

Test Material: Primisulfuron-methyl

MRID: 49447001

Title: Analytical Method (GRM070.02A) for Determination of CGA136872 in Soil

MRID: 49447002

Title: Primisulfuron-Methyl - Independent Laboratory Validation of Residue Method (AG-498) For the Determination of Primisulfuron-Methyl in Soil by High Performance Liquid Chromatography/UV Detection

EPA PC Code: 128973

OCSPP Guideline: 850.6100

For CDM Smith

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Analytical method for primisulfuron-methyl (CGA136872) in soil

Reports: ECM: EPA MRID No.: 49447002 (Appendix 1, pp. 72-91). Beidler, W., and K. Shoffner. 1986. CGA-136872 - ANALYTICAL METHOD FOR DETERMINATION OF CGA-136872 IN SOIL BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY. Report prepared and sponsored by CIBA-GEIGY CORPORATION, Greensboro, North Carolina, and submitted by Syngenta Crop Protection, LLC, Greensboro, North Carolina; 20 pages. CIBA-GEIGY Project ID: AG-498 and METHOD NO. AG-498 (Appendix 1, pp. 72, 76). Final report issued February 26, 1986.

ECM (as classified and submitted by registrant): EPA MRID No.: 49447001. Lin, K. 2014. Analytical Method (GRM070.02A) for Determination of CGA136872 in Soil. Report prepared, sponsored, and submitted by Syngenta Crop Protection, LLC, Greensboro, North Carolina; 49 pages. Syngenta Report No.: GRM070.02A and Task No.: TK0165281. Final report issued July 11, 2014.

ILV: EPA MRID No. 49447002. Perez, R., and A. Caro. 2014. Primisulfuron-Methyl - Independent Laboratory Validation of Residue Method (AG-498) For the Determination of Primisulfuron-Methyl in Soil by High Performance Liquid Chromatography/UV Detection. Report prepared by ADPEN Laboratories, Inc., Jacksonville, Florida, sponsored and submitted by Syngenta Crop Protection, LLC, Greensboro, North Carolina; 112 pages (including ECM, Appendix 1, pp. 72-91). Report and Task No.: TK0165281. ADPEN Study No.: 2K13-901-TK0165281 (Appendix 2, p. 93). Final report issued June 2, 2014.

Document No.: MRIDs 49447001 & 49447002

Guideline: 850.6100

Statements: ECM: Good Laboratory Practice (GLP) standards were not in effect for the study, but the study was "conducted in accordance with good and acceptable scientific practices" (Appendix 1, p. 74 of MRID 49447002). Signed and dated Data Confidentiality, GLP, and Authenticity Certification statements were provided (Appendix 1, pp. 73-74, 91). A Quality Assurance statement was not provided.

ILV: The study was conducted in compliance with USEPA GLP standards (p. 3 of MRID 49447002). Signed and dated Data Confidentiality, GLP, and Quality Assurance statements were provided (pp. 2-4). The certification of the authenticity of the study report is included in the Quality Assurance Statement (p. 4).

Classification: This analytical method is classified as unacceptable. The updated LC/MS/MS method in MRID 49447002 may be considered in an acceptable submission but the submission must include an ECM and ILV with the same methods. The independent laboratory modified the original ECM (HPLC/UV) to simplify the procedure and use newer detector (LC/MS/MS) technology, but Syngenta failed to conduct an internal validation of the LC/MS/MS method. Syngenta retains the HPLC/UV analysis as the primary analytical method

despite ILV findings that severe background interferences were observed in two soil types (sandy loam, clay loam), yet no significant interferences (<10% of LOQ) were observed with LC/MS/MS analysis of the clay loam soil. For the ECM HPLC/UV validation, only a single procedural recovery (n = 1) was reported at the LOQ for each soil matrix and no fortifications at 10× LOQ were reported. The determinations of the LOQ and LOD were not based on scientifically acceptable procedures. The ILV did not report LODs. The ECM does not require the HPLC/UV method to have a confirmatory method. For the ILV, LC/MS/MS method recovery results were corrected for matrix controls. For the ECM HPLC/UV validation, soil matrices were not characterized.

