificant modifications to the analytical parameters and equipment, as well as the fact that recoveries were not corrected for residues quantified in the controls and the same calibration range (0.050-25.0 ng/mL) was used for all analyses/analytes (pp. 9, 15-16; Appendix A, pp. 35-37; Appendix A, Appendix 1, pp. 40-91; Appendix C, pp. 101-116; Appendix D, p. 117, Appendix F, pp. 277-282 of MRID 51778718). The number of ILV trials was not reported, but the reviewer assumed that the ILV validation occurred with the first trial based on the lack of method modifications and reported communications of method issues.

8 Based on Figures 18-19, p. 49-50, of MRID 51778713. This contaminant did not affect the validity of the method since a confirmatory method is not usually required when LC/MS or GC/MS is used as the primary method to generate study data.

9 Based on Appendix E, pp. 186-192, of MRID 51778718.

10 Based on Appendix E, pp. 246-252, of MRID 51778718.

11 Based on Appendix E, pp. 206-207, of MRID 51778718. This contaminant did not affect the validity of the method since a confirmatory method is not usually required when LC/MS or GC/MS is used as the primary method to generate study data.

IV. Method Deficiencies and Reviewer's Comments

1. Since the reported method LOQs were not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQs are the lowest levels of method validation (LLMVs) rather than LOQs (pp. 13, 15; Appendix 2, pp. 81, 98 of MRID 51778713; p. 15; Appendix A, p. 35; Appendix A, Appendix 1, pp. 40, 57 of MRID 51778718). The lowest concentration tested with sufficiently accurate and precise recoveries is the LLMV. Based on the performance data submitted by the ILV and ECM, the LLMVs were equivalent to the respective ECM reported method LOQs for epyrifenacil (S-3100; V-10456) and its degradates in soil.

2. The ILV study report MRID 51778718 was submitted to validate Valent Method RM-52S-4A (pp. 9, 15 of MRID 51778718). ECM study report MRID 51778713 cited Valent Method RM-52S-4 as the analytical method which was validated by the performance data; however, both Valent Method RM-52S-4 and Valent Method RM-52S-4A were included in Appendix 2 of the ECM MRID 51778713. The only differences between Valent Method RM-52S-4 and Valent Method RM-52S-4A was the correction of typographical errors in Section 3 of Valent Method RM-52S-4 (Appendix 2, p. 103 of MRID 51778713).

3. In the ECM and ILV, the LOD was calculated by dividing the lowest calibration standard concentration by the effective matrix concentration in the sample extracts (Appendix 2, pp. 81, 98 of MRID 51778713; p. 15; Appendix A, Appendix 1, p. 57 of MRID 51778718). The reviewer noted that an ILV modification of the ECM method (Valent Method RM-52S-4 and Valent Method RM-52S-4A) was the use of the same calibration range (0.050-25.0 ng/mL) for all analyses/analytes; therefore, using the reported LOD calculation equation, the LOD for all analytes should be 0.0001 mg/kg since the lowest calibration standard was 0.05 ng/mL for all analytes. However, the ILV study report listed the same LODs for the analytes as the ECM. This typographical error should be corrected in the ILV study report.

4. The ILV soil matrix was not characterized; its soil texture and source were not specified but could be inferred by the reviewer from the raw data. In the ILV, the soil matrix was described only as untreated control samples of soil provided by the Sponsor and selected as the most difficult soil matrix (highest organic matter) from the terrestrial field dissipation study (p. 12 of MRID 51778718). No study number or citation was reported for the terrestrial field dissipation study, but the reviewer noted that the method validation sample identification numbers were "V-18-200320-NDSoil-x-n" (where x was UTC/LOQ/10XLOQ and n ranged 01 to 05) in the raw data spreadsheets and chromatograms (Appendix C, pp. 101-116; Appendix E, pp. 119-276). Therefore, the reviewer assumed that the ILV soil matrix was the soil from the North Dakota site of submitted epyrifenacil (S-3100; V-10456) terrestrial field dissipation (TFD) study (Valent Study No. V-18-200320; MRID 51781215). From this available data, the reviewer concluded that the ILV test soil texture was clay (USDA; however, the reviewer could not report soil characterization of the ILV test soil since the soil depth of the ILV test soil matrix was not reported.

