Analytical method for fluthiacet-methyl and its metabolites CGA-300402, CGA-300403, CGA-300404, CGA-327066, CGA-327067, CGA-330057, and CGA-330059 in soil

Reports:	ECM: EPA MRID No.: Syngenta No. 122-99. Chamkasem, N. 2001. Analytical Method for Determination of CGA-248757 and Its Degradates CGA-300402, CGA-300403, CGA-300404, CGA-327066, CGA-327067, CGA-330057, and CGA-330059 in Soil by High Performance Liquid Chromatography with Mass Spectrometric Detection. Syngenta Laboratory Study ID No. 122-99. Report prepared, sponsored, and submitted by Syngenta Crop Protection, LLC, Greensboro, North Carolina; 116 pages. Final report issued March 22, 2001.
Document No.: Guideline:	ILV: EPA MRID No. 50193201. Mannella, L. 2016. Independent Laboratory Validation of Analytical Methods for the Determination of Fluthiacet-methyl and Seven Metabolites in Soil and Water. EAG Project No. 2812W. FMC Tracking No. 2015AMT-FLU2297. Report prepared by EAG Laboratories-Hercules (Formerly doing business as PTRL West), Hercules, California, sponsored and submitted by FMC Corporation, Ewing, New Jersey; 226 pages. Final report issued November 2, 2016. Syngenta No. 122-99 & MRID 50193201 850.6100
Statements:	ECM: The study was conducted in accordance with the USEPA FIFRA Good Laboratory Practice (GLP) standards, with the exception that the company Syngenta Crop Protection resulted from the spin-off of Novartis' AG Agribusiness and its subsequent merger with Zeneca Agrochemcials (40 CFR Part 160; p. 3 of Syngenta No. 122-99). Signed and dated No Data Confidentiality, GLP, Quality Assurance and Authenticity statements were provided (pp. 2-3, 5, 26).
	ILV: The study was conducted in accordance with the USEPA FIFRA GLP standards (40 CFR Part 160; p. 3, 6 of MRID 50193201). Signed and dated No Data Confidentiality, GLP and Quality Assurance statements were provided (pp. 2-4). A certification of authenticity was included with the Quality Assurance statement.
Classification:	This analytical method is classified as ACCEPTABLE for CGA-248757 (fluthiacet-methyl, parent), CGA-300402, CGA-300403, CGA-300404, and CGA-330057 and UNACCEPTABLE for CGA-327066, CGA-327067 and CGA-330059 as the ILV did not support the LOQ/LOD (i.e., the single to noise at LOQ/LOD and 10x LOQ/LOD was too low). Significant matrix effects were observed, therefore matrix-matched standards must be used in application of this method. The study was not conducted to establish a true LOQ or LOD rather to confirm detection at specified value (i.e., reporting level). ILV did not support the LOQ/LOD for CGA-327066, CGA-327067 and CGA-330059. ILV linearity was not satisfactory for CGA-330059; ECM linearity was not satisfactory for the quantitation ion calibration curves of CGA-327067 and CGA-330059.

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

Executive Summary

The analytical method, Syngenta Report No. 122-99, is designed for the quantitative determination of fluthiacet-methyl and its seven metabolites CGA-300402, CGA-300403, CGA-300404, CGA-327066, CGA-327067, CGA-330057, and CGA-330059 in soil at the LOQ of 0.05 µg/kg using LC/MS/MS. The study was not conducted to establish a true LOQ or LOD rather to confirm detection at specified value (i.e., reporting level). The LOQ was defined as the lowest concentration fortified in the control samples which yielded adequate recovery, and the LOD was defined as lowest amount of the standard injected. The LOQ (0.0001 lbs/A field equivalent¹) is equal to the lowest toxicological level of concern in soil $(0.00017 \text{ lbs/A}^2)$. The ECM validated the method using characterized loam and sandy loam soil; the ILV validated the method for all analytes using characterized sandy loam soil. It could not be determined if the ILV sandy loam soil matrix was representative of TFD test soils due to lack of TFD information. The ILV validated the method for all analytes at both fortification levels after the second trial, with insignificant sample processing and analytical method modifications. The difference between the first and second trial was that the volume of acetonitrile was 9 mL in the first trial and 7 mL in the second trial. In the first trial, several individual and mean recoveries were <70%. Only one ion transition was monitored in the ECM while two ion transitions were monitored in the ILV for all analytes, except for CGA-300403. A confirmatory method is typically not required where GC/MS and/or LC/MS methods are used as the primary method. Based on the quantitation ion results, all ECM and ILV data was satisfactory regarding accuracy and precision, except for ECM performance data for CGA-300403 in one soil. ILV linearity was satisfactory for all analytes, except CGA-330059; ECM linearity was satisfactory for all analytes, except one soil each of CGA-300403, CGA-327067, and CGA-330059. However, ILV representative chromatograms did not support the LOQ/LOD for CGA-327066, CGA-327067 and CGA-330059 due to significant baseline noise or contaminants which prevented analyte

¹ Calculated using the equation: LOQ equivalent field detection = (LOQ)(soil depth)(soil density).

Where the soil depth was assumed to be 0.15 m and the soil density was assumed to be 1500 kg/m^3 .

² Terrestrial plant EC_{25} for dicot vegetative vigor studies.

peak distinction and resolution.