PC Code: 128973

Reviewer:

Andrew Shelby
Physical Scientist

Signature: 

Date: 1/21/2016

Page citations in this review refer to MRID 49447002, unless noted otherwise.

Executive Summary

The analytical method, Method No. AG-498, is designed for the quantitative determination of primisulfuron-methyl in soil using HPLC/UV. The method is quantitative for the analyte at the stated LOQ of 0.01 mg/kg. The LOQ is less than the lowest toxicological level of concern in soil of 0.0002 lb a.i./A for plants. The independent laboratory validated the method for analysis of primisulfuron-methyl at the LOQ and 10x LOQ in a sandy loam soil after one trial, with no major modifications to the method. However, the independent laboratory found the method was insufficiently rugged using a clay loam soil with resulting interferences and high background. The independent laboratory validated a modified method for primisulfuron-methyl at both fortification levels in the clay loam soil after replacing the HPLC/UV method with LC/MS/MS analysis and simplifying clean-up procedures. Syngenta submitted Analytical Method GRM070.02A to include the LC/MS/MS analysis method as optional for difficult soil matrices, but failed to conduct an internal validation of the LC/MS/MS method. In Analytical Method GRM070.02A, HPLC/UV analysis remains the primary method despite the ILV findings that severe background interferences were observed in both soil types with the HPLC/UV method, yet no significant interferences (<10% of LOQ) were observed with LC/MS/MS analysis of the clay loam soil. For the HPLC/UV method, primisulfuron-methyl is identified by retention time and quantified by peak height, with no confirmatory method.

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						
Primisulfuron-methyl	49447002 (Appendix 1, pp. 72-91) HPLC/UV method	49447002 HPLC/UV and LC/MS/MS methods		Soil ¹	26/02/1986	Syngenta Crop Protection, LLC	HPLC/UV LC/MS/MS	0.01 mg/kg
	49447001 HPLC/UV and LC/MS/MS methods, but no ECM validation data				11/07/2014			

¹ The ILV used sandy loam soil (19% clay, 4.2% organic matter) for the HPLC/UV method and clay loam soil (32% clay, 4.2% organic matter) for the LC/MS/MS method (Appendix 7, pp. 111-112 of MRID 49447002). The HPLC/UV method was insufficiently rugged with clay loam soil. The independent laboratory developed the LC/MS/MS method.

I. Principle of the Method

Soil (25 g) was fortified with primisulfuron-methyl (CGA136872) in acetonitrile for procedural recoveries (Appendix 1, pp. 80, 82). Uncharacterized soils from Mississippi, Nebraska, and New York were used for the validation (Appendix 1, p. 86). Soil samples (25 g) are extracted with 125 mL of acetonitrile:water:ammonium hydroxide (CH₃CN:H₂O:NH₄OH; 90:8:2, v:v:v) by shaking (mechanical shaker, speed not reported) for 1 hour (Appendix 1, pp. 78-80, Figure 1, p. 88). Soil and extract are separated by centrifugation (5,000 rpm, 10 minutes) and the extract filtered (Whatman 2V filter paper). A 25-mL aliquot (5-g equivalent) of the filtered extract is concentrated to aqueous (*ca.* 1-2 mL) by rotary evaporation (temperature not reported), reconstituted with 50 mL of 0.1M sodium carbonate (Na₂CO₃), and partitioned with 50 mL of toluene. The organic phase is discarded. The remaining aqueous phase is acidified to pH 2-3 with 10 mL of 1.2M phosphoric acid (H₃PO₄) and partitioned twice with methylene chloride (2 x 25 mL). Organic phases are combined, the solvent is removed by rotary evaporation (40-45°C), the residue is reconstituted in acetonitrile (5 mL), and then taken to dryness. The remaining residue is reconstituted in acetonitrile (5 mL) and applied to a Waters Alumina-A Sep-Pak solid phase extraction (SPE) cartridge pre-conditioned with acetonitrile:methanol (85:15, v:v) and acetonitrile. Primisulfuron-methyl is eluted with 15 mL of acetonitrile:methanol (85:15, v:v). The eluate is taken to dryness by rotary evaporation (temperature not specified) and the residues reconstituted in acetonitrile (0.5 mL, or multiple of 0.5 mL) for HPLC/UV analysis.