5. The ILV soil matrix (clay; see above) did not cover the range of soils used in the terrestrial field dissipation (TFD) studies since only one ILV test soil was included; however, the reviewer noted that the ILV test soil provided a difficult sample condition and was sourced from the terrestrial field dissipation study (p. 12 of MRID 51778718). 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 matrix) to analyze from the study to demonstrate how well the method performs.

   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. Additionally, the soil texture for the ECM test soil and ILV test soil were the same, and the ILV test soil was supplied by the Sponsor (Valent U.S.A. LLC; p. 12 of MRID 51778718). OCSPP 850.6100 guidance does not address the use of the same test matrix between the ECM and ILV validations.

   One epyrifenacil (S-3100; V-10456) TFD study (MRID 51781215) was submitted for review by PB&A/CSS Joint Venture personnel. The following soils were included in the epyrifenacil (S-3100; V-10456) TFD study: sandy loam (0-90 cm: 6-8% clay, 0.09-0.66% organic matter) [California site]; loamy sand (0-15 cm: 8% clay, 0.82% organic matter), sandy loam (15-30 cm: 18%, 0.91% organic matter), sandy clay loam (30-60 cm: 30-34% clay, 0.45-0.70% organic matter) and sandy clay (60-90 cm: 40-44% clay, 0.04-0.6% organic matter) [Georgia site]; sandy loam (0-45, 60-90 cm: 7-13% clay, 0.22-2.7% organic matter) and loam (45-60 cm: 25% clay, 0.83% organic matter) [Ontario, Canada site]; and clay (0-90 cm: 53-61% clay, 1.2-3.5% organic matter) [North Dakota site; Table 2, p. 30; Appendix G, Table 1, p. 454; Appendix H, Table 1, p. 943; Appendix I, Table 1, p. 1412; Appendix J, Table 1, p. 1911 of MRID 51781215]. The reviewer noted that soil samples in submitted epyrifenacil (S-3100; V-10456) TFD study MRID 51781215 were analyzed using three methods (RM-52S, RM-52S-2, and RM-52S-3) with the majority of samples analyzed with RM-52S-3, *Determination of Residues of V-10456, S-3100-CA, S-3100-DA, S-3100-CA-RD, S-3100-CA-UR, S-3100-DP, 4"-OH-S-3100-CA, and S-3100-DA-RD in Soil*.

6. The number of ILV trials was not reported, but the reviewer assumed that the ILV validation occurred with the first trial based on the lack of method modifications.

7. It could not be determined if the ILV was conducted independently from the ECM due to lack of data. Communications between the ILV and method developers was not reported or summarized, but the ILV Protocol stated that all contact with the Sponsor regarding the method would be documented in the raw data and reported (Appendix A, pp. 34 of MRID 51778718). The registrant stated there is no communication between ILV and ECM authors during the method validation process ((see the registrant's response on page 9). The ILV Protocol also stated that the ILV laboratory was unfamiliar with the method (Appendix A, p. 30 of MRID 51778718). The reviewer noted that the ILV Sponsor

Representative (Kirk Göhre, Valent U.S.A. LLC) was also an author of the ECM Methods Valent Method RM-52S-4 and Valent Method RM-52S-4A (Appendix 2, pp. 100, 122 of MRID 51778713).

8. The reported/calculated LOD for epyrifenacil (S-3100; V-10456), S-3100-CA, S-3100-DA, and S-3100-DP in the ECM and ILV was 0.0001 mg/kg which was 60% of the LOQ (p. 13 of MRID 51778713; p. 15 of MRID 51778718). Additionally, only one calibration standard was present below the LOQ fortification level for epyrifenacil (S-3100; V-10456), S-3100-CA, S-3100-DA, and S-3100-DP in the ECM and ILV. The calibration standard range should contain two calibration standards below and above the tested fortification levels for accuracy of quantitation at the LOQ and 10×LOQ.