	MR	ID						Limit of
Analyte(s) by Pesticide ¹	Environment al Chemistry Method	Independen t Laboratory Validation	EPA Review	Matri x	Method Date (dd/mm/yyy y)	Registrant	Analysis	Quantitatio n (LOQ)
Fluthiacet -methyl (CGA- 248757) CGA- 300402 CGA- 300403 CGA- 300404 CGA- 327066 CGA- 327067 CGA- 330057 CGA- 330059	Syngenta No. 122-99	50193201	ACCEPTABLE for CGA-248757 (fluthiacet- methyl, parent), CGA-300402, CGA-300403, CGA-300404, and CGA-330057 and UNACCEPTABL E for CGA- 327066, CGA- 327067 and CGA- 330059 4/22/2021	Soil ^{2,3}	22/03/2001	FMC Corporatio n	LC/MS/M S	0.05 µg/kg

Table 1. Analytical Method Summary

1 Fluthiacet-methyl = [[2-Chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1ylidene)amino]phenyl]thio]-methyl ester acetic acid; CGA-300402 = [[2-Chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1-ylidene)amino]phenyl]thio]-acetic acid; CGA-300403 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1-oxo-3-thioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2(3H)-yl)phenyl]thio]-acetic acid; CGA-300404 = [[2-Chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1ylidene)amino]phenyl]sulfinyl]-acetic acid; CGA-327066 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl)phenyl]thio]-acetic acid; CGA-327067 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl)phenyl]sulfinyl]-acetic acid; CGA-330057 = Methyl ester [[2-chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H-3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1ylidene)amino]phenyl]sulfinyl]-acetic acid; and CGA-330059 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1-oxo-3thioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2(3H)-yl)phenyl]sulfinyl]-acetic acid; cGA-30057 = Methyl ester [[2-chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H-3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1ylidene)amino]phenyl]sulfinyl]-acetic acid; and CGA-330059 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1-oxo-3thioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2(3H)-yl)phenyl]sulfinyl]-acetic acid.

- 2 In the ECM, Dundee loam soil (41% sand 50% silt 9% clay, pH 7.4, 1.1% organic matter) and Hanford sandy loam soil (61% sand 32% silt 7% clay, pH 7.4, 0.6% organic matter) were used in the study (USDA soil texture classification; Table 1, p. 27 of Syngenta No. 122-99). The soil sources and characterization laboratory were not reported.
- 3 In the ILV, the sandy loam soil (Sample ID: 2705W-033; 65% sand 27% silt 8% clay, pH 5.5 in 1:1 soil:water ratio, 0.96% organic matter) was obtained from Hickman, California, and characterized by Agvise Laboratories, Northwood, North Dakota (USDA soil texture characterization; p. 22; Appendix C, p. 213 of MRID 50193201).

I. Principle of the Method

Syngenta Report No. 122-99

Soil $(20 \pm 0.1 \text{ g})$ was weighed into a centrifugable polyallomer bottle and fortified with a mixed standard solution of fluthiacet-methyl (CGA-248757) and its seven metabolites in acetonitrile:0.05 M ammonium acetate in water, pH 5 (10:90, v:v) for procedural recoveries (pp. 10-15, 19-20 of Syngenta No. 122-99). The samples were extracted with acetonitrile:0.05 M ammonium acetate in water (50:50, v:v) via vigorous shaking for ca. 15 seconds then shaking on an orbital shaker for ca. 1 hours at room temperature. After centrifugation (ca. 8000 rpm for 8 minutes), the supernatant was decanted into a 100-mL graduated cylinder containing 2 drops of ammonium hydroxide. A Mega Bond Elut SAX Solid Phase Extraction (SPE) column (1 g/6 mL) was pre-conditioned with 10 mL of acetonitrile:0.05 M ammonium acetate in water (50:50, v:v; with 25 µL of ammonium hydroxide for each 50 mL of solvent). The column should not be allowed to run dry. An aliquot (80 mL) of the decanted extract was transferred into a 75-mL plastic reservoir on top of the SAX column and allowed to pass through the SPE column into a 150-mL beaker containing 50 µL of acetic acid. The SPE column was rinsed twice with ca. 5-10 mL of acetonitrile:0.05 M ammonium acetate in water (50:50, v:v; with 25 µL of ammonium hydroxide for each 50 mL of solvent), starting at the reservoir. The eluate and rinsates were combined and transferred to a 250-mL round bottom flask using methanol. The acetonitrile was removed from the sample via rotary evaporator at a water bath temperature of 20-30°C. The sample was diluted with 20 mL of 0.05 M ammonium acetate, pH 5, then applied to a Nexus Abselut column (1 g, 6 mL; pre-conditioned with 6 mL of methanol followed by 10 mL of 0.05 M ammonium acetate, pH 5). The column should not be allowed to run dry. The sample flask was rinsed with 2 x 5 mL of 0.05 M ammonium acetate, pH 5, which was applied to the column. The analytes were eluted from the column using *ca*. 12 mL acetonitrile into a 50-mL concentration tube calibrated to 5.0 mL. The calibration was done by adding 5.0 mL of 0.05 M ammonium acetate, pH 5, in water and marking the line with a waterproof fine-pointed pen. 0.5 mL of the 0.05 M ammonium acetate, pH 5, in water was added as a "water trap". The method noted that CGA-248757 has been found to irreversibly bind to glassware when taken to dryness by rotary evaporation. The acetonitrile was removed from the sample until ca. 0.5 mL remains via rotary evaporator at a water bath temperature of ca. 25-30°C. 500 µL of acetonitrile was added to the residue and vortex-mixed for ca. 1 min. The residue was diluted to 5 mL with 0.05 M ammonium acetate, pH 5, and vortex-mixed for *ca*. 30 seconds then sonicated for *ca*. 1 min. High-concentration samples were diluted, as necessary. Samples were analyzed by LC/MS/MS. The method noted that all laboratory equipment and glassware should be thoroughly cleaned prior to use. Additionally, several statements were made which indicated that the use of different soil matrices, laboratory SPE columns and LC/MS/MS instruments could require optimization of the method parameters.

A Method Flow Diagram was included (Figure 2, p. 66 of Syngenta No. 122-99).

Samples were analyzed using a Waters 2690 HPLC system and a Micromass Quattro Ultima MS with Ion-Spray interface (pp. 12, 15-17; Table 2, pp. 28-30 of Syngenta No. 122-99). The following LC conditions were used: An Upchurch (A-318) pre-column filter ($0.5 \mu m$), Phenomenex C-18 guard column, Develosil RPAQUEOUS-3 column (3.0 mm x 150 mm, 3 μm ,

column temperature 30°C), mobile phase of (A) 0.1% acetic acid in acetonitrile and (B) 0.1% acetic acid in water [percent A:B (v:v) at 0 min. 10:90, 20 min. 70:30, 23-25 min. 100:0, 25.1-32 min. 10:90], and injection volume of 50 µL. The following MS/MS conditions were used: positive electrospray ionization mode and multiple reaction monitoring (MRM). Analytes were identified using one ion pair transition as follows: m/z 404→404 for fluthiacet-methyl (CGA-248757), m/z 390→390 for CGA-300402, m/z 390→344 for CGA-300403, m/z 406→347 for CGA-300404, m/z 374→356 for CGA-327066, m/z 390→330 for CGA-327067, m/z 420→347 for CGA-330057, and m/z 406→346 for CGA-330059. Expected retention times are *ca*. 20.9, 17.5, 14.1, 12.7, 11.8, 7.9, 16.5, and 10.1 minutes for fluthiacet-methyl (CGA-330057, and CGA-3300402, CGA-300403, CGA-300404, CGA-327066, CGA-327067, CGA-330057, and CGA-330059, respectively.