Samples are analyzed using a Perkin-Elmer Series 4 LC with a LC85B Variable Wavelength UV Detector (Table I, p. 84). The following HPLC conditions were used: Zorbax-ODS column (4.6 mm x 250 mm, column temperature ambient), isocratic mobile phase of acetonitrile:0.02M monopotassium phosphate:0.02M phosphoric acid (CH₃CN:0.02M KH₂PO₄:0.02M H₃PO₄, 65:28:7, v:v:v), and UV detection at 234 nm. Injection volume was 20 µL. Expected retention time for primisulfuron-methyl is *ca.* 5.2 ± 0.15 minutes. A confirmatory method was not used.

ILV: The test compound and two soil matrices (sandy loam, clay loam) were supplied by Syngenta (pp. 12-13). For the sandy loam soil, the independent laboratory performed the extraction method as written, except primisulfuron-methyl was eluted from the SPE cartridge with 30 mL of acetonitrile:methanol (85:15, v:v; pp. 13-15; Table 1, p. 21). For analysis of sandy loam soil

extracts, the following modifications to the LC/UV conditions were made: Agilent 1100 HPLC with UV detector, Phenomenex Luna C18 column (4.6 mm x 250 mm, 5 μ m), and an isocratic mobile phase of 60.5% acetonitrile to 39.5% buffer of 0.02M KH₂PO₄:0.02M H₃PO₄ (80:20, v:v). Approximate retention time was 8.76 minutes for primisulfuron-methyl.

For the clay loam soil, the independent laboratory found the HPLC/UV method was insufficiently rugged showing interferences and high background (p. 11). Therefore, the HPLC/UV analysis was replaced with LC/MS/MS and the phase-phase partitions of the soil extract and SPE clean-up steps were omitted (pp. 15-16; Table 2, p. 22). Soil is extracted with acetonitrile:water:ammonium hydroxide as described above, then, after centrifugation, a 5-mL aliquot is filtered (0.45 μ m syringe filter). A 0.5-mL aliquot of the filtered extract is diluted with 10 mL of 0.2M ammonium acetate:acetonitrile (90:10, v:v) for LC/MS/MS analysis. Samples are analyzed using an Agilent 1290 UPLC system and Agilent 6490 Triple Quad MS with ElectroSpray interface. The following LC conditions were used: Zorbax Eclipse Plus C18 column (2.1 mm x 50 mm, 1.8 μ m, column temperature 40°C), an isocratic mobile phase of 0.2M ammonium acetate in water:acetonitrile (ratio not reported; the updated ECM reported the ratio as 97:3, v:v; p. 16 of MRID 49447001). Injection volume was 10 μ L. The following MS/MS conditions were used: positive ion mode and multiple reaction monitoring (MRM; Figures 22-43, pp. 48-69). Primisulfuron-methyl is identified using one ion transition: *m/z* 469.1→253.9. Expected retention time was *ca.* 4.5 minutes. A confirmatory method was not used.

LOQ and LOD: In the ECM and ILV, the LOQ for primisulfuron-methyl using HPLC/UV was 0.01 mg/kg (ppm; pp. 11, 17; Appendix 1, p. 76). In the ECM, the LOD for primisulfuron-methyl using HPLC/UV was reported as 1.0 ng (lowest calibration standard injected; Appendix 1, pp. 80, 84; Figure 2, p. 89). In the ILV, the LOQ for primisulfuron-methyl using LC/MS/MS was 0.01 mg/kg (ppm; pp. 11, 17). LODs were not reported in the ILV.

