

Analytical method for Atrazine, Simazine, Propazine, G-30033, G-28279, G-28273, Ametryn, Prometryn, GS-11354, GS-11355, GS-26831, S-Metolachlor, Metolachlor-ESA, Metolachlor-OA and Mesotrione in water

Reports: ECM 1: EPA MRID No.: 47629802. Huang, S.-B., T.J. Mayer, and R.A. Yokley. 2006. Atrazine: Method - Analytical Method for the Determination of Atrazine, Simazine, Propazine, G-30033, G-28279, G-28273, Ametryn, Prometryn, GS-11354, GS-11355, GS-26831, S-Metolachlor, Metolachlor-ESA, Metolachlor-OA and Mesotrione in Water Using Direct-Aqueous-Injection ESI-LC/MS/MS, Including Validation Data. Syngenta Study No.: T001681-06. Report prepared, sponsored and submitted by Syngenta Crop Protection, Inc., Greensboro, North Carolina; 96 pages. Final report issued October 4, 2006.

ECM 2: EPA MRID No.: 49960502. Perez, S.R. 2016. Mesotrione. Proactive Monitoring of Mesotrione in Vulnerable Community Water Systems. Analytical Phase Report. Report and Task Nos.: T017170-04. Study No.: ADPEN-901-T017170-04. Report prepared by ADPEN Laboratories, Inc., Jacksonville, Florida, sponsored and submitted by Syngenta Crop Protection, Inc., Greensboro, North Carolina; 96 pages. Final report issued May 4, 2016.

ILV: EPA MRID No. 49960503. Rees, S. 2014. Atrazine, Simazine, Propazine, G-30033, G-28279, G-28273, Ametryn, Prometryn, GS-11354, GS-11355, GS-26831, S-Metolachlor, Metolachlor-ESA, Metolachlor-OA and Mesotrione. Independent Laboratory Validation of Residue Method (Syngenta Number T001681-06) for the Determination of Atrazine, Simazine, Propazine, G-30033, G-28279, G-28273, Ametryn, Prometryn, GS-11354, GS-11355, GS-26831, S-Metolachlor, Metolachlor-ESA, Metolachlor-OA and Mesotrione in Water by LC-MS/MS. Final Report. Report and Study Nos.: 69608. Task No.: TK0049794. Report prepared by Morse Laboratories, LLC, Sacramento, California, and ABC Laboratories, Inc., Columbia, Missouri (p. 3), and sponsored and submitted by Syngenta Crop Protection, LLC, Greensboro, North Carolina; 766 pages (including page 385A). Final report issued May 9, 2014.

Document No.: MRIDs 47629802 & 49960502 & 49960503

Guideline: 850.6100

Statements: ECM 1: The study was conducted in accordance with the USEPA FIFRA Good Laboratory Practice (GLP) standards (40 CFR Part 160; p. 3 of MRID 47629802). Signed and dated No Data Confidentiality, GLP, and Quality Assurance statements were provided (pp. 2-4). An Authenticity statement was not included.

ECM 2: The study was not conducted in accordance with the USEPA FIFRA GLP standards (40 CFR Part 160; pp. 3, 5 of MRID 49960502). Signed and dated No Data Confidentiality, GLP, and Quality Assurance statements were

provided (pp. 2-3, 5-6). The Authenticity statement was included with the Quality Assurance statement.

ILV: The study was conducted in accordance with the USEPA GLP standards (40 CFR Part 160; p. 3 of MRID 49960503). Signed and dated No Data Confidentiality, GLP, and Quality Assurance statements were provided (pp. 2-4). The Authenticity statement was included with the Quality Assurance statement.

Classification: This analytical method is classified as **supplemental for mesotrione** in ground water, surface water, and deionized water. The method was not validated for treated/finished water. Since the reported method LOQs were not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQs are the lowest level of method validation (LLMVs) rather than LOQs. It could not be determined if an Updated ECM should be submitted since details of the necessary analytical corrections prior to ILV trial #2 were not reported.

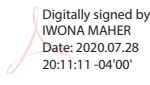
The following deficiencies were found in the ILV: The ILV did not validate the method for deionized or treated/finished water matrices. ILV performance data was not acceptable for the LOQ analyses in ground water of G-28279, prometryn, and S-metolachlor. The specificity of the method for G-28279, G-28273, GS-26831 and metolachlor-OA in surface and ground water and for atrazine and GS-11355 in surface water was not supported by ILV representative chromatograms. The method LOD was not reported.

The following deficiencies were found in ECM 1: No samples were prepared at the 10×LOQ fortification for G-28273 in the four water matrices. Individual correlation coefficients for linearity were not provided for any analyte, except atrazine. Representative chromatograms for all fortifications/matrices tested were not provided for review.