ILV

The independent laboratory performed the ECM as written, except that a different Nexus column [Agilent Nexus SPE (0.5 g/12 mL)] was used, 7 mL of acetonitrile instead of 12 mL was used to elute the analytes from the Nexus column, matrix-based calibration standard solutions were used, and insignificant analytical method modifications (pp. 21, 23, 31-34, 48 of MRID 50193201). An Agilent 1260 Series HPLC system and AB Sciex API 5500 Series Triple Quad MS was used. All LC and MS parameters were the same as the ECM, except that a confirmatory ion transition was also monitored for each analyte as follows: m/z 404 \rightarrow 404 (Q) and m/z 404 \rightarrow 344.1 (C) for fluthiacet-methyl (CGA-248757), m/z 390 \rightarrow 390 (Q) and m/z 390 \rightarrow 260 (C) for CGA-300402, m/z 390 \rightarrow 344 (Q) and m/z 390 \rightarrow 390 (C) for CGA-300403, m/z 406 \rightarrow 347 (Q) and m/z 406 \rightarrow 362 (C) for CGA-300404, m/z 374 \rightarrow 356 (Q) and m/z 374 \rightarrow 328 (C) for CGA-327066, m/z 390 \rightarrow 330 (Q) and m/z 390-314 (C) for CGA-327067, m/z 420-347 (Q) and m/z 420-217 (C) for CGA-330057, and m/z 406 \rightarrow 346 (Q) and m/z 406 \rightarrow 344 (C) for CGA-330059 (the quantitation ion transitions were the same as the only monitored ion transitions of the ECM). Approximate retention times were 20.7, 17.5, 14.1, 13.1, 11.9, 8.2, 16.4, and 10.4 minutes for fluthiacetmethyl (CGA-248757), CGA-300402, CGA-300403, CGA-300404, CGA-327066, CGA-327067, CGA-330057, and CGA-330059, respectively. The ILV modifications did not warrant an updated ECM.

LOQ and LOD

In the ECM and ILV, Limit of Quantification (LOQ) for fluthiacet-methyl (CGA-248757), CGA-300402, CGA-300403, CGA-300404, CGA-327066, CGA-327067, CGA-330057, and CGA-330059 in soil was 0.05 μ g/kg (pp. 9, 22, 25 of Syngenta No. 122-99; pp. 42, 45 of MRID 50193201). The Limit of Detection (LOD) for all analytes in soil was 4 pg (the lowest amount of standard injected; 0.00008 ng/µL calibration standard) in the ECM and 0.015 μ g/kg (30% of the LOQ) in the ILV.

II. Recovery Findings

ECM (Syngenta No. 122-99): For Syngenta Method No. 122-99, mean recoveries and relative standard deviations (RSD) were within guideline requirements (mean 70-120%; RSD \leq 20%) for analysis of fluthiacet-methyl and its transformation products CGA-300402, CGA-300403, CGA-300404, CGA-327066, CGA-327067, CGA-330057, and CGA-330059 in two soil matrices at fortification levels of 0.05 µg/kg (LOQ), 0.5 µg/kg (10×LOQ), and 5 µg/kg (100×LOQ), except for CGA-300403 in Hanford sandy loam soil at the LOQ, mean 67% (n = 4 for all analyses; Appendix I, pp. 109-116; DER Attachment 2). One ion pair transition was monitored for each analyte; a confirmatory method is typically not required where GC/MS and/or LC/MS methods are used as the primary method. Standard deviations and RSDs were reviewer-calculated based on data provided in the study report since the study author only provided overall statistics for the combined fortification data. Dundee loam soil (41% sand 50% silt 9% clay, pH 7.4, 1.1% organic matter) and Hanford sandy loam soil (61% sand 32% silt 7% clay, pH 7.4, 0.6% organic matter) were used in the study (USDA soil texture classification; Table 1, p. 27). The soil sources and characterization laboratory were not reported.

ILV (MRID 50193201): For Syngenta Method No. 122-99, mean recoveries and RSDs were within guidelines for analysis for analysis of fluthiacet-methyl (CGA-248757) and its transformation products CGA-300402, CGA-300403, CGA-300404, CGA-327066, CGA-327067, CGA-330057, and CGA-330059 in one soil matrix at fortification levels of 0.05 µg/kg (LOQ) and 0.5 µg/kg (10×LOQ), except for the confirmation ion analysis of CGA-327067 (LOQ: mean 55% RSD 47%; 10×LOQ: mean 47% RSD 45%; Table IV, pp. 64-71). Except for CGA-300403, analytes were identified and quantified using two ion transitions; quantitation ion and confirmation ion recovery results were comparable. CGA-300403 was identified and quantified using one ion pair transition; a confirmatory method is typically not required where GC/MS and/or LC/MS methods are used as the primary method. The reviewer noted that the unsatisfactory or absence of the confirmatory analysis did not affect the validity of the method since a confirmatory method is typically not required where GC/MS and/or LC/MS methods are used as the primary method. The sandy loam soil (Sample ID: 2705W-033; 65% sand 27% silt 8% clay, pH 5.5 in 1:1 soil:water ratio, 0.96% organic matter) was obtained from Hickman, California, and characterized by Agvise Laboratories, Northwood, North Dakota (USDA soil texture characterization; p. 22; Appendix C, p. 213). The method was validated for all analytes at both fortification levels in sandy loam soil after the second trial, with the following modifications: different Nexus column [Agilent Nexus SPE (0.5 g/12 mL)] was used, 7 mL of acetonitrile instead of 12 mL was used to elute the analytes from the Nexus column, matrixbased calibration standard solutions were used, and insignificant analytical method modifications (pp. 21, 23, 31-34, 44-45, 48). The difference between the first and second trial was that the volume of acetonitrile was 9 mL in the first trial and 7 mL in the second trial. In the first trial, several individual and mean recoveries were <70% (Appendix D, pp. 215-222).