9. ILV and ECM representative chromatograms showed some matrix interferences for S-3100-DP. In both sets of chromatograms, minor matrix interferences (<11% of the LOQ, based on peak area) were noted at the analyte RT and a nearby peak (RT 8.64-8.66 min.; peak height *ca*. <15% of LOQ peak height) was observed which interfered with analyte peak attenuation and integration (Figures 28-30, pp. 59-61, of MRID 51778713; Appendix E, pp. 226-237, of MRID 51778718). ECM representative chromatograms also showed some matrix interferences (<24% of the LOQ, based on peak area) for epyrifenacil (S-3100; V-10456; Figures 3-4, pp. 34-35, of MRID 51778713). These matrix interferences do not affect the specificity of the method for these analytes since the matrix interferences were <LOD (LOD = 0.0001 mg/kg = 60% of the LOQ; p. 13 of MRID 51778713; p. 15 of MRID 51778718). OCSPP Guideline 850.6100 states that interferences with peak areas <50% at the LOD "are not considered significant".

10. According to the analytical method (Valent Method RM-52S-4 and Valent Method RM-52S-4A), recovery results were corrected for residues quantified in the controls (p. 15 Appendix 2, pp. 95-98 of MRID 51778713). While peaks at the retention time of the analyte were integrated for epyrifenacil (S-3100; V-10456) and S-3100-DP in the untreated control soils, the "concentration found" for these residues in the controls was set to 0.0000 mg/kg (Appendix 5, pp. 147-162). Therefore, it was determined that no correction of the recoveries was performed in the ECM study

11. The determinations of the LOD and LOQ in the ECM and ILV were not based on scientifically acceptable procedures as defined in 40 CFR Part 136 (pp. 13, 15; Appendix 2, pp. 81, 98 of MRID 51778713; p. 15; Appendix A, p. 35; Appendix A, Appendix 1, pp. 40, 57 of MRID 51778718). In the ECM, no justifications or calculations for the LOQ were reported in the ECM; no calculations for the LOQ were reported in the ILV. In the ECM and ILV, the LOD was calculated by dividing the lowest calibration standard concentration by the effective matrix concentration in the sample extracts. Detection limits should not be based on the arbitrarily selected lowest concentration in the spiked samples.

    Since the LOQs were not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQs are the lowest levels of method validation (LLMVs) rather than LOQs.

12. Matrix effects were not studied in the ECM or ILV. Solvent-based calibration standards were used in the ECM and ILV (Appendix 2, pp. 85-86 of MRID 51778713 and Appendix A, p. 35; Appendix A, Appendix 1, pp. 44-45 of MRID 51778718).

13. In the ECM, the time requirement for the method was reported as *ca*. 8 hours for a batch of 17 samples for a trained analyst (p. 15 of MRID 51778713). In the ILV, the time requirement for the method was reported as *ca*. 1 working day for a batch of 19 samples (six calibration standards, a reagent blank, two untreated control samples, five samples fortified at the LOQ and five samples fortified at 10×LOQ; pp. 13-14 of MRID 51778718).

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.

Attachment 1: Chemical Names and Structures

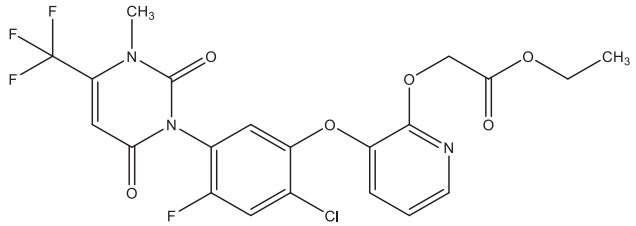
Epyrifenacil (S-3100; V-10456)

IUPAC Name: Ethyl [(3-{2-chloro-5-[3,6-dihydro-3-methyl-2,6-dioxo-4-(trifluoromethyl)pyrimidin-1(2H)-yl]-4-fluorophenoxy}-2-pyridyl)oxy]acetate

