

Test Material: Prosulfuron (CGA-152005)

MRID: 49805202

Title: Method Validation of Analytical Method Number ADPEN M1408: The Determination of Residues of CGA-152005 and Its Metabolites, CGA-300406, CGA-159902, and CGA150829 in Soil and Water Matrices Using LC-MS/MS

MRID: 49805201

Title: Independent Laboratory Validation (ILV) of Method ADPEN M1408: THE DETERMINATION OF RESIDUES OF CGA-152005 AND ITS METABOLITES, CGA-300406, CGA-159902, AND CGA150829 IN SOIL AND WATER MATRICES USING LC-MS/MS

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For CDM Smith

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Date: 7/13/16

Analytical method for prosulfuron (CGA152005) and its transformation products, CGA300406, CGA159902, and CGA150829, in soil and water

Reports: ECM: EPA MRID No.: 49805202. Perez, R., and A. Ratliff. 2016. Method Validation of Analytical Method Number ADPEN M1408: The Determination of Residues of CGA-152005 and Its Metabolites, CGA-300406, CGA-159902, and CGA150829 in Soil and Water Matrices Using LC-MS/MS. Study No.: ADPEN 2K15-804-0107. Report prepared by ADPEN Laboratories, Inc., Jacksonville, Florida, sponsored and submitted by Gowan Company, Yuma, Arizona; 271 pages. Final report completed December 16, 2015; Amended report completed January 12, 2016.

ILV: EPA MRID No.: 49805201. Perez, S., and A. Ratliff. 2015. Independent Laboratory Validation (ILV) of Method ADPEN M1408: THE DETERMINATION OF RESIDUES OF CGA-152005 AND ITS METABOLITES, CGA-300406, CGA-159902, AND CGA150829 IN SOIL AND WATER MATRICES USING LC-MS/MS. Study No.: ADPEN 2K15-804-0410. Report prepared by ADPEN Laboratories, Inc., Jacksonville, Florida, sponsored and submitted by Gowan Company, Yuma, Arizona; 156 pages. Final report issued October 29, 2015.

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Guideline: 850.6100

Statements: ECM: The study was conducted in compliance with USEPA Good Laboratory Practice (GLP) standards (p. 3 of MRID 49805202). Signed and dated Data Confidentiality, GLP, Quality Assurance, and Authenticity Certification statements were provided (pp. 2-5).

ILV: The study was conducted in compliance with USEPA FIFRA GLP standards (40 CFR 160; p. 3 of MRID 49805201). Signed and dated Data Confidentiality, GLP, Quality Assurance, and Authenticity Certification statements were provided (pp. 2-5).

Classification: This analytical method for water is classified as supplemental. The analytical methods were validated by the same company that developed the method (ADPEN), which was also the same company that analyzed the test samples, therefore, the analytical methods do not support the aquatic field dissipation study.

For Water and Soil Analyses: The ILV was not independent of the ECM. The specificity of the method was not demonstrated in the ECM chromatograms of CGA150829. The specificity of the method was not demonstrated in the ILV chromatograms of the confirmation ion of CGA159902. Insufficient chromatograms were provided to support all matrices of the ECM.

For Water Analysis: In the ILV, the number of samples was insufficient for all analyses at the LOQ, n = 4. In the ILV, the LOQ confirmation ion analyses of prosulfuron, CGA300406, and CGA159902 did not meet OCSPP Guidelines for precision and accuracy.

For Soil Analysis: In the ECM, no samples were prepared at 10×LOQ. In the ECM, the LOQ analysis of prosulfuron in the Texas soil 30-36” did not meet OCSPP Guidelines for precision and accuracy. ECM linear regressions were unsatisfactory ($r^2 < 0.995$) for the majority of the calibration curves of prosulfuron and CGA159902 and for several of the calibration curves of CGA150829. The LOD of CGA150829 differed between the ECM and ILV.

PC Code: 129031

Reviewer: Karen Milians, Chemist

Signature:

Date:

Page citations in this review refer to the page numbers located in the upper right corner of each page of the MRID.

Executive Summary

The analytical method, ADPEN M1408, is designed for the quantitative determination of prosulfuron (CGA152005) and its transformation products, CGA300406, CGA159902, and CGA150829, using HPLC/MS/MS at the LOQ of 0.01 ppb for water analysis and the LOQ of 0.1 ppb for soil analysis. The respective LOQ is less than the lowest toxicological level of concern in soil and water. The ILV was not independent of the ECM: the laboratory which performed the ILV was the same as that which performed the ECM; one of the co-authors was the same between the ILV and ECM; and there was some additional overlap of study personnel, including the Study Director. The water and soil matrices were not characterized or described in the ECM or ILV; it could not be determined if the ILV was provided with the most difficult matrix with which to validate the method. The ILV validated the method in water and soil with the first trial for all analytes with minor modifications to the analytical parameters (few monitored ion transitions were modified and a confirmation ion transition was monitored for CGA150829). For the water and soil analyses, the specificity of the method was not demonstrated in the ECM chromatograms of CGA150829 or in the ILV chromatograms of the confirmation ion of CGA159902. Additionally, insufficient ECM chromatograms were provided to support all matrices. For the ILV water analysis, the number of samples was insufficient for all analyses at the LOQ, $n = 4$. Also, the ILV water LOQ confirmation ion analyses of prosulfuron, CGA300406, and CGA159902 did not meet OCSPP Guidelines for precision and accuracy. For the ECM soil analysis, no samples were prepared at 10×LOQ, and the LOQ analysis of prosulfuron in the Texas soil 30-36” did not meet OCSPP Guidelines for precision and accuracy. Also, ECM soil linear regressions were unsatisfactory for the majority of the calibration curves of prosulfuron and CGA159902 and for several of the calibration curves of CGA150829. ECM sample recoveries for soil were corrected for residues quantified in the controls (*ca.* 2-25% of the LOQ). The LOD of CGA150829 in soil differed between the ECM and ILV.

Table 1. Analytical Method Summary

Analyte(s) by Pesticide ¹	MRID		EPA Review	Matrix	Method Date (dd/mm/yyyy)	Registrant	Analysis	Limit of Quantitation (LOQ)
	Environmental Chemistry Method	Independent Laboratory Validation						
Prosulfuron (CGA152005)	49805202 ²	49805201 ³		Water	16/12/2015 (Final report) ⁴	Gowan Company	LC/MS/MS	0.1 ppb
CGA300406					12/01/2016 (Amended final report) ⁴			
CGA159902								
CGA150829								
Prosulfuron (CGA152005)				Soil	15/12/2015 (Technical report) ⁵			0.01 ppb
CGA300406								
CGA159902								
CGA150829								

1 Prosulfuron (CGA152005) = 1-(4-Methoxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]urea. CGA300406 = 1-(4-Hydroxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]urea. CGA159902 = 2-(3,3,3-Trifluoropropyl)phenylsulfonylurea. CGA150829 = 2-Amino-4-hydroxy-6-methyl-1,3,5-triazine.

2 In the ECM, water samples from Louisiana and Texas were used in the study; no water characterization or further source description was reported (p. 11 of MRID 49805202). Soil samples from Louisiana (0-6") and Texas (0-6", 6-12", 12-24", 24-30", and 30-36") were used in the study; no soil characterization was reported.

3 In the ILV, water sample was provided by R&D Research Farm, Inc.; a sample code was provided, 150527001-001, but the water was not characterized (p. 16 of MRID 49805201). The water source was not further specified. The soil sample was provided by R&D Research Farm, Inc.; a sample code was provided, 150527001-002, but the soil was not characterized.