Table 2. Initial Validation Method Recoveries for Fluthiacet-methyl (CGA-248757) and ItsTransformation Products CGA-300402, CGA-300403, CGA-300404, CGA-327066, CGA-327067, CGA-330057, and CGA-330059 in Soil^{1,2}

Analyte ³	Fortification		Recovery Range (%)	Mean	Standard Deviation (%) ⁴	Relative Standard Deviation (%)⁴
	Level (µg/kg)	of rests	•	Indee Loam Soi		Deviation (76)
	0.05	4	80-117	92		19
Fluthiacet-methyl	0.05	4	77-97	92 88	17 8	19
(CGA-248757)	5.0		87-94	<u>88</u> 91	8	
		4				4
CC A 200402	0.05	4	79-103	94	11	12
CGA-300402	0.5	4	77-95	87	7	9
	0.05	4	72-80	80 73	5	8
CC A 200402		4				6
CGA-300403	0.5	4	81-95	89	6	7 4
	5.0	4	83-90	86	4 7	
CC A 200404	0.05	4	61-78	71		10
CGA-300404	0.5	4	75-82	79	3	4
	5.0	4	79-85	82	3	4
GG 1 227044	0.05	4	80-97	88	7	8
CGA-327066	0.5	4	95-108	100	6	6
	5.0	4	81-88	86	3	4
	0.05	4	91-103	98	6	6
CGA-327067	0.5	4	77-100	89	10	11
	5.0	4	87-94	90	3	3
	0.05	4	88-96	93	3	4
CGA-330057	0.5	4	92-98	96	3	3
	5.0	4	97-101	99	2	2
	0.05	4	86-122	96	18	19
CGA-330059	0.5	4	69-89	83	9	11
	5.0	4	84-94	90	4	5
			Hanfo	rd Sandy Loam	Soil	
	0.05	4	78-96	88	8	9
Fluthiacet-methyl	0.5	4	90-95	92	2	3
(CGA-248757)	5.0	4	90-99	94	4	4
	0.05	4	83-112	94	14	15
CGA-300402	0.5	4	80-87	84	3	4
	5.0	4	89-94	92	2	2
	0.05	4	58-72	67	6	10
CGA-300403	0.5	4	79-87	83	3	4
2011 200 102	5.0	4	85-93	90	4	4
	0.05	4	70-77	75	3	4
CGA-300404	0.5	4	80-83	82	1	2
	5.0	4	84-88	86	2	2
	0.05	4	77-104	92	12	13
			,, 101	/4		15
CGA-327066	0.5	4	89-93	91	2	2

Analyte ³	Fortification Level (µg/kg)		Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%) ⁴	Relative Standard Deviation (%) ⁴
	0.05	4	76-101	89	13	14
CGA-327067	0.5	4	88-102	97	6	6
	5.0	4	85-100	93	7	7
	0.05	4	92-97	94	2	2
CGA-330057	0.5	4	95-103	98	4	4
	5.0	4	93-98	96	2	2
	0.05	4	67-81	76	6	8
CGA-330059	0.5	4	69-90	81	9	11
	5.0	4	88-97	94	4	4

Data (recovery results were corrected when residues were quantified in the controls; pp. 20-21) were obtained from Appendix I, pp. 109-116 of Syngenta No. 122-99 and DER Attachment 2.

1 The Dundee loam soil (41% sand 50% silt 9% clay, pH 7.4, 1.1% organic matter) and Hanford sandy loam soil (61% sand 32% silt 7% clay, pH 7.4, 0.6% organic matter) were used in the study (USDA soil texture classification; Table 1, p. 27). The soil sources and characterization laboratory were not reported.

- 2 Analytes were identified using one ion pair transition as follows: $m/z \ 404 \rightarrow 404$ for fluthiacet-methyl (CGA-248757), $m/z \ 390 \rightarrow 390$ for CGA-300402, $m/z \ 390 \rightarrow 344$ for CGA-300403, $m/z \ 406 \rightarrow 347$ for CGA-300404, $m/z \ 374 \rightarrow 356$ for CGA-327066, $m/z \ 390 \rightarrow 330$ for CGA-327067, $m/z \ 420 \rightarrow 347$ for CGA-330057, and $m/z \ 406 \rightarrow 346$ for CGA-330059.
- $3 \ Fluthiacet-methyl = [[2-Chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1-ylidene)amino]phenyl]thio]-methyl ester acetic acid; CGA-300402 = [[2-Chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1-ylidene)amino]phenyl]thio]-acetic acid; CGA-300403 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1-oxo-3-thioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2(3H)-yl)phenyl]thio]-acetic acid; CGA-300404 = [[2-Chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1-ylidene)amino]phenyl]sulfinyl]-acetic acid; CGA-327066 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl)phenyl]thio]-acetic acid; CGA-327067 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl)phenyl]sulfinyl]-acetic acid; CGA-330057 = Methyl ester [[2-chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H-3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1-ylidene)amino]phenyl]sulfinyl]-acetic acid; and CGA-330059 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl)phenyl]sulfinyl]-acetic acid; and CGA-330059 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1-oxo-3-thioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-1-ylidene)amino]phenyl]sulfinyl]-acetic acid; and CGA-330059 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1-oxo-3-thioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl)phenyl]sulfinyl]-acetic acid.$
- 4 Standard deviations and relative standard deviations were reviewer-calculated based on data provided in the study report since the study author only provided overall statistics for the combined fortification data (see DER Attachment 2).