The following deficiencies were found in ECM 2: ECM 2 did not validate the method for mesotrione in surface, ground or treated/finished water matrices. No samples were prepared at the 10×LOQ fortification for mesotrione in deionized water. One of the ECM 2 data sets for mesotrione had an insufficient number of samples and unidentified water matrix; the linearity of the other ECM 2 data set for mesotrione had deficiencies. The method LOD was not reported.

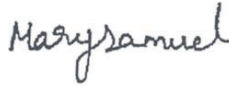
PC Code: 122990 (Mesotrione), 080803 (Atrazine), 080807 (Simazine), 080808 (Propazine), 080801 (Ametryn), 080805 (Prometryn), and 108801 (S-Metolachlor)

EFED Final Reviewer: Iwona L. Maher
Chemist

Signature: IWONA MAHER
Date:  Digitally signed by IWONA MAHER
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CDM/CSS- Lisa Muto, M.S.,

Signature: 

Dynamac JV	Environmental Scientist	Date:	04/30/2020
Reviewers:	Mary Samuel, M.S., Environmental Scientist	Signature:	
		Date:	04/30/2020

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 Method No. T001681-06 (ECM 1), is designed for the quantitative determination of atrazine, simazine, propazine, G-30033, G-28279, ametryn, prometryn, GS-11354, GS-11355, GS-26831, S-metolachlor, metolachlor-ESA, metolachlor-OA and mesotrione in water at the LOQ of 0.05 µg/L and of G-28273 in water at the LOQ of 0.50 µg/L using LC/MS/MS. **The method was not designed to resolve the stereoisomers of racemic mixtures, and the method was not validated for analytes containing thiomethyl groups in treated/finished water due to instability in the presence of chlorine, i.e., ametryn, prometryn, GS-11354, GS-11355, GS-26831, and mesotrione.** The respective LOQ (rather LLMV) is less than the lowest toxicological level of concern in water for mesotrione. Based on the performance data submitted by the ILV and/or ECMs, the LLMVs were equivalent to the reported method LOQs for all analytes in surface and ground water, except for G-28279, prometryn, and S-metolachlor in ground water (LLMV = 0.5 µg/L).

The ECM 1 validated the method for nine of the fifteen analytes using four characterized water matrices (deionized, ground, surface, and treated water) and for the other six analytes using three of the four characterized water matrices (deionized, ground, and surface water). The ECM 2 validated the method for mesotrione in uncharacterized deionized water and an unspecified water using Syngenta Method No. T001681-06. The ILV validated the method for all fifteen analytes using two characterized water matrices (surface and ground) in the second trial, with insignificant analytical instrument and parameter modifications. The first trial was unsuccessful due to low recoveries (individual recoveries, 17-67%) for ametryn, prometryn, propazine, and S-metolachlor in surface water. The second trial was initiated after instrument maintenance and correcting suppression matrix effects. The ILV was performed as a validation of ECM 1. Deionized water and treated/finished water were not included as ILV test water matrices. Although communications regarding remedying the low recoveries occurred between the ILV study author and Syngenta Study Sponsor/Monitor (not involved with ECM 1), details of the necessary analytical corrections were not reported, so it could not be determined if an Updated ECM should be submitted. The reviewer also believed that ILV performance and specificity data suggested that matrix-matched standards and/or a more rigorous samples processing procedure may be necessary to improve method reproducibility.

In ECM 1 and ECM 2, analytes were identified and quantified using one ion transition. In the ILV, three ion transitions were reported, but only one ion transition was used for quantification. A confirmatory method is not usually required when LC/MS or GC/MS is used as the primary method to generate data.

All ILV performance data was satisfactory at 0.05 µg/L and 0.5 µg/L in surface and ground water for atrazine, simazine, propazine, G-30033, ametryn, GS-11354, GS-11355, GS-26831, metolachlor-ESA, metolachlor-OA and mesotrione. All ILV performance data was satisfactory at 0.05 µg/L and 0.5 µg/L in surface water for atrazine G-28279, prometryn, and S-metolachlor; however, performance data was only satisfactory at 0.5 µg/L in ground water for these analytes. ILV performance data was satisfactory for G-28273 at 0.5 µg/L and 5.0 µg/L in surface and ground water. ILV linearity was acceptable for all analytes/matrices. ILV specificity was acceptable for all analytes in both matrices, except for G-28279, G-28273, GS-26831 and metolachlor-OA in surface and ground water and for atrazine and GS-11355 in surface water. Although matrix interferences were not observed in most of the unacceptable chromatograms, baseline noise interfered with analyte peak integration, and analyte peak was small compared to baseline noise and hard to distinguish. The LOD was not reported in the ILV.