4 From ADPEN Study No. 2K15-804-0107 (p. 1 of MRID 49805202; see Reviewer's Comment #11).

5 From ADPEN Method No. ADPEN-M1408 (Appendix 6, p. 192 of MRID 49805202).

I. Principle of the Method

Water Samples: Samples (10.0 mL) were placed in 15-mL polypropylene test tubes and fortified, if necessary (p. 17; Appendix 6, pp. 201-203 of MRID 49805202). An aliquot (*ca.* 0.45 mL) was filtered using a 0.2 μm syringe filter. The initial 0.1-0.2 mL of the filtrate was disposed and the remaining aliquot was transferred to an autosampler vial for analysis by LC-MS/MS.

Soil Samples: Samples (10.0 g) were placed in 50-mL polypropylene test tubes and fortified, if necessary (pp. 15, 17; Appendix 6, pp. 197-198, 202-204 of MRID 49805202). The samples were extracted with 25 mL of methanol:water + 10 mM sodium phosphate (or 10 mM ammonium acetate; 85:15, v:v) via shaking on an Omni Bead Ruptor for 1 minute at 4 m/s. After centrifugation (30 minutes at 4150 rpm), the supernatant was separated. An aliquot of the supernatant (5 mL) was concentrated under nitrogen using evaporation (Turbo Vap or N-Evap) at 50°C to a final volume of 0.75 mL (final volume was *ca.* 2 mL for the 15-mL control sample). The residue was reconstituted to a final volume of 5 mL using HPLC grade water (15 mL for the control diluent). After shaking by hand for 20 seconds and centrifugation (30 minutes at 4150 rpm), the supernatant was filtered (0.2 μm) and transferred to autosampler vials for analysis by LC-MS/MS. The method noted that samples fortified at concentrations higher than the LOQ should be diluted down to the LOQ concentration range.

LC/MS/MS for Prosulfuron, CGA300406 and CGA159902: Samples are analyzed using an Agilent 1290 Infinity HPLC System coupled with an AB Sciex Triple Quad 6500 in Turbo Spray Ionization Mode (550°C; API 6500 - MS Instrument #27; pp. 18-19 of MRID 49805202). The following LC conditions were used: Acquity-HSS T3 C18 column (2.1 mm x 150 mm, 1.8 μm ; column temperature 50°C), mobile phase of (A) 0.1% formic acid in water and (B) 0.1% formic acid in acetonitrile [percent A:B (v:v) at 0.00-0.50 min. 99.0:1.0, 2.40 min. 40:60, 4.26-5.25 min. 0.0:100.0, 5.26-5.75 min. 99.0:1.0], and injection volume of 40 μL . The following MS/MS conditions were used: negative ion polarity and multiple reaction monitoring (MRM). Two ion pair transitions were monitored for each analyte (quantitative and confirmatory, respectively): m/z 418.0 \rightarrow 138.9 and m/z 418.0 \rightarrow 106.8 for prosulfuron, m/z 404.1 \rightarrow 125.1 and m/z 404.1 \rightarrow 82.0 for CGA300406, and m/z 252.1 \rightarrow 212.1 and m/z 252.1 \rightarrow 102.1 for CGA159902. Expected retention times were *ca.* 4.45, 3.62 and 3.80 minutes for prosulfuron, CGA300406 and CGA159902, respectively.

LC/MS/MS for CGA150829: The following LC/MS/MS conditions were modified from above: positive ion polarity and ion pair transition m/z 141.0 \rightarrow 57.1 (pp. 18-19 of MRID 49805202). Expected retention time was *ca.* 2.46 minutes. Only one ion transition was monitored due to lower sensitivity (Appendix 6, p. 209).

The method noted that matrix-matched standards were necessary to eliminate strong matrix suppression and enhancement observed during method development with or without cleanup (Appendix 6, p. 209).

ILV: The extraction procedures were performed exactly as written in the ECM, except that the reconstitution solvent was not specified in the soil extraction (pp. 16-17; Tables 1-2, pp. 23-24 of MRID 49805201). The samples are analyzed for analytes by HPLC/MS/MS using an Agilent 1290 UPLC system and an Agilent 6490 Triple Quad MS with ElectroSpray Ionization (ESI; 200°C; Table 19, p. 42). The LC parameters were the same as those of the ECM. Two ion pair transitions

were monitored for all analytes (quantitative and confirmatory, respectively): m/z 418.08 \rightarrow 138.90 and m/z 418.08 \rightarrow **251.90** for prosulfuron, m/z 404.06 \rightarrow 124.90 and m/z 404.06 \rightarrow 82.00 for CGA300406, m/z 252.03 \rightarrow 211.90 and m/z 252.03 \rightarrow **127.9** for CGA159902, and m/z 141.08 \rightarrow 57.00 and m/z **141.08** \rightarrow **42.10** for CGA150829 (those that differed significantly from those of the ECM were **bolded**). Observed retention times were *ca.* 4.15, 3.35-3.37, 3.54-3.56, and 2.19-2.20 minutes for prosulfuron, CGA300406, CGA159902, and CGA150829, respectively (Figures 2-33, pp. 52-127).

LOQ and LOD - water: In the ECM and ILV, LOQ and LOD were 0.01 ppb and 0.002 ppb, respectively, for all analytes (pp. 11, 30-31; Appendix 6, p. 209 of MRID 49805202; p. 10 of MRID 49805201).

LOQ and LOD - soil: In the ECM and ILV, LOQ was 0.1 ppb for all analytes (pp. 11, 30-31; Appendix 6, p. 209 of MRID 49805202; p. 10 of MRID 49805201). In the ECM, the LODs were reported to be 0.02 ppb for prosulfuron, CGA300406 and CGA159902 and 0.06 ppb for CGA150829. In the ILV, the LOD was reported to be 0.02 ppb for all analytes.

II. Recovery Findings

ECM - water (MRID 49805202): Mean recoveries and relative standard deviations (RSDs) were within guidelines (mean 70-120%; RSD \leq 20%) for analysis of prosulfuron (CGA152005) and its transformation products, CGA300406, CGA159902, and CGA150829, at fortification levels of 0.01 ppb (LOQ) and 0.1 ppb (10 \times LOQ) in water matrices (Tables 4.1.1-4.1.2, pp. 21-22). Two ion transitions were monitored for each analyte, except CGA150829. Results of the quantitation and confirmation ion transitions were fairly comparable for prosulfuron, CGA300406 and CGA159902. Calculations allowed for the correction of sample recoveries for residues quantified in the controls; however, no residues were quantified in the controls (p. 20; Appendix 5, pp. 128-141). Water samples from Louisiana and Texas were used in the study; no water characterization or further source description was reported (p. 11).

ECM - soil (MRID 49805202): Mean recoveries and RSDs were within guidelines for analysis of prosulfuron (CGA152005) and its transformation products, CGA300406, CGA159902, and CGA150829, at fortification levels of 0.1 ppb (LOQ) and 10 ppb (100 \times LOQ) in soil matrices, except for prosulfuron at the LOQ in the Texas soil 30-36" where means were 127% and 131% for the quantitation and confirmation ions, respectively (Tables 4.1.3-4.1.9, pp. 23-29; DER Attachment 2). No samples were prepared at 10 \times LOQ. The study authors excluded one sample from the statistical analysis for prosulfuron at the LOQ in the Texas soil 30-36", $n = 4$ (116% mean, 7.5% RSD for quantitation ion; 122% mean, 8.0% RSD for confirmation ion; reported by the study authors; Table 4.1.9, p. 29). The results provided in the DER were reviewer-calculated using all samples, $n = 5$. Two ion transitions were monitored for each analyte, except CGA150829. Results of the quantitation and confirmation ion transitions were comparable for prosulfuron, CGA300406 and CGA159902. Calculations allowed for the correction of sample recoveries for residues quantified in the controls; residues were quantified in the controls for prosulfuron in the Texas soil 6-12" (both ions, *ca.* 2-16% of the LOQ), 24-30" (both ions, *ca.* 22-25% of the LOQ) and 30-36" (confirmation ion, *ca.* 3% of the LOQ), CGA300406 in the Texas soil 24-30" (quantitation ion, *ca.* 3% of the LOQ), and CGA159902 in the Texas soil 24-30" (quantitation ion, *ca.* 4% of the LOQ; control residue percentages were reviewer-quantified using reported data in Appendix 5; p. 20;

Appendix 5, pp. 142-190). Soil samples from Louisiana (0-6") and Texas (0-6", 6-12", 12-24", 24-30", and 30-36") were used in the study; no soil characterization was reported (p. 11).