Table 3. Independent Validation Method Recoveries for Fluthiacet-methyl (CGA-248757) and Its Transformation Products CGA-300402, CGA-300403, CGA-300404, CGA-327066, CGA-327067, CGA-330057, and CGA-330059 in Soil^{1,2}

Analyte ³	Fortification Level (µg/kg)			Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
		of resus	5, 5	andy Loam Soil	Deviation (70)	Deviation (70)
				Quantitation Ion		
Fluthiacet-methyl	0.05 (LOQ)	5	80-106	90	12	13
(CGA-248757)	0.5	5	74-102	84	11	13
, , ,	0.05 (LOQ)	44	88-101	93	6	6
CGA-300402	0.5	5	70-81	75	5	7
	0.05 (LOQ)	5	73-87	79	7	9
CGA-300403	0.5	5	70-97	82	10	12
	0.05 (LOQ)	5	81-100	87	8	9
CGA-300404	0.5	5	85-108	92	10	11
	0.05 (LOQ)	5	61-114	91	20	22
CGA-327066	0.5	5	91-110	98	10	10
001 0070/7	0.05 (LOQ)	5	101-118	108	8	7
CGA-327067	0.5	5	91-112	99	8	8
CC 4 220057	0.05 (LOQ)	5	77-102	90	10	11
CGA-330057	0.5	5	81-106	90	11	12
CC A 220050	0.05 (LOQ)	5	77-96	87	8	9
CGA-330059	0.5	5	77-99	84	9	11
			C	Confirmation Ion		
Fluthiacet-methyl	0.05 (LOQ)	5	69-96	82	10	12
(CGA-248757)	0.5	5	74-97	80	10	13
CGA-300402	0.05 (LOQ)	5	70-100	84	13	15
CGA-300402	0.5	5	70-98	80	12	15
CGA-300403	0.05 (LOQ)	5		No vichle confi	rmation ion was	found
CGA-300403	0.5	5		No viable com	iniation ion was	Toulia
CGA-300404	0.05 (LOQ)	5	60-98	79	15	19
CUA-300404	0.5	5	81-105	92	9	10
CGA-327066	0.05 (LOQ)	5	92-112	102	9	9
CGA-327000	0.5	5	82-106	90	11	12
CGA-327067	0.05 (LOQ)	5	23-95	55	26	47
CUA-327007	0.5	5	18-75	47	21	45
CGA-330057	0.05 (LOQ)	5	78-101	90	9	10
COA-330037	0.5	5	82-106	90	11	12
CGA-330059	0.05 (LOQ)	5	92-121	105	11	10
CGA-330039	0.5	5	93-125	104	13	13

Data (recovery results were corrected when residues were quantified in the controls; p. 37) were obtained from Table IV, pp. 64-71 of MRID 50193201.

1 The sandy loam soil (Sample ID: 2705W-033; 65% sand 27% silt 8% clay, pH 5.5 in 1:1 soil:water ratio, 0.96% organic matter) was obtained from Hickman, California, and characterized by Agvise Laboratories, Northwood, North Dakota (USDA soil texture characterization; p. 22; Appendix C, p. 213).

2 Two ion pair transitions were monitored (quantitation and confirmation, respectively): $m/z 404 \rightarrow 404$ (Q) and $m/z 404 \rightarrow 344.1$ (C) for fluthiacet-methyl (CGA-248757), $m/z 390 \rightarrow 390$ (Q) and $m/z 390 \rightarrow 260$ (C) for CGA-300402, $m/z 390 \rightarrow 344$ (Q) and $m/z 390 \rightarrow 390$ (C; deemed non-viable) for CGA-300403, $m/z 406 \rightarrow 347$ (Q) and $m/z 406 \rightarrow 362$ (C) for CGA-300404, $m/z 374 \rightarrow 356$ (Q) and $m/z 374 \rightarrow 328$ (C) for CGA-327066, $m/z 390 \rightarrow 330$ (Q)

and m/z 390 \rightarrow 314 (C) for CGA-327067, m/z 420 \rightarrow 347 (Q) and m/z 420 \rightarrow 217 (C) for CGA-330057, and m/z 406 \rightarrow 346 (Q) and m/z 406 \rightarrow 344 (C) for CGA-330059 (the quantitation ion transitions were the same as the only monitored ion transitions of the ECM).

- $3 \ Fluthiacet-methyl = [[2-Chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1-ylidene)amino]phenyl]thio]-methyl ester acetic acid; CGA-300402 = [[2-Chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1-ylidene)amino]phenyl]thio]-acetic acid; CGA-300403 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1-oxo-3-thioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2(3H)-yl)phenyl]thio]-acetic acid; CGA-300404 = [[2-Chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1-ylidene)amino]phenyl]sulfinyl]-acetic acid; CGA-327066 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl)phenyl]thio]-acetic acid; CGA-327067 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl)phenyl]sulfinyl]-acetic acid; CGA-330057 = Methyl ester [[2-chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H-3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1-ylidene)amino]phenyl]sulfinyl]-acetic acid; and CGA-330059 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl)phenyl]sulfinyl]-acetic acid; and CGA-330059 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1-oxo-3-thioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-1-ylidene)amino]phenyl]sulfinyl]-acetic acid; and CGA-330059 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1-oxo-3-thioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2(3H)-yl)phenyl]sulfinyl]-acetic acid.$
- 4 The recovery of one of the samples was not used for statistical analysis since it was deemed an outlier. The reviewer could not calculate statistics using 5 replicates since the raw data was not provided (Table IV, p. 65)...

III. Method Characteristics

In the ECM and ILV, LOQ for fluthiacet-methyl (CGA-248757), CGA-300402, CGA-300403, CGA-300404, CGA-327066, CGA-327067, CGA-330057, and CGA-330059 in soil were 0.05 μ g/kg (pp. 9, 22, 25 of Syngenta No. 122-99; pp. 39-40, 42, 45 of MRID 50193201). In the ECM, the LOQ was defined as the lowest concentration fortified in the control samples which yielded adequate recovery. The LOD for all analytes in soil was 4 pg (the lowest amount of standard injected; 0.00008 ng/µL calibration standard) in the ECM and 0.015 µg/kg (30% of the LOQ; 0.06 ng/mL in the calibration standard solution using the current methodology) in the ILV. In the ECM and ILV, no calculations or comparisons of the LOQ or LOD to background noise were provided.