II. Recovery Findings

ECM (MRID 49447002, Appendix 1, pp. 72-91; HPLC/UV): Only individual (per fortification level) procedural recoveries for soils from terrestrial field dissipation studies at three locations were reported to support validation of the ECM (Appendix 1, p. 83; Table III, p. 86). Therefore, statistics (mean, standard deviation, RSD) for the recovery results per fortification level and soil matrix could not be generated. All individual recovery results were within 70-120% at fortification levels of 0.01 mg/kg (LOQ), 0.05 mg/kg (5x LOQ), 0.20 mg/kg (20x LOQ) and 1.00 mg/kg (100x LOQ). Recovery results for soil fortified at 10x LOQ (0.10 mg/kg) were not reported. Primisulfuron-methyl was identified by retention time and quantified by peak height; a confirmatory method was not used (Appendix 1, Table II, p. 85; Figures 2-3, pp. 89-90). The soil matrices were not characterized.

ILV (MRID 49447002): Mean recoveries and relative standard deviations (RSDs) were within guidelines (mean 70-120%; RSD \leq 20%) for analysis of primisulfuron-methyl in a sandy loam soil using HPLC/UV and in a clay loam soil using LC/MS/MS at fortification levels of 0.01 mg/kg (LOQ) and 0.1 mg/kg (10x LOQ; Tables 5-6, pp. 25-26). The method was validated for primisulfuron-methyl at both fortification levels in the sandy loam soil using HPLC/UV after one trial, with minor modifications to the method (pp. 11, 14-15, 17). The HPLC/UV method was found to be insufficiently rugged using the clay loam soil (p. 11; Table 4, p. 24). Therefore, the method was validated for primisulfuron-methyl at both fortification levels in the clay loam soil after

replacing the HPLC/UV method with LC/MS/MS analysis and elimination of the phase-phase partition and SPE cleanup steps (pp. 11, 15, 17). Although "severe background interferences" were observed for the sandy loam soil using the HPLC/UV method, the sandy loam soil was not analyzed using the modified LC/MS/MS method (pp. 11, 18; Figures 9-20, pp. 35-46). The soils were characterized by Agvise Laboratories, Northwood, North Dakota (Appendix 7, pp. 111-112).

Table 2. Initial Validation Method Recoveries for Primisulfuron-methyl in Soil using HPLC/UV

Soil ¹	Fortification Level (mg/kg)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
Mississippi	0.01 (LOQ)	1	88	-- ²	--	--
	0.05	1	87	--	--	--
	0.20	1	95	--	--	--
	1.00	1	94	--	--	--
Nebraska	0.01 (LOQ)	1	101	--	--	--
	0.05	1	89	--	--	--
	0.20	1	89	--	--	--
	1.00	1	91	--	--	--
New York	0.01 (LOQ)	1	86	--	--	--
	0.05	1	77	--	--	--
	0.20	1	72	--	--	--
	1.00	1	94	--	--	--

Data (recovery results) were obtained from Appendix 1, Table III, p. 86. The study authors reported that "At a screening level of 0.01 ppm, no residues were found in any of the control samples." (Appendix 1, p. 83).

1 Soil characterizations were not reported.

2 Not applicable, n = 1.

Table 3a. Independent Validation Method Recoveries for Primisulfuron-methyl in Sandy Loam Soil using HPLC/UV

Soil ¹	Fortification Level (mg/kg)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
Sandy Loam	0.01 (LOQ)	5	104-122	114	7.7	6.8
	0.10	5	97-104	102	2.8	2.8

Data (uncorrected recovery results) were obtained from Table 6, p. 26; Appendix 5, pp. 105-106.