ILV – water (MRID 49805201): Mean recoveries and relative standard deviations (RSDs) were within guidelines (mean 70-120%; RSD \leq 20%) for analysis of prosulfuron (CGA152005) and its transformation products, CGA300406, CGA159902, and CGA150829, at fortification levels of 0.01 ppb (LOQ) and 0.1 ppb (10 \times LOQ) in water matrices, except for the LOQ confirmation ion analyses of prosulfuron (RSD 22.0%), CGA300406 (RSD 60%), and CGA159902 (mean 129%, RSD 34%; pp. 11-12; Tables 2-9, pp. 25-32; DER Attachment 2). The number of samples was insufficient for all analyses at the LOQ (n = 4). The study authors excluded one sample from the confirmation ion statistical analyses of CGA300406 and CGA159902, n = 3 (103% mean, 25.2% RSD for CGA300406; 107% mean, 8.1% RSD for CGA159902; reported by the study authors; Table 5, p. 28 and Table 7, p. 30). The results provided in the DER were reviewer-calculated using all samples, n = 4. Two ion transitions were monitored for each analyte; results of the quantitation and confirmation ion transitions were comparable. The water sample was provided by R&D Research Farm, Inc.; a sample code was provided, 150527001-001, but the water was not characterized (p. 16). The water source was not further specified. The method was validated with the first trial for all analytes with minor modifications to the analytical parameters (p. 20; Table 19, p. 42).

ILV – soil (MRID 49805201): Mean recoveries and RSDs were within guidelines for analysis of prosulfuron (CGA152005) and its transformation products, CGA300406, CGA159902, and CGA150829, at fortification levels of 0.1 ppb (LOQ) and 1.0 ppb (10 \times LOQ) in soil matrices (pp. 11-12; Tables 10-17, pp. 33-40). Two ion transitions were monitored for each analyte; results of the quantitation and confirmation ion transitions were comparable. The soil sample was provided by R&D Research Farm, Inc.; a sample code was provided, 150527001-002, but the soil was not characterized (p. 16). The method was validated with the first trial for all analytes with minor modifications to the analytical parameters (p. 20; Table 19, p. 42).

Table 2a. Initial Validation Method Recoveries for Prosulfuron (CGA152005) and Its Transformation Products, CGA300406, CGA159902, and CGA150829 in Water^{1,2,3}

Analyte	Fortification Level (ppb)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
LA Water						
Quantitation ion transition						
Prosulfuron (CGA152005)	0.01 (LOQ)	5	94-98	96	1.5	1.5
	0.1	5	93-97	95	1.7	1.8
CGA300406	0.01 (LOQ)	5	104-107	105	1.5	1.4
	0.1	5	119-122	120	1.3	1.1
CGA159902	0.01 (LOQ)	5	91-97	94	2.5	2.7
	0.1	5	90-95	93	1.6	1.7
CGA150829	0.01 (LOQ)	5	87-100	92	5.5	6.0
	0.1	5	94-108	101	5.3	5.2
Confirmation ion transition						
Prosulfuron (CGA152005)	0.01 (LOQ)	5	92-104	99	4.7	4.8
	0.1	5	98-100	99	0.9	0.9
CGA300406	0.01 (LOQ)	5	104-112	108	2.9	2.6
	0.1	5	118-121	120	1.5	1.3
CGA159902	0.01 (LOQ)	5	92-110	102	7.3	7.1
	0.1	5	91-97	93	2.7	2.9
TX Water						
Quantitation ion transition						
Prosulfuron (CGA152005)	0.01 (LOQ)	5	101-103	102	0.8	0.8
	0.1	5	99-104	102	2.0	2.0
CGA300406	0.01 (LOQ)	5	105-111	108	2.9	2.7
	0.1	5	104-109	106	2.0	1.9
CGA159902	0.01 (LOQ)	5	89-103	94	5.2	5.6
	0.1	5	94-95	95	0.6	0.7
CGA150829	0.01 (LOQ)	5	97-103	101	2.4	2.4
	0.1	5	94-100	98	3.0	3.0
Confirmation ion transition						
Prosulfuron (CGA152005)	0.01 (LOQ)	5	99-105	102	2.3	2.3
	0.1	5	102-104	103	1.0	1.0
CGA300406	0.01 (LOQ)	5	100-118	111	7.3	6.6
	0.1	5	103-106	105	1.5	1.5
CGA159902	0.01 (LOQ)	5	75-100	85	10.1	12.0
	0.1	5	91-96	94	2.1	2.2

Data (uncorrected recovery results; p. 20; Appendix 5, pp. 128-141) were obtained from Tables 4.1.1-4.1.2, pp. 21-22 of MRID 49805202.

1 Water samples from Louisiana and Texas were used in the study; no water characterization or further source description was reported (p. 11).

2 Prosulfuron (CGA152005) = 1-(4-Methoxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]urea. CGA300406 = 1-(4-Hydroxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]urea. CGA159902 = 2-(3,3,3-Trifluoropropyl)phenylsulfonylurea. CGA150829 = 2-Amino-4-hydroxy-6-methyl-1,3,5-triazine.

3 Two ion pair transitions were monitored for prosulfuron, CGA300406, and CGA159902 (quantitative and confirmatory, respectively): m/z 418.0 \rightarrow 138.9 and m/z 418.0 \rightarrow 106.8 for prosulfuron, m/z 404.1 \rightarrow 125.1 and m/z 404.1 \rightarrow 82.0 for CGA300406, and m/z 252.1 \rightarrow 212.1 and m/z 252.1 \rightarrow 102.1 for CGA159902 (pp. 18-19). Only one ion pair transition was monitored for CGA150829: m/z 141.0 \rightarrow 57.1.