Analyte ¹			CGA-248757	CGA-300402	CGA-300403	CGA-300404	CGA-327066	CGA-327067	CGA-330057	CGA-330059		
Limit of Quantitation (LOQ)	ECM ILV			0.05 µg/kg								
Limit of	ECM			(the lo	owest amount of		pg ed; 0.00008 ng/µl	L calibration sta	ndard)			
Detection (LOD) ²	ILV		(30% of the LO	Q; 0.06 ng/mL ir		µg/kg standard solution	n using the curre	ent methodology)		
		LOQ and 10×LOQ	$r^2 = 0.9994$ (D) $r^2 = 0.9998$ (H)	$r^2 = 0.9998$ (D & H)	$r^2 = 0.9998 (D)$ $r^2 = 0.9946 (H)$	$r^2 = 0.9990$	$r^2 = 0.9982$ (D) $r^2 = 0.9986$ (H)	$r^2 = 0.9934$ (D)	$r^2 = 0.9998$ (D)	$r^2 = 0.9924$ (D)		
Linearity (calibration	ECM ⁴	100×LOQ	-2 0,0002	$r^2 = 0.9990$ (D & H)	$r^2 = 0.9972$ (D & H)	$r^2 = 0.9996$ (D & H)	$r^2 = 0.9986$ (D & H)	$r^2 = 0.9988$ (D & H)	$r^2 = 0.9996$ (D & H)	$r^2 = 0.9994$ (D & H)		
curve r ² and concentration		Range		· · ·		4-40 pg (0.0000	08-0.0008 ng/µL)		, <i>,</i> ,	· · · ·		
range) ³	ILV		$r^2 = 0.9996 (Q)$ $r^2 = 0.9988 (C)$			$r^2 = 0.9994$ (Q & C)	$r^2 = 0.9964$ (Q) $r^2 = 0.9968$ (C)		$r^2 = 0.9992 (Q)$ $r^2 = 0.9996 (C)$			
		Range	0.06-0.8 ng/mL									
			Only quantitation ion transition monitored. ⁸									
Repeatable	ECM ^{6,7}		Yes at LOQ, 100×LOQ (char and sandy	racterized loam	Yes at LOQ, 10×LOQ and 100×LOQ (characterized loam soil). No at LOQ; yes at 10×LOQ and 100×LOQ (characterized sandy loam soil)	Yes at LOQ, 10	0×LOQ and 100>		rized loam and s	andy loam soil)		
	ILV ^{9,10}		Yes at LOQ a (characterized s		Yes at LOQ and 10×LOQ; no C analysis. ⁸ (characterized sandy loam soil)	Yes at LOQ and 10×LOQ (characterized sandy loam soil)	No at LOQ (22% RSD), yes at 10×LOQ. (characterized sandy loam soil)	Yes at LOQ and 10×LOQ, no for C (mean 47-55% RSD 45-47%). ⁸ (characterized sandy loam soil)	Yes at LOQ	and 10×LOQ andy loam soil)		

Table 4. Method Characteristics for Fluthiacet-methyl (CGA-248757) and Its Transformation Products CGA-300402, CGA-300403, CGA-300404, CGA-327066, CGA-327067, CGA-330057, and CGA-330059 in Soil

Analyte ¹		 CGA-248757	CGA-300402	CGA-300403	CGA-300404	CGA-327066	CGA-327067	CGA-330057	CGA-330059
Reproducible					Yes at LOQ	and 10×LOQ			
		The LOQ peaks	s in representativ	ve chromatograr	ns were small co	ompared to basel	ine noise in the	majority of the c	hromatograms.
	ECM	Yes, n	o matrix interfe	rences were obs	erved.	Yes, no matrix interferences were observed; however, baseline noise (<i>ca.</i> 20% of the LOQ based on peak height) interfered with LOQ peak integration.	interferences were observed; however, baseline noise (<i>ca.</i> 5-10%	Yes, matrix interferences were <10% of LOQ (based on peak area).	
Specific	ILV	Yes, no matrix were observed; peak was smal baseline	however, LOQ l compared to	the LOQ based	Yes, matrix interferences were <i>ca</i> . 7% of the LOQ based on peak height (Q).	No matrix interferences were observed; however, Q ion LOQ and 10×LOQ peaks were significantly compromised by baseline noise. ¹¹	nearby baseline peak	Yes, matrix interferences were <i>ca</i> . 1% of the LOQ based on peak height (Q).	neight;

Data were obtained from pp. 9, 22, 25; Appendix I, pp. 109-116 (recovery results); Tables 4-6, pp. 31-54 (correlation coefficients); Figures 5-6, pp. 81-98 (chromatograms) of Syngenta No. 122-99; pp. 39-40, 42, 45; Table IV, pp. 64-71 (recovery results); Figure 6, pp. 120-134 (calibration curves); Figures 2, 4, 11-12, pp. 80-87, 96-103, 167-182 (chromatograms) of MRID 50193201; DER Attachment 2. D = Dundee Soil; H = Hanford Soil. Q = Quantitation ion transition; C = Confirmation ion transition.

1 Fluthiacet-methyl = [[2-Chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1-ylidene)amino]phenyl]thio]-methyl ester acetic acid; CGA-300402 = [[2-Chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1-ylidene)amino]phenyl]thio]-acetic acid; CGA-300403 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1-oxo-3-thioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2(3H)-yl)phenyl]thio]-acetic acid; CGA-300404 = [[2-Chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-2(3H)-yl)phenyl]thio]-acetic acid; CGA-300404 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-1-ylidene)amino]phenyl]sulfinyl]-acetic acid; CGA-327066 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl)phenyl]thio]-acetic acid; CGA-327066 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl)phenyl]thio]-acetic acid; CGA-327067 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl]phenyl]thio]-acetic acid; CGA-327067 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl]phenyl]thio]-acetic acid; CGA-327067 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl]phenyl]thio]-acetic acid; CGA-327067 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-

1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl)phenyl]sulfinyl]-acetic acid; CGA-330057 = Methyl ester [[2-chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H-3H-

[1,3,4] thiadiazolo[3,4-a] pyridazin-1-ylidene) amino] phenyl] sulfinyl] - acetic acid; and CGA-330059 = [[2-Chloro-4-fluoro-5-[(tetrahydro-1-oxo-3-thioxo-1H-1)] + (tetrahydro-1-oxo-3-thioxo-1H-1)] + (tetrahydro-1-oxo-3-thioxo-1H-1) + (tetrahydro-1-oxo-3-thio

[1,2,4]triazolo[1,2-a]pyridazin-2(3H)-yl)phenyl]sulfinyl]-acetic acid.