All ECM 1 performance data was satisfactory at 0.05 µg/L and 0.5 µg/L for atrazine, simazine, propazine, G-30033, G-28279, S-metolachlor, metolachlor-ESA, and metolachlor-OA in four water matrices (deionized, ground, surface, and treated water). All ECM 1 performance data was satisfactory at 0.05 µg/L and 0.5 µg/L for ametryn, prometryn, GS-11354, GS-11355, GS-26831, and mesotrione in three water matrices (deionized, ground, and surface water). ECM 1 performance data was satisfactory for G-28273 at 0.5 µg/L in four water matrices (deionized, ground, surface, and treated water); no samples prepared at 5.0 µg/L. ECM 1 linearity data was acceptable; however, individual correlation coefficients for linearity were only provided for atrazine. ECM 1 did not provide full support for the specificity of the method because chromatograms were only provided for the surface water matrix and chromatograms were not provided for all fortifications tested.

All ECM 2 performance data was satisfactory at 0.05 µg/L for mesotrione in deionized water; no samples prepared at 0.5 µg/L. In unspecified water, ECM 2 performance data was satisfactory at 0.05 µg/L and 0.5 µg/L for mesotrione; however, only three replicates were prepared for each fortification. ECM 2 linearity was not satisfactory for two of 13 sample sets of mesotrione in deionized water. The LOD was not reported in the ECM 2.

Table 1. Analytical Method Summary

Analyte(s) by Pesticide	MRID		EPA Review	Matrix	Method Date (dd/mm/yyyy)	Registrant	Analysis	Limit of Quantitation (LOQ)*
	Environmental Chemistry Method	Independent Laboratory Validation						
Mesotrione	47629802 ¹ & 49960502 ²	49960503 ^{3,4}		Ground, Surface, and Deionized Water	04/10/2006 (ECM 1) 04/05/2016 (ECM 2)	Syngenta Crop Protection, Inc.	LC/MS/MS	0.05 µg/L
G-28273	47629802 ¹				0.50 µg/L			
Atrazine					0.05 µg/L			
G-30033								
G-28279								
Simazine								
Propazine								
Ametryn								
Prometryn								
GS-11354								
GS-11355								
GS-26831								
<i>S</i> - Metolachlor								
Metolachlor- ESA								
Metolachlor- OA								
G-28273		47629802 ¹	None submitted			Finished/ Treated Water	04/10/2006	
Atrazine				0.05 µg/L				
G-30033								
G-28279								
Simazine								
Propazine								
<i>S</i> - Metolachlor								
Metolachlor- ESA								
Metolachlor- OA								

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

1 MRID 47629802 = ECM 1 (Syngenta Method T001681-06). In the ECM 1, deionized water (Picopure purification system; pH 6.4, hardness 3.0 mg equivalent CaCO₃/L, 4.0 ppm total dissolved solids), ground (well; pH 7.1, hardness 43 mg equivalent CaCO₃/L, 108 ppm total dissolved solids), surface water (reservoir; pH 6.2, hardness 15 mg equivalent CaCO₃/L, 14 ppm total dissolved solids), and treated/finished water (pH 7.5, hardness 81 mg equivalent CaCO₃/L, 162 ppm total dissolved solids) were used in the study (pp. 15-16; Appendix 1, p. 70 of MRID 47629802). The deionized water was collected from Syngenta laboratory L-2021. The ground and treated

- water were collected from two separate residential water supplies: residential well in Summerfield, North Carolina, and residential tap in Belews Creek, North Carolina, respectively. The surface water was collected from a local municipality reservoir, a small lake in Kernersville, North Carolina. The water characterization was provided by Agvise Laboratories (Northwood, North Dakota).
- 2 MRID 49960502 = ECM 2. Syngenta Method T001681-06 was used for sample analysis; however, mesotrione was the only analyte for fortifications (pp. 14-16 of MRID 49960502). ECM 2 referenced ECM 1 (p. 17). For the Method Verification set, water samples were only described as “simulated samples” (pp. 14-15, 17; Tables 3-4, pp. 21-22). For the Method Performance set, no water description was reported; the reviewer determined that deionized water was used based on Figures 4-5, pp. 90-91 of MRID 49960502. No water characterization was provided.
 - 3 In the ILV, the surface (Sample ID: RIMV00312-0001 SURFACE; pH 7.3, hardness 27 mg equivalent CaCO₃/L, 58 ppm total dissolved solids) and ground water (Sample ID: RIMV00312-0002 GROUND; pH 7.5, hardness 59 mg equivalent CaCO₃/L, 122 ppm total dissolved solids) matrices used in the study were provided by the Sponsor and characterized by Agvise Laboratories (Northwood, North Dakota; p. 23; Appendix 8, pp. 764-765 of MRID 49960503). Water sources were not reported.
 - 4 The ILV was performed as a validation of ECM 1 (p. 14 of MRID 49960503).