Table 2b. Initial Validation Method Recoveries for Prosulfuron (CGA152005) and Its Transformation Products, CGA300406, CGA159902, and CGA150829 in Soil^{1,2,3}

Analyte	Fortification Level (ppb)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
TX Soil (0-6")						
Quantitation ion transition						
Prosulfuron (CGA152005)	0.1 (LOQ)	5	78-87	82	3.7	4.5
	10	5	81-89	86	3.5	4.1
CGA300406	0.1 (LOQ)	5	99-105	101	3.2	3.1
	10	5	96-100	99	16	1.6
CGA159902	0.1 (LOQ)	5	88-96	93	3.1	3.3
	10	5	90-95	92	1.9	2.1
CGA150829	0.1 (LOQ)	5	88-99	93	3.9	4.2
	10	5	86-97	92	4.5	4.9
Confirmation ion transition						
Prosulfuron (CGA152005)	0.1 (LOQ)	5	75-82	79	2.8	3.5
	10	5	82-91	88	3.5	4.0
CGA300406	0.1 (LOQ)	5	101-106	104	2.4	2.3
	10	5	97-102	99	2.4	2.4
CGA159902	0.1 (LOQ)	5	87-103	95	7.0	7.3
	10	5	91-96	94	2.3	2.5
LA Soil (0-6")						
Quantitation ion transition						
Prosulfuron (CGA152005)	0.1 (LOQ)	5	86-91	88	2.4	2.7
	10	5	88-94	91	2.2	2.5
CGA300406	0.1 (LOQ)	5	93-99	96	2.3	2.4
	10	5	94-98	97	1.6	1.6
CGA159902	0.1 (LOQ)	5	83-90	87	3.0	3.4
	10	5	87-92	90	1.9	2.1
CGA150829	0.1 (LOQ)	5	81-88	83	3.0	3.7
	10	5	78-88	82	3.6	4.4
Confirmation ion transition						
Prosulfuron (CGA152005)	0.1 (LOQ)	5	83-91	89	3.4	3.9
	10	5	88-94	91	2.2	2.5
CGA300406	0.1 (LOQ)	5	88-104	93	6.4	6.9
	10	5	93-97	95	2.0	2.1
CGA159902	0.1 (LOQ)	5	90-96	94	2.7	2.8
	10	5	88-93	91	1.8	1.9
TX Soil (6-12")						
Quantitation ion transition						
Prosulfuron (CGA152005)	0.1 (LOQ)	5	79-91	84	4.9	5.8
	10	5	82-86	84	1.6	1.9
CGA300406	0.1 (LOQ)	5	94-103	100	3.6	3.6
	10	5	100-109	106	3.4	3.2
CGA159902	0.1 (LOQ)	5	86-96	91	3.9	4.4
	10	5	89-95	91	2.6	2.8
CGA150829	0.1 (LOQ)	5	97-108	101	4.0	4.0
	10	5	86-98	93	5.1	5.5

Analyte	Fortification Level (ppb)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
Confirmation ion transition						
Prosulfuron (CGA152005)	0.1 (LOQ)	5	78-90	86	5.4	6.4
	10	5	82-85	84	1.2	1.5
CGA300406	0.1 (LOQ)	5	96-110	103	6.6	6.5
	10	5	104-107	106	1.6	1.5
CGA159902	0.1 (LOQ)	5	84-94	90	4.6	5.1
	10	5	86-94	90	3.4	3.7
TX Soil (12-18")						
Quantitation ion transition						
Prosulfuron (CGA152005)	0.1 (LOQ)	5	87-94	90	3.0	3.3
	10	5	89-94	92	1.7	1.9
CGA300406	0.1 (LOQ)	5	91-103	97	4.3	4.5
	10	5	94-98	96	1.5	1.5
CGA159902	0.1 (LOQ)	5	84-94	87	4.0	4.6
	10	5	85-89	87	1.4	1.6
CGA150829	0.1 (LOQ)	5	80-99	90	6.9	7.7
	10	5	79-85	81	2.3	2.8
Confirmation ion transition						
Prosulfuron (CGA152005)	0.1 (LOQ)	5	89-95	91	2.8	3.1
	10	5	91-94	93	1.3	1.4
CGA300406	0.1 (LOQ)	5	89-95	93	2.6	2.8
	10	5	93-98	96	1.8	1.9
CGA159902	0.1 (LOQ)	5	78-84	82	2.8	3.4
	10	5	84-90	87	2.4	2.7
TX Soil (18-24")						
Quantitation ion transition						
Prosulfuron (CGA152005)	0.1 (LOQ)	5	81-90	86	4.1	4.8
	10	5	94-97	95	1.3	1.4
CGA300406	0.1 (LOQ)	5	88-101	95	5.3	5.6
	10	5	91-98	95	2.7	2.8
CGA159902	0.1 (LOQ)	5	79-89	85	4.7	5.5
	10	5	84-92	89	3.5	3.9
CGA150829	0.1 (LOQ)	5	84-94	87	5.3	6.1
	10	5	85-91	87	2.8	3.3
Confirmation ion transition						
Prosulfuron (CGA152005)	0.1 (LOQ)	5	81-95	89	5.9	6.6
	10	5	91-96	94	1.8	1.9
CGA300406	0.1 (LOQ)	5	93-106	95	9.5	10.0
	10	5	89-100	94	4.1	4.4
CGA159902	0.1 (LOQ)	5	83-108	92	9.6	10.4
	10	5	83-90	88	3.0	3.4
TX Soil (24-30")						
Quantitation ion transition						
Prosulfuron (CGA152005)	0.1 (LOQ)	5	72-80	77	3.1	4.1
	10	5	77-82	80	1.8	2.3
CGA300406	0.1 (LOQ)	5	86-96	91	3.9	4.2
	10	5	91-97	95	2.4	2.5

Analyte	Fortification Level (ppb)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
CGA159902	0.1 (LOQ)	5	84-94	89	4.1	4.6
	10	5	85-90	88	1.5	1.7
CGA150829	0.1 (LOQ)	5	78-102	87	10.8	12.3
	10	5	81-90	85	3.2	3.8
Confirmation ion transition						
Prosulfuron (CGA152005)	0.1 (LOQ)	5	71-80	76	4.3	5.6
	10	5	77-80	79	1.0	1.3
CGA300406	0.1 (LOQ)	5	88-103	95	5.6	5.8
	10	5	95-99	97	1.8	1.8
CGA159902	0.1 (LOQ)	5	84-97	90	5.0	5.5
	10	5	85-91	89	2.4	2.8
TX Soil (30-36")						
Quantitation ion transition						
Prosulfuron (CGA152005)	0.1 (LOQ)	5 ⁴	108-168	127	24	19
	10	5	98-102	100	1.7	1.7
CGA300406	0.1 (LOQ)	5	93-102	97	3.5	3.6
	10	5	92-99	96	2.4	2.5
CGA159902	0.1 (LOQ)	5	86-96	91	3.8	4.2
	10	5	93-95	94	0.8	0.9
CGA150829	0.1 (LOQ)	5	74-86	80	5.1	6.4
	10	5	79-86	82	2.9	3.5
Confirmation ion transition						
Prosulfuron (CGA152005)	0.1 (LOQ)	5 ⁴	112-166	131	21	16
	10	5	98-102	100	2.0	2.0
CGA300406	0.1 (LOQ)	5	91-103	96	5.0	5.2
	10	5	93-97	95	1.6	1.7
CGA159902	0.1 (LOQ)	5	78-99	88	7.8	8.9
	10	5	91-95	92	1.6	1.8

Data (recovery results were corrected for residues quantified in the controls; p. 20; Appendix 5, pp. 142-190) were obtained from Tables 4.1.3-4.1.9, pp. 23-29 of MRID 49805202 and DER Attachment 2.

1 Soil samples from Louisiana (0-6") and Texas (0-6", 6-12", 12-24", 24-30", and 30-36") were used in the study; no soil characterization was reported (p. 11).

2 Prosulfuron (CGA152005) = 1-(4-Methoxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]urea. CGA300406 = 1-(4-Hydroxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]urea. CGA159902 = 2-(3,3,3-Trifluoropropyl)phenylsulfonylurea. CGA150829 = 2-Amino-4-hydroxy-6-methyl-1,3,5-triazine.

3 Two ion pair transitions were monitored for prosulfuron, CGA300406, and CGA159902 (quantitative and confirmatory, respectively): m/z 418.0 \rightarrow 138.9 and m/z 418.0 \rightarrow 106.8 for prosulfuron, m/z 404.1 \rightarrow 125.1 and m/z 404.1 \rightarrow 82.0 for CGA300406, and m/z 252.1 \rightarrow 212.1 and m/z 252.1 \rightarrow 102.1 for CGA159902 (pp. 18-19). Only one ion pair transition was monitored for CGA150829: m/z 141.0 \rightarrow 57.1.