1 USDA classification (Appendix 7, p. 112).

Table 3b. Independent Validation Method Recoveries for Primisulfuron-methyl in Clay Loam Soil using LC/MS/MS

Soil ¹	Fortification Level (mg/kg)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
Clay Loam	0.01 (LOQ)	5	81-86	84	2.0	2.3
	0.10	5	92-94	93	1.0	1.1

Data (corrected recovery results) were obtained from Table 5, p. 25; Appendix 5, p. 107.

1 USDA classification (Appendix 7, p. 111).

III. Method Characteristics

In the ECM and ILV, the LOQ for primisulfuron-methyl in soil was 0.01 mg/kg (ppm; pp. 11, 17; Appendix 1, p. 76 of MRID 49447002; p. 21 of MRID 49447001). The updated ECM defined the LOQ as the lowest analyte concentration at which the methodology has been validated and a mean recovery of 70-110% and RSD of $\leq 20\%$ has been obtained. The updated ECM defined the LOD as the lowest analyte concentration detectable above the mean amplitude of the background noise in an untreated matrix control sample at the corresponding retention time and an estimate of the LOD can be taken as three times the background noise. The updated ECM did not specify LODs for either the HPLC/UV or LC/MS/MS method. For the original ECM HPLC/UV validation, the LOD for primisulfuron-methyl was 1.0 ng (lowest calibration standard injected; Appendix 1, pp. 80, 84; Figure 2, p. 89 of MRID 49447002). LODs were not reported in the ILV.

Table 4. Method Characteristics for Primisulfuron-methyl in Soil

		HPLC/UV	LC/MS/MS
Limit of Quantitation (LOQ)		0.01 mg/kg	0.01 mg/kg
Limit of Detection (LOD)		1.0 ng (0.05 ng/ μ L) injected.	Not reported.
Linearity (calibration curve r^2 and concentration range)	ECM: ¹	$r^2 = 0.99990$	Not performed.
	ILV:	$r^2 = 0.99991$	$r^2 = 0.99882590$
	Range:	0.05-2.0 ng/ μ L (1.0-40.0 ng)	0.01-5.0 pg/ μ L
Repeatable	ECM:	Undetermined, n = 1 at all fortification levels.	Not performed.
	ILV:	Yes at LOQ and 10x LOQ (sandy loam soil).	Yes at LOQ and 10x LOQ (clay loam soil).
Reproducible		Yes.	Analysis method developed by independent laboratory. Internal validation of LC/MS/MS method not performed by Syngenta.
Specific	ECM:	Chromatograms for only one (NE) of three soils (MS, NE, NY; all uncharacterized). Chromatogram of NE soil control showed significant matrix interference. No confirmatory method.	Not performed.
	ILV:	"Severe background interferences were observed". No confirmatory method.	Interferences were <10% of the LOQ (based on mean peak area at LOQ). ²

Data were obtained from p. 21 of MRID 49447001; p. 18; Figure 1, p. 27; Figures 8-15, pp. 34-41; Figure 21, p. 47; Figures 31-38, pp. 57-64; Appendix 1, p. 76; Tables I-III, pp. 84-86; Figure 3, p. 90 of MRID 49447002.

Linearity is satisfactory when $r^2 \geq 0.995$.

1 ECM coefficient of determination (r^2) value is reviewer-generated from reported correlation coefficient (r) value (Appendix 1, Table II, p. 85 of MRID 49447002; DER Attachment 2).

2 A confirmatory method was not used; however, a confirmatory method is typically not required where GC/MS and LC/MS methods are used as the primary method.

IV. Method Deficiencies and Reviewer's Comments

1. MRID 49447001 was submitted by the registrant, Syngenta, as Analytical Method GRM070.02A to update Method No. AG-498 and implement significant modifications to the original ECM (AG-498) as recommended by an independent laboratory (ADPEN Laboratories; p. 9 of MRID 49447001). However, all of the recovery results and chromatograms presented in MRID 49447001 are data generated by ADPEN Laboratories as part of the ILV of Method No. AG-498 (MRID 49447002). The author, Kaijun Lin, of the updated ECM report was the study monitor for the ILV (Appendix 6, p. 108 of MRID 49447002). The original ECM, Method No. AG-498, with validation data, is appended to the ILV study report (Appendix 1, pp. 72-91 of MRID 49447002).