I. Principle of the Method

ECM 1 MRID 47629802 (Syngenta Method T001681-06)

Samples (9.0 mL) was fortified, as necessary, with 1.0 mL of individual 0.0005 µg/mL standard solutions in methanol (pp. 7, 12-13 of MRID 47629802). The sample was further diluted, if necessary. An aliquot (800-1000 µL, *ca.* 1 mL) was transferred to an autosampler vial and analyzed by LC/MS/MS. Note: water samples were to be filtered or centrifuged prior to analysis, if necessary.

Samples were analyzed using a Perkin Elmer Series 200 HPLC coupled to an Applied Biosystems/MDS Sciex API 4000 triple quadrupole MS (pp. 13-14; Table 2, pp. 20-21 of MRID 47629802). The following LC conditions were used: Zorbax SB-AQ column (4.6 mm x 50 mm, 3.5 µm, column temperature 25°C), ColumnSaver filter, mobile phase of (A) 0.1% formic acid in water and (B) 0.1% formic acid in acetonitrile [percent A:B (v:v) at 0.0 min. 95:5, 2.0-3.0 min. 5:95, 4.0-6.0 min. 95:5], and injection volume of 50 µL. The following MS/MS conditions were used: temperature 700°C, positive (all analytes, except Metolachlor-ESA, Metolachlor-OA, and Mesotrione) or negative (Metolachlor-ESA, Metolachlor-OA, and Mesotrione) mode, and multiple reaction monitoring (MRM). Analytes were identified using one ion pair transition as follows: *m/z* 145.7→104.0 for G-28273, *m/z* 158.2→110.0 for GS-26831, *m/z* 174.2→96.2 for G-28279, *m/z* 186.1→96.0 for GS-11355, *m/z* 188.3→104.0 for G-30033, *m/z* 200.3→158.0 for GS-11354, *m/z* 202.1→132.1 for simazine, *m/z* 216.1→174.2 for atrazine, *m/z* 228.2→186.1 for ametryn, *m/z* 242.0→158.2 for prometryn, *m/z* 230.2→145.9 for propazine, *m/z* 284.2→176.3 for S-metolachlor, *m/z* 328.2→121.0 for metolachlor-ESA, *m/z* 278.1→206.3 for metolachlor-OA, and *m/z* 338.0→290.8 for mesotrione. Expected retention times were 1.91, 1.85, 2.16, 2.01, 2.29, 2.10, 2.48, 2.60, 2.28, 2.38, 2.70, 2.87, 2.35, 2.44-2.57, and 2.55 minutes for G-28273, GS-26831, G-28279, GS-11355, G-30033, GS-11354, Simazine, Atrazine, Ametryn, Prometryn, Propazine, S-Metolachlor, Metolachlor-ESA, Metolachlor-OA, and Mesotrione, respectively.

The study author reported that 1) Metolachlor-OA was typically two peaks and both were integrated for quantification and 2) the method was not designed to resolve the stereoisomers of racemic mixtures (p. 14; Table 2, p. 21).

ECM 2 MRID 49960502 (Report and Task No.s T017170-04)

Samples were processed and analyzed as in Syngenta Method T001681-06; however, mesotrione was the only analyte for fortifications (pp. 14-17 of MRID 49960502). The sample was further diluted, if necessary. An aliquot (1 mL) was transferred to an autosampler vial and analyzed by LC/MS/MS. Samples were centrifuged prior to analysis if sample was cloudy or particulates were visible.

Samples were analyzed using an Agilent 1200 Binary Pump SL HPLC coupled to an Applied Biosystems API 4000 QT MS (Tables 1-2, pp. 19-20 of MRID 49960502). The following LC conditions were used: Zorbax SB-AQ column (4.6 mm x 50 mm, 5 μ , column temperature 25°C), mobile phase of (A) 0.1% formic acid in water and (B) formic acid in water (assumed by reviewer to be a typographical error) [percent A:B (v:v) at 0.00 min. 95.0:5.0, 1.15 min. 38.3:61.7, 2.00-3.00-4.00 min. 5.0:95.0, 4.10-6.0 min. 95.0:5.0], and injection volume of 40 μ L. The following MS/MS conditions were used: temperature 550°C, negative mode, and multiple reaction monitoring (MRM). Mesotrione was identified using one ion pair transition as follows: m/z 337.91 \rightarrow 290.90 for mesotrione. Expected retention time was 3.46 minutes. The LC/MS/MS conditions were similar to those of Syngenta Method T001681-06.