4 The study authors excluded one sample from the statistical analysis, $n = 4$ (116% mean, 7.5% RSD for quantitation ion; 122% mean, 8.0% RSD for confirmation ion; Table 4.1.9, p. 29). The results provided were reviewer-calculated using all samples, $n = 5$ (see DER Attachment 2).

Table 3a. Independent Validation Method Recoveries for Prosulfuron (CGA152005) and Its Transformation Products, CGA300406, CGA159902, and CGA150829 in Water¹

Analyte	Fortification Level (ppb)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
Water						
Quantitation ion transition						
Prosulfuron (CGA152005)	0.01 (LOQ)	4	73-100	84	11.5	13.7
	0.1	6	84-89	87	1.6	1.8
CGA300406	0.01 (LOQ)	4	82-117	98	14.7	15.0
	0.1	6	98-110	104	4.3	4.2
CGA159902	0.01 (LOQ)	4	104-115	108	5.5	5.1
	0.1	6	86-103	94	6.0	6.3
CGA150829	0.01 (LOQ)	4	98-100	99	0.7	0.7
	0.1	6	102-107	104	1.8	1.8
Confirmation ion transition						
Prosulfuron (CGA152005)	0.01 (LOQ)	4	80-129	97	21.4	22.0
	0.1	6	85-95	90	4.8	5.4
CGA300406	0.01 (LOQ)	4⁴	15-130	91	49	60
	0.1	6	91-109	101	7.3	7.2
CGA159902	0.01 (LOQ)	4⁴	97-194	129	44	34
	0.1	6	86-107	93	7.5	8.0
CGA150829	0.01 (LOQ)	4	112-118	114	2.5	2.2
	0.1	6	95-101	98	1.9	2.0

Data (uncorrected recovery results; pp. 17-18; Appendix C, pp. 141-156) were obtained from pp. 11-12; Tables 2-9, pp. 25-32 of MRID 49805201 and DER Attachment 2.

1 The water sample was provided by R&D Research Farm, Inc.; a sample code was provided, 150527001-001, but the water was not characterized (p. 16). The water source was not further specified.

2 Prosulfuron (CGA152005) = 1-(4-Methoxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]urea. CGA300406 = 1-(4-Hydroxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]urea. CGA159902 = 2-(3,3,3-Trifluoropropyl)phenylsulfonylurea. CGA150829 = 2-Amino-4-hydroxy-6-methyl-1,3,5-triazine.

3 Two ion pair transitions were monitored for all analytes (quantitative and confirmatory, respectively): m/z 418.08 → 138.90 and m/z 418.08 → **251.90** for prosulfuron, m/z 404.06 → 124.90 and m/z 404.06 → 82.00 for CGA300406, m/z 252.03 → 211.90 and m/z 252.03 → **127.90** for CGA159902, and m/z 141.08 → 57.00 and m/z **141.08** → **42.10** for CGA150829 (those that differed significantly from those of the ECM were **bolded**; Table 19, p. 42).

4 The study authors excluded one sample from the statistical analysis, $n = 3$ (103% mean, 25.2% RSD for CGA300406; 107% mean, 8.1% RSD for CGA159902; Table 5, p. 28 and Table 7, p. 30). The results provided were reviewer-calculated using all samples, $n = 4$ (see DER Attachment 2).

Table 3b. Independent Validation Method Recoveries for Prosulfuron (CGA152005) and Its Transformation Products, CGA300406, CGA159902, and CGA150829 in Soil¹

Analyte	Fortification Level (ppb)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
Soil						
Quantitation ion transition						
Prosulfuron (CGA152005)	0.1 (LOQ)	5	91-100	97	3.4	3.5
	1.0	5	90-98	94	3.1	3.3
CGA300406	0.1 (LOQ)	5	64-84	74	8.7	11.8
	1.0	5	79-92	83	5.4	6.5
CGA159902	0.1 (LOQ)	5	95-115	106	7.2	6.8
	1.0	5	91-114	102	8.3	8.2
CGA150829	0.1 (LOQ)	5	90-96	93	2.6	2.8
	1.0	5	85-94	89	3.2	3.6
Confirmation ion transition						
Prosulfuron (CGA152005)	0.1 (LOQ)	5	79-96	87	8.3	9.5
	1.0	5	81-98	92	7.6	8.3
CGA300406	0.1 (LOQ)	5	70-99	82	13.9	16.9
	1.0	5	71-99	85	14.1	16.6
CGA159902	0.1 (LOQ)	5	98-122	113	9.8	8.7
	1.0	5	103-119	112	6.1	5.5
CGA150829	0.1 (LOQ)	5	99-107	103	2.9	2.8
	1.0	5	87-92	90	1.9	2.1

Data (uncorrected recovery results; pp. 17-18; Appendix C, pp. 141-156) were obtained from pp. 11-12; Tables 10-17, pp. 33-40 of MRID 49805201.

1 The soil sample was provided by R&D Research Farm, Inc.; a sample code was provided, 150527001-002, but the soil was not characterized (p. 16).

2 Prosulfuron (CGA152005) = 1-(4-Methoxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]urea. CGA300406 = 1-(4-Hydroxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]urea. CGA159902 = 2-(3,3,3-Trifluoropropyl)phenylsulfonylurea. CGA150829 = 2-Amino-4-hydroxy-6-methyl-1,3,5-triazine.

3 Two ion pair transitions were monitored for all analytes (quantitative and confirmatory, respectively): m/z 418.08 → 138.90 and m/z 418.08 → **251.90** for prosulfuron, m/z 404.06 → 124.90 and m/z 404.06 → 82.00 for CGA300406, m/z 252.03 → 211.90 and m/z 252.03 → **127.90** for CGA159902, and m/z 141.08 → 57.00 and m/z **141.08** → **42.10** for CGA150829 (those that differed significantly from those of the ECM were **bolded**; Table 19, p. 42).

IV. Method Deficiencies

In the ECM and ILV, LOQs were 0.1 ppb in soil and 0.01 ppb in water for all analytes (pp. 11, 30-31; Appendix 6, p. 209 of MRID 49805202; p. 10 of MRID 49805201). In the ECM, the LOQ was defined as the lowest fortification level which was validated in the study. In the ECM and ILV, the LOD in water was 0.002 ppb for all analytes. In the ECM, the LODs in soil were reported to be 0.02 ppb for prosulfuron, CGA300406 and CGA159902 and 0.06 ppb for CGA150829. In the ILV, the LOD in soil was reported to be 0.02 ppb for all analytes. No justification or calculations were provided to support the LOQs. In the ECM and ILV, the LODs were defined as 20% of the LOQ for all analytes/matrices, except for CGA150829 in soil where the LOD was defined as 60% of the LOQ in the ECM.