- 2 LOD reported in the ILV differed from that reported in the ECM.
- 3 ECM and ILV coefficient of determination (r²) values are reviewer-generated from reported correlation coefficient (r) values (1/x weighting; Figure 8, pp. 58-63 of Syngenta No. 122-99; Appendix 6, pp. 183-193 of MRID 49447003; DER Attachment 2). Solvent-based calibration standards.
- 4 The reviewer assumed that the linear regression was performed with 1/x weighting.
- 5 The proposed C ion transition was deemed non-viable by the ILV.
- 6 In the ECM, Dundee loam soil (41% sand 50% silt 9% clay, pH 7.4, 1.1% organic matter) and Hanford sandy loam soil (61% sand 32% silt 7% clay, pH 7.4, 0.6% organic matter) were used in the study (USDA soil texture classification; Table 1, p. 27 of Syngenta No. 122-99). The soil sources and characterization laboratory were not reported.
- 7 Standard deviations and relative standard deviations were reviewer-calculated based on data provided in the study report since the study author did not report these values (see DER Attachment 2).
- 8 A confirmatory method is typically not required where GC/MS and/or LC/MS methods are used as the primary method.
- 9 In the ILV, the sandy loam soil (Sample ID: 2705W-033; 65% sand 27% silt 8% clay, pH 5.5 in 1:1 soil:water ratio, 0.96% organic matter) was obtained from Hickman, California, and characterized by Agvise Laboratories, Northwood, North Dakota (USDA soil texture characterization; p. 22; Appendix C, p. 213 of MRID 50193201).
- 10 The ILV validated the method for all analytes at both fortification levels in sandy loam soil after the second trial, with the following modifications: different Nexus column [Agilent Nexus SPE (0.5 g/12 mL)] was used, 7 mL of acetonitrile instead of 12 mL was used to elute the analytes from the Nexus column, matrix-based calibration standard solutions were used, and insignificant analytical method modifications (pp. 21, 23, 31-34, 44-45, 48 of MRID 50193201). The difference between the first and second trial was that the volume of acetonitrile was 9 mL in the first trial and 7 mL in the second trial. In the first trial, several individual and mean recoveries were <70% (Appendix D, pp. 215-222).
- 11 Based on Figures 11 and 12, pp. 171 and 179 of MRID 50193201.
- 12 Based on Figures 11 and 12, pp. 172 and 180 of MRID 50193201.
- 13 Based on Figures 11 and 12, pp. 174 and 182 of MRID 50193201.

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

IV. Method Deficiencies and Reviewer's Comments

1. The ILV representative chromatograms did not support the specificity of the method for CGA-327066, CGA-327067 and CGA-330059. For CGA-327067, LOQ and 10×LOQ peaks (quantitation and confirmation) were not resolved from nearby baseline peak noise; the analyte peaks were conjoined with contaminant peaks (Figures 11 and 12, pp. 172 and 180 of MRID 50193201). Matrix interferences were 13% (Q) and 35% (C) of the LOQ based on peak height. For CGA-327066 and CGA-330059, the resolution of the quantitation ion LOQ and 10×LOQ peaks were significantly compromised by baseline noise (Figures 11 and 12, pp. 171, 174, 179 and 182). Additionally, for CGA-330059, matrix interferences were 20% (Q) and 33% (C) of the LOQ based on peak height.

In the ECM, the LOQ peaks in representative chromatograms were small compared to baseline noise in the majority of the chromatograms (Figure 5-6, pp. 81-98 of Syngenta No. 122-99).

- 2. The ECM and ILV soil matrices were characterized but no terrestrial field dissipation study (TFD) was referenced for those soils. Additionally, no TFD studies were provided to the reviewer; therefore, the reviewer could not determine if the ILV sandy loam soil matrix was representative of TFD test soils.
- 3. ILV linearity was not satisfactory for CGA-330059 [$r^2 = 0.9932$ (Q), 0.9896 (C); Figure 6, pp. 120-134 of MRID 50193201; DER Attachment 2]. ECM linearity was not satisfactory for the calibration curves of CGA-300403 ($r^2 = 0.9946$, Hanford soil), CGA-327067 ($r^2 = 0.9934$, Dundee soil) and CGA-330059 ($r^2 = 0.9924$, Dundee soil); the reviewer assumed that the r values in the study report were 1/x weighted (Tables 4-6, pp. 31-54 of Syngenta No. 122-99; DER Attachment 2).
- 4. ECM performance data was not satisfactory for CGA-300403 in Hanford sandy loam soil at the LOQ, mean 67% (n = 4; Appendix I, pp. 109-116 of Syngenta No. 122-99; DER Attachment 2). OCSPP guidelines state that mean recoveries and RSDs were within 70-120% and $\leq 20\%$, respectively. ECM performance data was satisfactory at 10×LOQ and 100×LOQ in the Hanford sandy loam soil and for the LOQ, 10×LOQ and 100×LOQ in the Dundee loam soil.

ILV performance data was not satisfactory for the confirmation ion analysis of CGA-327067 (LOQ: mean 55% RSD 47%; $10 \times LOQ$: mean 47% RSD 45%; Table IV, pp. 64-71 of MRID 50193201). The reviewer noted that this deviation did not have an effect of the validity of the method since a confirmatory method is typically not required where GC/MS and/or LC/MS methods are used as the primary method. ILV performance data had low recoveries of the quantitation ion of CGA-327066 (LOQ: range 61%-114%, Table IV), the confirmation ion of CGA-300404 (LOQ: range 60%-98%, Table IV), and high recovery of the confirmation ion of CGA-330059(LOQ: range 92%-121%, $10 \times LOQ$: range 93%-125%, Table IV).