ILV

The independent laboratory performed the ECM as written, except for insignificant modifications of analytical instrumentation and parameters (pp. 14, 26-32, 38 of MRID 49960503). An Acquity UPLC coupled to an AB Sciex QTRAP 6500 MS was used. The following LC conditions were used: Zorbax SB-AQ column (4.6 mm x 50 mm, 3.5 μ m, column temperature 25°C), Phenomenex guard cartridge (Widopore C18, 4 x 2.0 mm), mobile phase of (A) 0.1% formic acid in water and (B) 0.1% formic acid in acetonitrile [percent A:B (v:v) at 0.0 min. 95.0:5.0, 2.0-4.0 min. 5.0:95.0, 4.0-6.0 min. 95.0:5.0], and injection volume of 10 μ L. The following MS/MS conditions were used: temperature 550°C, positive (all analytes, except Metolachlor-ESA, Metolachlor-OA, and Mesotrione) or negative (Metolachlor-ESA, Metolachlor-OA, and Mesotrione) mode, and multiple reaction monitoring (MRM). Analytes were identified using three ion pair transitions (primary, confirmatory 1, and confirmatory 2, respectively) as follows: m/z 216 \rightarrow 174, m/z 216 \rightarrow 104, and m/z 216 \rightarrow 132 for atrazine, m/z 202 \rightarrow 132, m/z 202 \rightarrow 124, and m/z 202 \rightarrow 104 for simazine, m/z 230 \rightarrow 146 and m/z 230 \rightarrow 188 for propazine (only two monitored ion transitions), m/z 188 \rightarrow 104, m/z 188 \rightarrow 146, and m/z 188 \rightarrow 110 for G-30033, m/z 174 \rightarrow 96, m/z 174 \rightarrow 104, and m/z 174 \rightarrow 146 for G-28279, m/z 146 \rightarrow 104, m/z 146 \rightarrow 110, and m/z 146 \rightarrow 79 for G-28273, m/z 228 \rightarrow 186, m/z 228 \rightarrow 116, and m/z 228 \rightarrow 138 for ametryn, m/z 242 \rightarrow 158, m/z 242 \rightarrow 200, and m/z 242 \rightarrow 152 for prometryn, m/z 200 \rightarrow 158, m/z 200 \rightarrow 116, and m/z 200 \rightarrow 110 for GS-11354, m/z 186 \rightarrow 96, m/z 186 \rightarrow 158, and m/z 186 \rightarrow 91 for GS-11355, m/z 158 \rightarrow 110, m/z 158 \rightarrow 116, and m/z 158 \rightarrow 85 for GS-26831, m/z 284 \rightarrow 176, m/z 284 \rightarrow 252, and m/z 284 \rightarrow 212 for S-metolachlor, m/z 328 \rightarrow 121, m/z 328 \rightarrow 192, and m/z

328→135 for metolachlor-ESA, m/z 278→206, m/z 278→174, and m/z 278→158 for metolachlor-OA, and m/z 338→291, m/z 338→212, and m/z 338→248 for mesotrione. Approximate retention times were *ca.* 2.6, 2.5, 2.7, 2.3, 2.2, 1.9, 2.3, 2.4, 2.1, 2.0, 1.8, 2.8, 2.4, 2.5, and 2.5 minutes for Atrazine, Simazine, Propazine, G-30033, G-28279, G-28273, Ametryn, Prometryn, GS-11354, GS-11355, GS-26831, S-Metolachlor, Metolachlor-ESA, Metolachlor-OA, and Mesotrione, respectively. In the ILV, the injection volume was reduced from 50 μ L to 10 μ L, and one or two confirmatory ion transitions were monitored. Quantification was performed using only one ion transition, the primary ion transition (p. 30; Figure 1, pp. 75-89). The ILV primary ion transition were similar to those of the ECM. The ILV modifications did not warrant an updated ECM.

LOQ/LOD

In the ECM 1 and ILV, Limits of Quantification (LOQs) in water were 0.50 μ g/L for G-28273 and 0.05 μ g/L for Atrazine, Simazine, Propazine, G-30033, G-28279, G-28273, Ametryn, Prometryn, GS-11354, GS-11355, GS-26831, S-Metolachlor, Metolachlor-ESA, Metolachlor-OA, and Mesotrione (pp. 13, 17 of MRID 47629802; pp. 9, 34, of MRID 49960503). In the ECM 1, the Limits of Detection (LODs) in water were 10 pg (equivalent to 0.2 pg/ μ L, 0.2 μ g/L) for G-28273 and 1.0 pg (equivalent to 0.02 pg/ μ L, 0.02 μ g/L) for Atrazine, Simazine, Propazine, G-30033, G-28279, Ametryn, Prometryn, GS-11354, GS-11355, GS-26831, S-Metolachlor, Metolachlor-ESA, Metolachlor-OA, and Mesotrione. The LODs were not reported in the ILV. In ECM 2, the LOQ for mesotrione in water was reported as 0.05 μ g/L; the LOD was not reported (p. 17 of MRID 49960502).