Table 4a. Method Characteristics for Prosulfuron (CGA152005) and Its Transformation Products, CGA300406, CGA159902, and CGA150829 in Water

Analyte ¹		Prosulfuron (CGA152005)	CGA300406	CGA159902	CGA150829
Limit of Quantitation (LOQ)		0.01 ppb			
Limit of Detection (LOD)		0.002 ppb			
Linearity (calibration curve r^2 and concentration range)	ECM ²	$r^2 = 0.9986-1.0000$ (Q)	$r^2 = 0.9986$ (Q)	$r^2 = 0.9986-0.9994$ (Q)	$r^2 = 0.9994-0.9998$ (Q) ³
		$r^2 = 0.9982-0.9998$ (C)	$r^2 = 0.9986-0.9996$ (C)	$r^2 = 0.9982-0.9990$ (C)	
	0.002-0.3 ng/mL				
	ILV	A ⁴	$r^2 = 0.99979892$ (Q) $r^2 = 0.99981069$ (C)	$r^2 = 0.99966252$ (Q) $r^2 = 0.99906274$ (C)	$r^2 = 0.99973420$ (Q) $r^2 = 0.99979387$ (C)
B ⁵		$r^2 = 0.9996$ (Q/C)	$r^2 = 0.9994$ (Q) $r^2 = 0.9982$ (C)	$r^2 = 0.9994$ (Q) $r^2 = 0.9996$ (C)	$r^2 = 0.9970$ (Q) $r^2 = 0.9982$ (C)
		0.002-10 ng/mL (0.00008-0.4 ng)			
Repeatable	ECM ⁶		Yes at LOQ and 10×LOQ. Two uncharacterized, unspecified water matrices were used.		
	ILV ⁷	Q	Yes at LOQ and 10×LOQ, but n = 4 at the LOQ.		
		C	Yes at 10×LOQ; No at LOQ (RSD 22.0% ; n = 4).	Yes at 10×LOQ; No at LOQ (RSD 60% ; n = 4). ⁸	Yes at 10×LOQ; No at LOQ (mean 129% ; RSD 34% ; n = 4). ⁸
		One uncharacterized, unspecified water matrix was used.			
Reproducible		Yes at 10×LOQ; Yes at LOQ, but n = 4. LOQ confirmation analysis was not validated for most analytes. ⁹ First trial with minor analytical modifications.			
Specific	ECM	Yes. Interferences were <5% of LOQ, based on peak area, at analyte retention times.			No . Analyte peak and peak integration was barely discernable due to major baseline noise at LOQ. ¹⁰
		Only chromatograms for LA water were provided.			
	ILV	Yes. Interferences were <i>ca.</i> <10% of LOQ, based on peak area, at analyte retention times for all analyses, except CGA159902 C ion. ⁹			
		Minor baseline noise and minor nearby peak interfered with analyte peak integration.	Interferences were <10% of LOQ, based on peak area, at analyte retention time.	Interferences were <i>ca.</i> 11% of LOQ (Q) and <i>ca.</i> 43% of the LOQ (C), based on peak height, at analyte retention time. C ion peak was barely discernable from the baseline noise at the LOQ. ¹¹	Interferences were <5% of LOQ, based on peak area, at analyte retention time.

Data were obtained from pp. 11, 30-31; Tables 4.1.1-4.1.2, pp. 21-22 (recovery results); Appendix 2, pp. 40-53 (calibration curves); Appendix 3, pp. 111-121 (chromatograms); Appendix 5, pp. 128-141 (calibration correlation coefficients); Appendix 6, p. 209 of MRID 49805202; pp. 10-12; Tables 2-9, pp. 25-32 (recovery results); Figure 1, p. 44-51 (calibration curves); Figures 6-21, pp. 100-115 (reagent blank and water chromatograms); Appendix C, pp. 141-148 (calibration correlation coefficients) of MRID 49805201 and DER Attachment 2. Q = quantitation ion transition; C = confirmation ion transition.

¹ Prosulfuron (CGA152005) = 1-(4-Methoxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]urea. CGA300406 = 1-(4-Hydroxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-

- phenylsulfonyl]urea. CGA159902 = 2-(3,3,3-Trifluoropropyl)phenylsulfonylurea. CGA150829 = 2-Amino-4-hydroxy-6-methyl-1,3,5-triazine.
- 2 ECM correlation coefficients for all analytes were reviewer-calculated from r values of 0.9993-1.0000 (Q) and 0.9991-0.9999 (C; matrices/analytes combined; Appendix 2, pp. 40-53; Appendix 3, pp. 128-141 of MRID 49805202; DER Attachment 2).
 - 3 In the ECM, two ion pair transitions were monitored for prosulfuron, CGA300406, and CGA159902 (quantitative and confirmatory); only one ion pair transition was monitored for CGA150829 (pp. 18-19 of MRID 49805202).
 - 4 One set of calibration curves with linear regression were provided (Figure 1, p. 44-51 of MRID 49805201). The reviewer determined that these were from the water analysis via comparison of the data in Figure 1 and Appendix C, pp. 141-148. Only "1/x weighted" r values were reported in Appendix C; however, the reviewer noted that the "1/x weighted" r values reported in Appendix C matched the r² values reported in Figure 1.
 - 5 The reported r² values were reviewer calculated based on the provided r values of 0.9985-0.9998 (Q) and 0.9991-0.9998 (C; analytes combined; Appendix C, pp. 141-148; DER Attachment 2).
 - 6 In the ECM, water samples from Louisiana and Texas were used in the study; no water characterization or further source description was reported (p. 11 of MRID 49805202).
 - 7 In the ILV, water sample was provided by R&D Research Farm, Inc.; a sample code was provided, 150527001-001, but the water was not characterized (p. 16 of MRID 49805201). The water source was not further specified.
 - 8 The ILV study authors excluded one sample from the statistical analysis in the LOQ confirmation ion for CGA300406 and CGA159902, n = 3 (103% mean, 25.2% RSD for CGA300406; 107% mean, 8.1% RSD for CGA159902; Table 5, p. 28 and Table 7, p. 30). The results provided were reviewer-calculated using all samples, n = 4 (see DER Attachment 2).
 - 9 A confirmatory method is not usually required when LC/MS and GC/MS is the primary method.
 - 10 Based on Appendix 3, pp. 120-121 of MRID 49805202.
 - 11 Based on Figures 16-17, pp. 110-111 of MRID 49805201.

Table 4b. Method Characteristics for Prosulfuron (CGA152005) and Its Transformation Products, CGA300406, CGA159902, and CGA150829 in Soil¹

Analyte ¹	Prosulfuron (CGA152005)	CGA300406	CGA159902	CGA150829	
Limit of Quantitation (LOQ)	0.1 ppb				
Limit of Detection (LOD)	ECM	0.02 ppb		0.06 ppb	
	ILV	0.02 ppb			
Linearity (calibration curve r ² and concentration range)	ECM ²	r ² = 0.9817 -0.9980 (Q)	r ² = 0.9968-0.9998 (Q)	r ² = 0.9906 -0.9990 (Q)	r ² = 0.9896 -0.9980 (Q) ³
		r ² = 0.9809 -0.9982 (C)	r ² = 0.9972-0.9996 (C)	r ² = 0.9898 -0.9978 (C)	
	0.008-0.6 ng/mL (0.00032-0.024 ng)				
	ILV ⁴	r ² = 0.9988 (Q) r ² = 0.9994 (C)	r ² = 0.9984 (Q) r ² = 0.9982 (C)	r ² = 0.9988 (Q) r ² = 0.9986 (C)	r ² = 0.9982 (Q) r ² = 0.9978 (C)
Repeatable	ECM ⁵	Yes at LOQ and 100×LOQ for all soil/depths, except for LOQ in TX soil 30-36” (means 127% Q and 131% C). ⁶	Yes at LOQ and 100×LOQ.		
		No samples prepared at 10×LOQ. Two uncharacterized soil matrices were used: samples from one depth for one soil and samples from six depths for the other soil.			
	ILV ⁷	Yes at LOQ and 10×LOQ. One uncharacterized, unspecified water matrix was used.			
Reproducible	Yes at LOQ and 10×LOQ. First ILV trial with minor analytical modifications.				
Specific	ECM	Yes. Interferences were <5% of LOQ, based on peak area, at analyte retention times.		No . Analyte peak and peak integration was barely discernable due to major baseline noise at LOQ and 10×LOQ; nearby baseline noise peaks were 50-200% LOQ peak height. ⁸	
		Only chromatograms for TX soil 0-6” were provided. Residues quantified in the controls of Texas soil 6-12”, 24-30” and 30-36” were ca. 2-25% of the LOQ. ⁹			
	ILV	Yes. Interferences were <10% of LOQ, based on peak area, at analyte retention times. Minor baseline noise interfered with analyte peak integration.	Peak tailing was observed in the LOQ and 10×LOQ chromatogram of Q ion peak.	C ion peak was poorly resolved from the baseline noise at the LOQ. ¹⁰	Baseline was sloped in C ion chromatograms.