5. The estimations of the LOQ and LOD in ECM and ILV were not based on scientifically

acceptable procedures as defined in 40 CFR Part 136 (pp. 9, 22, 25 of Syngenta No. 122-99; pp. 39-40, 42, 45 of MRID 50193201). In the ECM, the LOQ was defined as the lowest concentration fortified in the control samples which yielded adequate recovery. The LOD for all analytes in soil was 4 pg (the lowest amount of standard injected; 0.00008 ng/ μ L calibration standard) in the ECM and 0.015 μ g/kg (30% of the LOQ; 0.06 ng/mL in the calibration standard solution using the current methodology) in the ILV. In the ECM and ILV, no calculations or comparisons of the LOQ or LOD to background noise were provided. The LOD of the ECM differed from that of the ILV. Detection limits should not be based on the arbitrarily selected lowest concentration in the spiked samples.

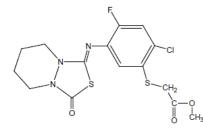
- 6. The reviewer noted that the LOD of ECM appeared to be *ca*. 50% of LOQ based on the peak areas of the 4 pg calibration standard and LOQ samples (Tables 4-6, pp. 31-54 of Syngenta No. 122-99).
- 7. The ILV study author provided communication details between the ILV laboratory personnel and the Sponsor Representative (Audrey Chen, FMC Corporation; pp. 3, 46-47 of MRID 50193201). These communications included communication of trial success or failure and approval of ILV modifications.
- 8. The reviewer noted that, although CGA-300403 was only identified and quantified using one ion pair transition in the ILV due to lack of a viable confirmation compound in the soil analysis, CGA-300403 was identified and quantified using two ion pair transitions in the ILV water analysis (Table III, p. 58; Table IV, p. 66 of MRID 50193201).
- 9. The matrix effects were determined to be significant in the ILV (p. 43; Table II, pp. 53-55 of MRID 50193201). Matrix-matched standards were used. Solvent standards were used in the ECM (based on ILV modifications; p. 48).
- 10. 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 *ca*. 26 hours (4 calendar days), with *ca*. 6 hours for preparation, *ca*. 16 hours for extraction and clean-up, and *ca*. 4 hours for LC/MS/MS analysis (pp. 40-41 of MRID 50193201).
- 11. In the ILV, the storage stability of the standard solutions was determined to be up to 108 days under refrigeration (4-10°C); the soil extracts were determined to stable for up to 7 days under refrigeration (4-10°C; pp. 45-46; Appendix E, pp. 224, 226 of MRID 50193201).
- 12. In this ILV/ECM only three major degradates of fluthiacet-methyl were identified and quantified (CGA-300402, CGA-300403, and CGA-327066). No ECM/ILV exists for other major residues of concern, including IN VLH91-000, M7, M13, and VAP41-000.

V. References

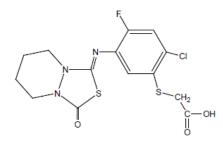
- U.S. Environmental Protection Agency. 2012. Ecological Effects Test Guidelines, OCSPP 850.6100, Environmental Chemistry Methods and Associated Independent Laboratory Validation. Office of Chemical Safety and Pollution Prevention, Washington, DC. EPA 712-C-001.
- 40 CFR Part 136. Appendix B. Definition and Procedure for the Determination of the Method Detection Limit-Revision 1.11, pp. 317-319. Attachment 1: Chemical Names and Structures

Fluthiacet-methyl (CGA-248757)

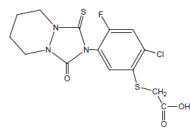
IUPAC Name:	Not reported
CAS Name:	[[2-Chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4-
	a]pyridazin-1-ylidene)amino]phenyl]thio]-methyl ester acetic acid
CAS Number:	117337-19-6
SMILES String:	Not found



CGA-300402	
IUPAC Name:	Not reported
CAS Name:	[[2-Chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1-ylidene)amino]phenyl]thio]-acetic acid
CAS Number:	149253-65-6
SMILES String:	Not found



CGA-300403	
IUPAC Name:	Not reported
CAS Name:	[[2-Chloro-4-fluoro-5-[(tetrahydro-1-oxo-3-thioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2(3H)-yl)phenyl]thio]-acetic acid
CAS Number:	Not available
SMILES String:	Not found



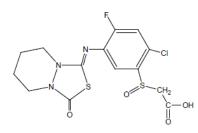
CGA-300404 IUPAC Name:

CAS Name:

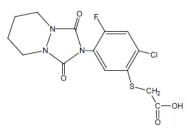
CAS Number:

SMILES String:

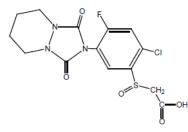
Not reported [[2-Chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4a]pyridazin-1-ylidene)amino]phenyl]sulfinyl]-acetic acid Not available Not found



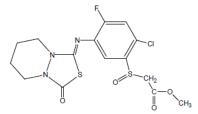
CGA-327066	
IUPAC Name:	Not reported
CAS Name:	[[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl)phenyl]thio]-acetic acid
CAS Number:	Not available
SMILES String:	Not found



CGA-327067	
IUPAC Name:	Not reported
CAS Name:	[[2-Chloro-4-fluoro-5-[(tetrahydro-1,3-dioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2-(3H)-yl)phenyl]sulfinyl]-acetic acid
CAS Number:	Not available
SMILES String:	Not found



CGA-330057	
IUPAC Name:	Not reported
CAS Name:	Methyl ester [[2-chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H-3H- [1,3,4]thiadiazolo[3,4-a]pyridazin-1-ylidene)amino]phenyl]sulfinyl]- acetic acid
CAS Number:	Not available
SMILES String:	Not found



CGA-330059	
IUPAC Name:	Not reported
CAS Name:	[[2-Chloro-4-fluoro-5-[(tetrahydro-1-oxo-3-thioxo-1H-[1,2,4]triazolo[1,2-a]pyridazin-2(3H)-yl)phenyl]sulfinyl]-acetic acid
CAS Number:	Not available
SMILES String:	Not found