The independent laboratory validated the method for primisulfuron-methyl at both fortification levels in a sandy loam soil using HPLC/UV after one trial, with minor modifications to the method (pp. 11, 14-15, 17 of MRID 49447002). The modifications were as follows: primisulfuron-methyl was eluted from the SPE cartridge with 30 mL of acetonitrile:methanol (85:15, v:v), an Agilent 1100 HPLC with UV detector was used, a Phenomenex Luna C18 column (4.6 mm x 250 mm, 5 μ m) was used, and the isocratic mobile phase was 60.5% acetonitrile to 39.5% buffer of 0.02M KH_2PO_4 :0.02M H_3PO_4 (80:20, v:v; pp. 13-15; Table 1, p. 21). These modifications are not considered substantial changes to the HPLC/UV method.

For the clay loam soil, the independent laboratory found the HPLC/UV method was insufficiently rugged showing interferences and high background (p. 11 of MRID 49447002). Therefore, the HPLC/UV analysis was replaced with LC/MS/MS and the phase-phase partitions of the soil extract and SPE clean-up steps were omitted (pp. 15-16; Table 2, p. 22). The independent laboratory successfully validated the LC/MS/MS method using clay loam soil. These modifications are considered substantial changes to the method.

Syngenta submitted the updated ECM report (MRID 49447001) to include the LC/MS/MS analysis method as optional, but failed to conduct an internal validation of the LC/MS/MS method. In addition, in the updated ECM report, HPLC/UV analysis remains the primary method despite the ILV findings that "Severe background interferences were observed in both soil types..." with the HPLC/UV method, yet no significant interferences (<10% of LOQ) were observed with the LC/MS/MS method using the clay loam soil (p. 18; Figures 8-15, pp. 34-41; Figures 31-38, pp. 57-64 of MRID 49447002).

2. For the ECM HPLC/UV validation, only a single procedural recovery ($n = 1$) was reported for each fortification level [0.01 (LOQ), 0.05, 0.20, 1.00 ppm] in each soil matrix, and no fortifications were reported at $10\times$ LOQ (Appendix 1, Table III, p. 86 of MRID 49447002).
3. The determination of the LOQ and LOD were not based on scientifically acceptable procedures as defined in 40 CFR Part 136, Appendix B. The updated ECM defined the LOQ as the lowest analyte concentration at which the methodology has been validated and a mean recovery of 70-110% and RSD of $\leq 20\%$ has been obtained (p. 21 of MRID 49447001). The updated ECM defined the LOD as the lowest analyte concentration detectable above the mean amplitude of the background noise in an untreated matrix control sample at the corresponding retention time and an estimate of the LOD can be taken as three times the background noise. The updated ECM did not specify LODs for either the

HPLC/UV or LC/MS/MS method. For the original ECM HPLC/UV validation, the LOD for primisulfuron-methyl was 1.0 ng (lowest calibration standard injected; Appendix 1, pp. 80, 84; Figure 2, p. 89 of MRID 49447002). LODs were not reported in the ILV.

Detection limits should not be based on the arbitrarily selected lowest concentration in the spiked samples. Additionally, the lowest toxicological level of concern in soil was not reported. An LOQ above toxicological levels of concern results in an unacceptable method classification.

4. For the "primary" HPLC/UV method, primisulfuron-methyl is identified by retention time and quantified by peak height, and a confirmatory method is not used (pp. 15-16; Appendix 1, p. 45 of MRID 49447001).

For the "optional" LC/MS/MS method, primisulfuron-methyl is identified using one ion pair transition, and a confirmatory method is not used (pp. 16-17; Appendix 2, p. 46 of MRID 49447001). Typically, a confirmatory method is not required where GC/MS and/or LC/MS methods are used as the primary method(s) to generate study data.