Data were obtained from pp. 11, 30-31; Tables 4.1.3-4.1.9, pp. 23-29 (recovery results); Appendix 2, pp. 40-53 (calibration curves); Appendix 3, pp. 100-110 (chromatograms); Appendix 5, pp. 142-190 (calibration correlation coefficients); Appendix 6, p. 209 of MRID 49805202; pp. 10-12; Tables 10-17, pp. 33-40 (recovery results); Figure 1, p. 44-51 (calibration curves); Figures 6-9, pp. 100-109 (reagent blank chromatograms); Figures 22-33, pp. 116-127 (soil chromatograms); Appendix C, pp. 149-156 (calibration correlation coefficients) of MRID 49805201 and DER Attachment 2. Q = quantitation ion transition; C = confirmation ion transition.

¹ Prosulfuron (CGA152005) = 1-(4-Methoxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-

- phenylsulfonyl]urea. CGA300406 = 1-(4-Hydroxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]urea. CGA159902 = 2-(3,3,3-Trifluoropropyl)phenylsulfonylurea. CGA150829 = 2-Amino-4-hydroxy-6-methyl-1,3,5-triazine.
- 2 ECM correlation coefficients for all analytes were reviewer-calculated from r values of 0.9908-0.9999 (Q) and 0.9904-0.9998 (C; matrices/depths/analytes combined; Appendix 2, pp. 40-53; Appendix 3, pp. 142-190 of MRID 49805202; DER Attachment 2).
 - 3 In the ECM, two ion pair transitions were monitored for prosulfuron, CGA300406, and CGA159902 (quantitative and confirmatory); only one ion pair transition was monitored for CGA150829 (pp. 18-19 of MRID 49805202).
 - 4 The reported r^2 values were reviewer calculated based on the provided r values of 0.9991-0.9994 (Q) and 0.9989-0.9997 (C; analytes combined; Appendix C, pp. 149-156; DER Attachment 2).
 - 5 In the ECM, soil samples from Louisiana (0-6") and Texas (0-6", 6-12", 12-24", 24-30", and 30-36") were used in the study; no soil characterization was reported (p. 11 of MRID 49805202).
 - 6 The study authors excluded one sample from the statistical analysis of prosulfuron at the LOQ in TX soil 30-36", n = 4 (116% mean, 7.5% RSD for quantitation ion; 122% mean, 8.0% RSD for confirmation ion; Table 4.1.9, p. 29 of MRID 49805202). The results provided were reviewer-calculated using all samples, n = 5 (see DER Attachment 2).
 - 7 In the ILV, the soil sample was provided by R&D Research Farm, Inc.; a sample code was provided, 150527001-002, but the soil was not characterized (p. 16 of MRID 49805201).
 - 8 Based on Appendix 3, pp. 109-110 of MRID 49805202.
 - 9 Control residue percentages were reviewer-quantified using reported data in Appendix 5, pp. 142-190 of MRID 49805202.
 - 10 Based on Figure 29, p. 123 of MRID 498052021. A confirmatory method is not usually required when LC/MS and GC/MS is the primary method.
- Linearity is satisfactory when $r^2 \geq 0.995$.

IV. Method Deficiencies and Reviewer's Comments

1. The ILV was not independent of the ECM. According to the OCSPP guidelines, if the laboratory that conducted the validation belonged to the same organization as the originating laboratory, the analysts, study director, equipment, instruments, and supplies of the two laboratories must have been distinct and operated separately and without collusion, and the analysts and study director of the ILV must have been unfamiliar with the method both in its development and subsequent use in field studies. The laboratory which performed the ILV was the same as that which performed the ECM, ADPEN Laboratories, Inc., Jacksonville, Florida, and one of the co-authors (Alisia Ratliff, Project Coordinator) was the same between the ILV and ECM (pp. 1, 10; p. 192 of MRID 49805202; pp. 1, 7 of MRID 49805201). The Laboratory Manager, Steven Perez, for the ECM was the Study Director for the ILV. Additionally, the Study Monitor and Sample Custodian was the same in the ECM and ILV. Even though the reviewer noted that no communication between the ECM and ILV was reported prior to or during the ILV method validation and the ILV analytical laboratory equipment was distinct from that of the ECM, the overlap of study personnel between the ECM and ILV prevented the ILV from being considered independent of the ECM.
2. Matrices were not characterized in ILV and ECM. The matrices of the ECM were only soil depth and/or source location (p. 11 of MRID 49805202). In the ILV, the matrices were only described with a sample code (p. 16 of MRID 49805201). The reviewer also noted that the matrices of the ILV were reported with a sample number which began with "LA"; the reviewer could not determine if this denotation indicated that the ILV matrices were from LA, as they were in the ECM (Appendix C, pp. 141-156 of MRID 49805201). It could not be determined if the ILV was provided with the most difficult matrix with which to validate the method.

3. For the ILV analysis in water, the number of samples was insufficient for all analyses at the LOQ, $n = 4$ (pp. 11-12; Tables 2-9, pp. 25-32 of MRID 49805201). The study authors explained that “one matrix control sample (water) was fortified at the high fortification level (0.1 ppb) instead of at the LOQ (0.01 ppb); therefore, four LOQ and six 10×LOQ recoveries are being reported instead of five and five as per protocol” (p. 20).

For the ECM analysis in soil, no samples were prepared at 10×LOQ (Tables 4.1.3-4.1.9, pp. 23-29 of MRID 49805202).

OCSPP guidelines recommend that a minimum of five spiked replicates were analyzed at each concentration (*i.e.*, minimally, the LOQ and 10× LOQ) for each analyte.

4. The following method recoveries did not meet OCSPP Guideline 850.6100 criteria for precision and accuracy [mean recoveries for replicates at each spiking level between 70% and 120% and relative standard deviations (RSD) $\leq 20\%$].

For the ECM analysis in soil, prosulfuron at the LOQ in the Texas soil 30-36” where means were 127% and 131% for the quantitation and confirmation ions, respectively (Tables 4.1.3-4.1.9, pp. 23-29 of MRID 49805202; DER Attachment 2). The study authors excluded one sample from the statistical analysis for prosulfuron at the LOQ in the Texas soil 30-36”, $n = 4$ (116% mean, 7.5% RSD for quantitation ion; 122% mean, 8.0% RSD for confirmation ion; reported by the study authors; Table 4.1.9, p. 29). The results provided in the DER were reviewer-calculated using all samples, $n = 5$.

For the ILV analysis in water, the LOQ confirmation ion analyses of prosulfuron (RSD 22.0%), CGA300406 (RSD 60%), and CGA159902 (mean 129%, RSD 34%; pp. 11-12; Tables 2-9, pp. 25-32 of MRID 49805201; DER Attachment 2). The study authors excluded one sample from the confirmation ion statistical analyses of CGA300406 and CGA159902, $n = 3$ (103% mean, 25.2% RSD for CGA300406; 107% mean, 8.1% RSD for CGA159902; reported by the study authors; Table 5, p. 28 and Table 7, p. 30). The results provided in the DER were reviewer-calculated using all samples, $n = 4$.