CAS Name: Ethyl 2-[[3-[2-chloro-5-[3,6-dihydro-3-methyl-2,6-dioxo-4-(trifluoromethyl)-1(2H)-pyrimidinyl]-4-fluorophenoxy]-2-pyridinyl]oxy]acetate

CAS Number: 353292-31-6

SMILES String: O=C(N1C2=CC(OC3=CC=CN=C3OCC(OCC)=O)=C(Cl)C=C2F)C=C(C(F)(F)F)N(C)C1=O



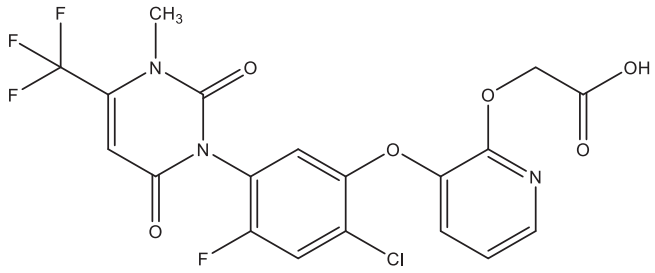
S-3100-CA

IUPAC Name: 2-((3-(2-Chloro-4-fluoro-5-(3-methyl-2,6-dioxo-4-(trifluoromethyl)-3,6-dihydropyrimidin-1(2H)-yl)phenoxy)pyridin-2-yl)oxy)acetic acid

CAS Name: Not reported

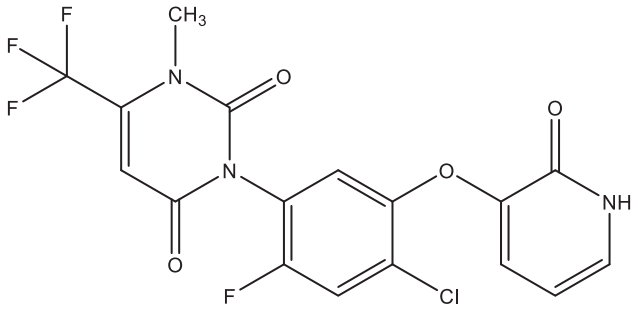
CAS Number: Not reported

SMILES String: O=C(N1C2=C(F)C=C(Cl)C(OC3=CC=CN=C3OCC(O)=O)=C2)C=C(C(F)(F)F)N(C)C1=O



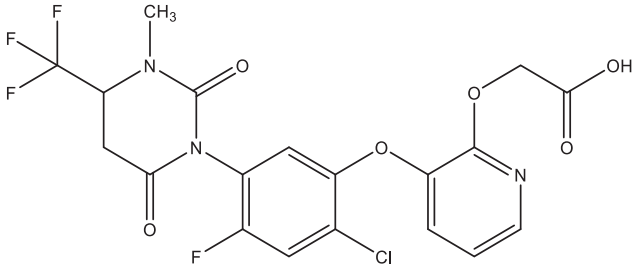
S-3100-DA

IUPAC Name: 3-(4-Chloro-2-fluoro-5-((2-oxo-1,2-dihydropyridin-3-yl)oxy)phenyl)-1-methyl-6-(trifluoromethyl)pyrimidine-2,4(1H,3H)-dione
CAS Name: Not reported
CAS Number: Not reported
SMILES String: O=C(N1C2=C(F)C=C(Cl)C(OC3=CC=CNC3=O)=C2)C=C(C(F)(F)F)N(C)C1=O



S-3100-CA-RD

IUPAC Name: 2-((3-(2-Chloro-4-fluoro-5-(3-methyl-2,6-dioxo-4-(trifluoromethyl)tetrahydropyrimidin-1(2H)-yl)phenoxy)pyridin-2-yl)oxy)acetic acid
CAS Name: Not reported
CAS Number: Not reported
SMILES String: O=C(N1C2=C(F)C=C(Cl)C(OC3=CC=CN=C3OCC(O)=O)=C2)CC(C(F)(F)F)N(C)C1=O