5. For the ILV, HPLC/UV analysis recovery results were uncorrected, but the LC/MS/MS analysis recovery results were corrected for residues in the matrix controls (Appendix 4, p. 101; Appendix 5, pp. 105-107 of MRID 49447002).
6. Characterizations for the soils used for the ECM validation of the HPLC/UV method were not reported. The soils were from terrestrial field dissipation studies conducted in Mississippi, Nebraska, and New York (Appendix 1, pp. 83; Table III, p. 86 of MRID 49447002). The purity of the test compound used was not specified, only described as "Standard CGA-136872" (Appendix 1, p. 78).
7. For the ILV, the 0.2M ammonium acetate in water:acetonitrile isocratic mobile phase ratio was not reported (p. 16 of MRID 49447002). In the updated ECM, the isocratic mobile phase ratio was reported as 97:3 (v:v; p. 16 of MRID 49447001).
8. For the ECM HPLC/UV validation, a reagent blank chromatogram, Nebraska soil spiked sample at 10x LOQ, and chromatograms for the Mississippi and New York soil matrices were not provided. Individual calibration standard data with regression curve analysis were provided, but a plot of the standard curve was not provided (Appendix 1, Table II, p. 85 of MRID 49447002). The chromatogram of LOQ spiked Nebraska soil sample showed the primisulfuron-methyl peak was barely attenuated above baseline noise (Appendix 1, Figure 3, p. 90).

In the updated ECM, the study author reported that "No significant matrix effects were observed in the soil types tested..." (p. 21 of MRID 49447001). However, for the original ECM validation using HPLC/UV analysis, a chromatogram of the Nebraska soil control showed significant matrix interference (Appendix 1, Figure 3, p. 90 of MRID 49447002). Chromatograms of matrix controls for the other two soil matrices (Mississippi, New York) used to validate the ECM HPLC/UV method were not provided, and Syngenta did not provide validation data for the updated LC/MS/MS method developed by the independent laboratory.

9. The original ECM HPLC/UV method was used in terrestrial dissipation studies (Appendix 1, p. 83 of MRID 49447002). However, insufficient information was provided to determine if the LOQ is less than 10% of the expected or actual peak concentration of the test compound in the field.
10. The following typographical error was noted in the updated ECM report, section **8.1 Matrix** (p. 20 of MRID 49447001): "No significant matrix effects were observed in the water types tested..." should read "in the soil types tested...".
11. It was reported for the ILV that a single analyst can complete a set of thirteen samples (one reagent blank, two matrix controls, and ten fortified samples) in two working days for the HPLC/UV procedure and in one day for the LC/MS/MS procedure, with instrument analysis performed overnight (p. 18 of MRID 49447002).

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.
- 40 CFR Part 136. Appendix B. Definition and Procedure for the Determination of the Method Detection Limit-Revision 1.11, pp. 317-319.

Attachment 1: Chemical Names and Structures**Primisulfuron-methyl (CGA-136872)**

IUPAC Name: Methyl 2-[4,6-bis(difluoromethoxy)pyrimidin-2-yl]carbamoylsulfamoyl]benzoate.
2-{3-[4,6-Bis(difluoromethoxy)-pyrimidin-2-yl]-ureidosulfonyl} benzoic acid methyl ester.

CAS Name: Methyl 2-[[[[[4,6-bis(difluoromethoxy)-2-pyrimidinyl]amino]carbonyl]amino]sulfonyl]benzoate.
Benzoic acid, 2-[[[[[4,6-bis(difluoromethoxy)-2-pyrimidinyl]amino]carbonyl]amino]sulfonyl]-, methyl ester.

CAS Number: 86209-51-0

SMILES String: COC(=O)c1ccccc1S(=O)(=O)NC(=O)Nc2nc(OC(F)F)cc(OC(F)F)n2