5. The specificity of the method for water and soil matrices was not demonstrated in the ECM chromatograms of CGA150829 (Appendix 3, pp. 109-110; Appendix 3, pp. 120-121 of MRID 49805202). In the water and soil representative chromatograms, the analyte peak and peak integration was barely discernable due to major baseline noise at LOQ. In the soil, baseline noise even interfered at the 10×LOQ fortification. Also, nearby peaks of the baseline noise were 50-200% of the LOQ peak height.

The specificity of the method for water and soil matrices was not demonstrated in the ILV chromatograms of the confirmation ion of CGA159902 (Figure 17, p. 111; Figure 29, p. 123 of MRID 49805201). The confirmation ion peak was barely discernable from the baseline noise at the LOQ and matrix interferences in water were *ca.* 43% of the LOQ, based on peak height, at analyte retention time. The reviewer noted that a confirmatory method is not usually required when LC/MS and GC/MS is the primary method.

6. The following ECM linear regressions were unsatisfactory ($r^2 < 0.995$): prosulfuron (Q/C) in all soil matrices, except TX soil 30-36”; CGA159902 (Q/C) in Texas soils 6-12”, 12-24”

and 24-30"; and CGA150829 (Q) in Texas soils 6-12" and 24-30" (Appendix 2, pp. 40-53; Appendix 5, pp. 142-190 of MRID 49805202). Linearity is satisfactory when $r^2 \geq 0.995$.

7. In the ECM, only chromatograms for LA water and TX soil 0-6" samples were provided (Appendix 3, pp. 100-121; Appendix 5, pp. 128-190 of MRID 49805202). Chromatograms were not provided for the TX water, LA soil 0-6" and Texas soils 6-12", 12-24", 24-30", and 30-36". OCSPP guidelines states that representative chromatograms should be provided for reagent blanks, matrix blanks, standard curves, and spiked samples at the LOQ and $10 \times$ LOQ for all analytes in each matrix.

Additionally, chromatograms of the reagent blanks were not included.

8. The estimations of the LOQ in ECM and ILV were not based on scientifically acceptable procedures as defined in 40 CFR Part 136 (pp. 11, 30-31; Appendix 6, p. 209 of MRID 49805202; p. 10 of MRID 49805201). No calculations were reported in ECM or ILV to support the method LOQ. In the ECM, the LOQ was defined as the lowest fortification level which was validated in the study. In the ECM and ILV, the LODs were defined as 20% of the LOQ for all analytes/matrices, except for CGA150829 in soil where the LOD was defined as 60% of the LOQ in the ECM.

The LOD of CGA150829 in soil differed between the ECM and ILV.

Additionally, the lowest toxicological levels of concern in soil and water for the analytes were not reported in the ECM and ILV. An LOQ above toxicological levels of concern results in an unacceptable method classification

9. The sample recoveries for soil were corrected in the ECM. Calculations allowed for the correction of sample recoveries for residues quantified in the controls; residues were quantified in the controls for prosulfuron in the Texas soil 6-12" (both ions, *ca.* 2-16% of the LOQ), 24-30" (both ions, *ca.* 22-25% of the LOQ) and 30-36" (confirmation ion, *ca.* 3% of the LOQ), CGA300406 in the Texas soil 24-30" (quantitation ion, *ca.* 3% of the LOQ), and CGA159902 in the Texas soil 24-30" (quantitation ion, *ca.* 4% of the LOQ; control residues were reviewer-quantified using reported data in Appendix 5; p. 20; Appendix 5, pp. 142-190 of MRID 49805202). Sample recoveries for water were not corrected in the ECM since no residues were quantified in the controls (p. 20; Appendix 5, pp. 128-141).
10. The ILV modifications of analytical method were minor (p. 20; Table 19, p. 42 of MRID 49805201). A few monitored ion transitions were modified, and a confirmation ion transition was monitored for CGA150829. No modifications of the extraction method were reported. An updated ECM was not recommended to incorporate these ILV modifications since a confirmatory method is not usually required when LC/MS and GC/MS is the primary method.
11. The reviewer noted that the method date of the ECM (Final report completed December 16, 2015; Amended report completed January 12, 2016; p. 1 of MRID 49805202) was after the report date of the ILV (Final report issued October 29, 2015; p. 1 of MRID 49805201). The ECM Original Method (ADPEN-M1408) was dated December 15, 2015, which was still after the ILV date (Appendix 6, p. 192 of MRID 49805202).

12. The ECM Original Method (ADPEN-M1408; Appendix 6 of MRID 49805202) has 2 LC conditions, one for water samples and one for soil samples (Appendix 6, pp. 206-207 of MRID 49805202). The only difference between the two LC conditions was the mobile phase gradient time frames and run time. The ECM internal validation followed the water LC conditions.
13. ECM MRID 49805202 was an amended report. The changes made to the amended final report were listed in Appendix 7, p. 271 of MRID 49805202. The changes involved adding the Technical Report, the ECM Original Method, of Appendix 6 and all of the updates required for that addition.
14. In the Technical Report, the study author noted that matrix enhancement and suppression was observed and the use of matrix-matched standards was necessary (Appendix 6, p. 209 of MRID 49805202).
15. In the ILV, the total time required to perform the extraction was *ca.* 6 hours for a set of 30 water samples and *ca.* 8 hours for a set of 20-30 soil samples (p. 19 of MRID 49805201). The time for LC/MS/MS analysis was not reported. These same time requirements were also reported in the Technical Method (Appendix 6, p. 209 of MRID 49805202).
16. Communications between the ILV and Study Monitor were reported as only the discussion of the successful completion of the first trial (p. 19 of MRID 49805201). No other communication was reported.

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.

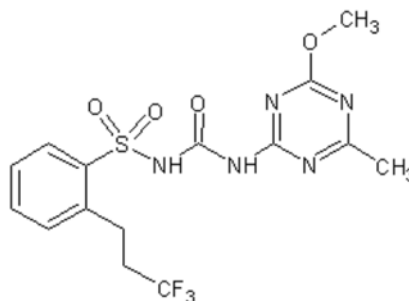
Attachment 1: Chemical Names and Structures**Prosulfuron (CGA152005)**

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CAS Name: 1-(4-Methoxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]urea

CAS Number: 94125-34-5

SMILES String: Not found

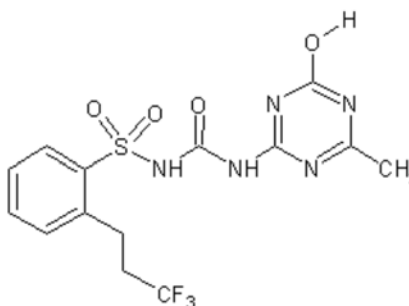
**CGA300406 (CSAA382278)**

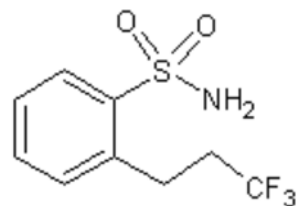
IUPAC Name: 1-(4-Hydroxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]urea

CAS Name: Not reported

CAS Number: Not reported

SMILES String: Not found



CGA159902 (CSAA148355)**IUPAC Name:** 2-(3,3,3-Trifluoropropyl)phenylsufonylurea**CAS Name:** Not reported**CAS Number:** Not reported**SMILES String:** Not found**CGA150829 (CSAA139483)****IUPAC Name:** 2-Amino-4-hydroxy-6-methyl-1,3,5-triazine**CAS Name:** Not reported**CAS Number:** Not reported**SMILES String:** Not found