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

II. Recovery Findings

ECM 1 (MRID 47629802 - Syngenta Method T001681-06): Mean recoveries and relative standard deviations (RSD) were within guideline requirements (mean 70-120%; RSD \leq 20%) for analysis of atrazine, simazine, propazine, G-30033, G-28279, S-metolachlor, metolachlor-ESA, and metolachlor-OA in four water matrices (deionized, ground, surface, and treated water) at fortification levels of 0.05 μ g/L (LOQ), 0.10 μ g/L (2 \times LOQ), 0.50 μ g/L (10 \times LOQ), and 3.0 μ g/L (60 \times LOQ), except for metolachlor-OA in surface water at 0.10 μ g/L (RSD 26%) and G-30033 at 0.10 μ g/L in deionized water (RSD 22%) and in treated water (RSD 21%; Tables 3-6, pp. 22-43). Mean recoveries and RSDs were within guidelines for analysis of ametryn, prometryn, GS-11354, GS-11355, GS-26831, and mesotrione in three water matrices (deionized, ground, and surface water) at fortification levels of 0.05 μ g/L (LOQ), 0.10 μ g/L (2 \times LOQ), 0.50 μ g/L (10 \times LOQ), and 3.0 μ g/L (60 \times LOQ), except for mesotrione in surface water at 0.10 μ g/L (mean 133% RSD 68%). Mean recoveries and RSDs were within guidelines for analysis of G-28273 in four water matrices (deionized, ground, surface, and treated water) at fortification levels of 0.50 μ g/L (LOQ) and 3.0 μ g/L (6 \times LOQ); no samples were prepared at 5.0 μ g/L (10 \times LOQ). For several analyte recoveries at 0.10 μ g/L in a few matrices, statistics were reviewer-calculated (n =

10) since the study report statistics excluded one of the recovery values due to presumed laboratory error (n = 9). Analytes were identified and quantified using one ion transition; a confirmatory method is not usually required when LC/MS or GC/MS is used as the primary method to generate data. According to the calculation method, recovery results were corrected when residues were quantified in the controls (p. 15). The deionized water (Picopure purification system; pH 6.4, hardness 3.0 mg equivalent CaCO₃/L, 4.0 ppm total dissolved solids), ground (well; pH 7.1, hardness 43 mg equivalent CaCO₃/L, 108 ppm total dissolved solids), surface water (reservoir; pH 6.2, hardness 15 mg equivalent CaCO₃/L, 14 ppm total dissolved solids), and treated/finished water (pH 7.5, hardness 81 mg equivalent CaCO₃/L, 162 ppm total dissolved solids) were used in the study (pp. 15-16; Appendix 1, p. 70). The deionized water was collected from Syngenta laboratory L-2021. The ground and treated water were collected from two separate residential water supplies: residential well in Summerfield, North Carolina, and residential tap in Belews Creek, North Carolina, respectively. The surface water was collected from a local municipality reservoir, a small lake in Kernersville, North Carolina. The water characterization was provided by Agvise Laboratories (Northwood, North Dakota).

ECM 2 (MRID 49960502 - Syngenta Method T001681-06): Mean and RSDs were within guidelines for analysis of mesotrione at fortification levels of 0.05 µg/L (LOQ), 0.50 µg/L (10×LOQ), and 5.0 µg/L (100×LOQ) in the Method Verification set; however, an insufficient number of samples (n = 3) was prepared for each fortification (p. 17; Table 3, p. 21). Water samples were not characterized and only described as “simulated samples” (pp. 14-15, 17). Mean and RSDs were within guidelines for analysis of mesotrione at fortification levels of 0.05 µg/L (LOQ) and 5.0 µg/L (100×LOQ) in Method Performance set; no samples were prepared at 0.50 µg/L (10×LOQ; p. 17; Table 4, p. 22). No water description or characterization was reported; the reviewer determined that deionized water was used based on Figures 4-5, pp. 90-91 of MRID 49960502. Mesotrione was identified and quantified using one ion transition; a confirmatory method is not usually required when LC/MS or GC/MS is used as the primary method to generate data. According to the calculation method, recovery results were corrected when residues were quantified in the controls (p. 16). Samples were processed and analyzed as in Syngenta Method T001681-06; however, mesotrione was the only analyte for fortification (pp. 14-16). ECM 2 referenced ECM 1 (p. 17).