S-3100-CA-UR

IUPAC Name:	2-((3-(2-Chloro-4-fluoro-5-(3-methylureido)phenoxy)pyridin-2-yl)oxy)acetic acid
CAS Name:	Not reported
CAS Number:	Not reported
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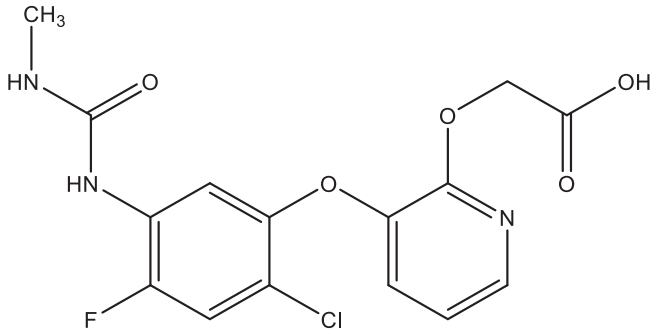
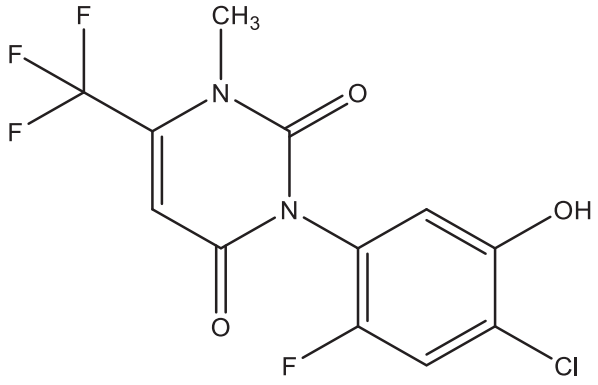


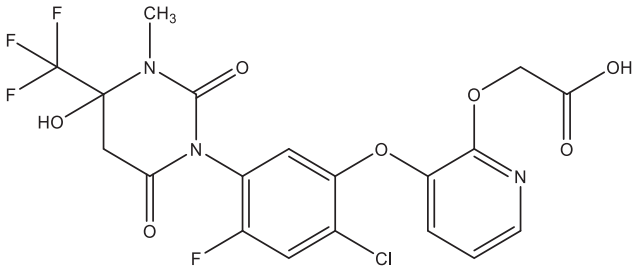
S-3100-DP

IUPAC Name:	3-(4-Chloro-2-fluoro-5-hydroxyphenyl)-1-methyl-6-(trifluoromethyl)pyrimidine-2,4(1H,3H)-dione
CAS Name:	Not reported
CAS Number:	Not reported
SMILES String:	O=C(N1C2=C(F)C=C(Cl)C(O)=C2)C=C(C(F)(F)F)N(C)C1=O



4′′-OH-S-3100-CA

IUPAC Name: 2-((3-(2-Chloro-4-fluoro-5-(4-hydroxy-3-methyl-2,6-dioxo-4-(trifluoromethyl)tetrahydropyrimidin-1(2H)-yl)phenoxy)pyridin-2-yl)oxy)acetic acid
CAS Name: Not reported
CAS Number: Not reported
SMILES String: O=C(N1C2=C(F)C=C(Cl)C(OC3=CC=CN=C3OCC(O)=O)=C2)CC(C(F)(F)F)(O)N(C)C1=O



S-3100-DA-RD

IUPAC Name: 3-(4-Chloro-2-fluoro-5-((2-oxo-1,2-dihydropyridin-3-yl)oxy)phenyl)-1-methyl-6-(trifluoromethyl)dihydropyrimidine-2,4(1H,3H)-dione
CAS Name: Not reported
CAS Number: Not reported
SMILES String: O=C(N1C2=C(F)C=C(Cl)C(OC3=CC=CNC3=O)=C2)CC(C(F)(F)F)N(C)C1=O