ILV (MRID 49960503): Mean recoveries and RSDs were within guidelines for analysis of atrazine, simazine, propazine, G-30033, G-28279, ametryn, prometryn, GS-11354, GS-11355, GS-26831, S-metolachlor, metolachlor-ESA, metolachlor-OA and mesotrione in two water matrices at fortification levels of 0.05 µg/L (LOQ) and 0.50 µg/L (10×LOQ), except for the LOQ analyses in ground water of G-28279 (RSD 26%), prometryn (mean 69%), and S-metolachlor (mean 68%; Tables 2-3, pp. 44-73). Mean recoveries and RSDs were within guidelines for analysis of G-28273 in two water matrices at fortification levels of 0.50 µg/L (LOQ) and 5.0 µg/L (10×LOQ). Analytes were identified using two or three ion transitions but quantified using only one ion transition; a confirmatory method is not usually required when LC/MS or GC/MS is used as the primary method to generate data. According to the calculation method, recovery results were corrected when residues were quantified in the controls. The surface (Sample ID: RIMV00312-0001 SURFACE; pH 7.3, hardness 27 mg equivalent CaCO₃/L, 58 ppm total dissolved solids) and ground water (Sample ID: RIMV00312-0002 GROUND; pH 7.5, hardness

59 mg equivalent CaCO₃/L, 122 ppm total dissolved solids) matrices used in the study were provided by the Sponsor and characterized by Agvise Laboratories (Northwood, North Dakota; p. 23; Appendix 8, pp. 764-765). Water sources were not reported. The method was validated for all analytes in surface and ground water matrices at both fortification levels after the second trial, with insignificant analytical instrument and parameter modifications (pp. 9, 14, 26-34, 38 of MRID 49960503). The first trial was unsuccessful due to inconsistent recoveries for various analytes [low recoveries (individual recoveries, 17-67%) for ametryn, prometryn, propazine, and S-metolachlor in surface water; Appendix 7, pp. 733-744]. The second trial was initiated after instrument maintenance and correcting matrix effects (suppression; p. 9). The ILV was performed as a validation of ECM 1 (p. 14). Deionized water and treated/finished water were not included as ILV test water matrices. Although communications regarding remedying the low recoveries occurred between the ILV study author and Syngenta Study Sponsor/Monitor (not part of ECM 1), details of the necessary analytical corrections were not reported, so it could not be determined if an Updated ECM should be submitted (Appendix 6, pp. 575, 650-654).

Table 2. Initial Validation Method Recoveries for Atrazine, Simazine, Propazine, G-30033, G-28279, G-28273, Ametryn, Prometryn, GS-11354, GS-11355, GS-26831, S-Metolachlor, Metolachlor-ESA, Metolachlor-OA and Mesotrione in Water

Analyte	Fortification Level (µg/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
ECM 1 – MRID 47629802 (Syngenta Method T001681-06)^{1,2}						
Deionized Water						
Atrazine	0.05 (LOQ)	10	102-113	107	3.7	3.4
	0.10	10 ³	51.8-110	97	17	17
	0.50	10	99.6-109	104	3.3	3.2
	3.0	10	101-107	105	2.0	1.9
G-30033	0.05 (LOQ)	10	90.8-111	102	6.7	6.5
	0.10	10 ³	37.0-114	96	22	22
	0.50	10	94.6-114	102	5.9	5.8
	3.0	10	99.9-105	102	1.7	1.7
G-28279	0.05 (LOQ)	10	92.4-117	105	10	9.5
	0.10	10 ³	47.4-116	102	20	20
	0.50	10	101-114	109	4.1	3.7
	3.0	10	108-117	112	3.8	3.4
G-28273	0.50	10	82.4-109	100	9.0	9.1
	3.0	10	96.1-101	98.7	1.8	1.8
Simazine	0.05 (LOQ)	10	91.6-107	99	5.7	5.8
	0.10	10 ³	60.2-103	94	12	13
	0.50	10	95.2-103	99.4	3.0	3.0
	3.0	10	98.7-105	101	1.9	1.9
Propazine	0.05 (LOQ)	10	93.5-101	97.7	2.4	2.4
	0.10	10 ³	67.4-103	93	11	12
	0.50	10	94.6-101	99.3	2.1	2.2
	3.0	10	94.7-100	96.7	1.6	1.7
Ametryn	0.05 (LOQ)	10	83.0-95.6	89.7	3.4	3.8
	0.10	10 ³	69.7-95.4	90.6	7.5	8.3
	0.50	10	90.2-96.2	93.8	2.2	2.3
	3.0	10	94.5-99.9	97.3	1.8	1.8
Prometryn	0.05 (LOQ)	10	90.3-98.2	94.8	2.6	2.7
	0.10	10 ³	78.6-98.9	94.7	5.9	6.3
	0.50	10	92.9-97.2	94.9	1.5	1.6
	3.0	10	91.9-97.9	95.8	1.7	1.8
GS-11354	0.05 (LOQ)	10	89.8-105	98.8	4.9	4.9
	0.10	10 ³	44.5-105	95	18	19
	0.50	10	93.1-103	98.7	3.0	3.0
	3.0	10	98.0-102	100	1.4	1.4
GS-11355	0.05 (LOQ)	10	89.2-112	99.3	6.1	6.2
	0.10	10 ³	71.4-108	102	11	11
	0.50	10	99.2-114	107	4.9	4.6
	3.0	10	97.3-105	101	2.6	2.6

Analyte	Fortification Level (µg/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
GS-26831	0.05 (LOQ)	10	90.8-121	107	12	11
	0.10	10 ³	87.0-117	107	9	8
	0.50	10	94.4-117	108	7.5	6.9
	3.0	10	96.0-109	103	4.4	4.2
S-Metolachlor	0.05 (LOQ)	10	73.6-115	100	11	11
	0.10	10 ³	65.6-112	90	13	14
	0.50	10	97.6-108	103	3.6	3.5
	3.0	10	93.3-105	98.8	3.5	3.6
Metolachlor-ESA	0.05 (LOQ)	10	87.1-98.7	93.8	4.0	4.3
	0.10	10	88.8-98.9	95.6	3.6	3.8
	0.50	10	95.0-103	98.9	2.4	2.4
	3.0	10	94.0-101	97.2	2.4	2.5
Metolachlor-OA	0.05 (LOQ)	10	91.4-103	97.8	3.8	3.8
	0.10	10	94.6-107	99.9	4.5	4.5
	0.50	10	98.7-105	101	2.5	2.5
	3.0	10	90.6-99.8	95.5	3.3	3.3
Mesotrione	0.05 (LOQ)	10	83.6-102	93.9	5.7	6.1
	0.10	10	94.2-105	98.5	3.4	3.5
	0.50	10	96.1-104	101	2.5	2.5
	3.0	10	96.6-102	98.6	1.8	1.8
Ground (Well) Water						
Atrazine	0.05 (LOQ)	10	91.8-113	101	7.2	7.1
	0.10	10	89.7-110	100	5.8	5.8
	0.50	10	95.6-104	100	2.4	2.4
	3.0	10	97.3-105	101	2.3	2.2
G-30033	0.05 (LOQ)	10	91.6-104	98.6	4.2	4.3
	0.10	10	90.8-106	100	5.1	5.1
	0.50	10	99.2-108	103	2.8	2.7
	3.0	10	97.3-103	101	1.9	1.9
G-28279	0.05 (LOQ)	10	93.8-115	105	7.4	7.1
	0.10	10	91.4-117	105	7.3	7.0
	0.50	10	98.7-108	103	3.3	3.2
	3.0	10	105-117	110	5.0	4.5
G-28273	0.50 (LOQ)	10	103-122	112	6.4	5.7
	3.0	10	100-114	107	4.4	4.1
Simazine	0.05 (LOQ)	10	96.8-111	106	4.9	4.7
	0.10	10	85.8-105	100	5.2	5.2
	0.50	10	100-104	103	1.3	1.2
	3.0	10	98.7-106	101	2.2	2.1
Propazine	0.05 (LOQ)	10	88.0-103	96.8	5.8	6.0
	0.10	10	85.5-103	94.6	5.4	5.8
	0.50	10	96.6-103	99.0	1.8	1.9
	3.0	10	95.9-103	100	2.1	2.1

Analyte	Fortification Level (µg/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
Ametryn	0.05 (LOQ)	10	93.1-101	97.3	2.4	2.4
	0.10	10	97.9-103	100	1.6	1.6
	0.50	10	99.4-105	102	2.0	1.9
	3.0	10	104-109	107	1.9	1.8
Prometryn	0.05 (LOQ)	10	98.6-106	102	2.7	2.7
	0.10	10	97.5-102	100	1.6	1.6
	0.50	10	97.5-106	101	2.7	2.6
	3.0	10	101-107	105	1.9	1.8
GS-11354	0.05 (LOQ)	10	97.4-105	100	2.5	2.5
	0.10	10	95.4-104	100	3.2	3.2
	0.50	10	96.3-103	100	2.3	2.3
	3.0	10	101-110	104	2.9	2.8
GS-11355	0.05 (LOQ)	10	96.4-110	102	4.4	4.4
	0.10	10	94.4-105	100	4.2	4.1
	0.50	10	98.4-106	103	2.6	2.5
	3.0	10	99.3-105	102	2.1	2.1
GS-26831	0.05 (LOQ)	10	87.2-116	98.2	8.1	8.3
	0.10	10	87.6-110	99.1	6.5	6.6
	0.50	10	100-114	106	4.9	4.6
	3.0	10	94.0-119	107	6.8	6.4
S-Metolachlor	0.05 (LOQ)	10	89.2-118	107	10	9.5
	0.10	10	91.2-113	100	7.7	7.7
	0.50	10	95.6-105	101	3.5	3.4
	3.0	10	93.3-104	98.0	3.4	3.5
Metolachlor-ESA	0.05 (LOQ)	10	92.8-113	103	5.7	5.5
	0.10	10	97.2-105	102	3.0	3.0
	0.50	10	99.2-105	102	2.0	1.9
	3.0	10	98.0-103	100	1.7	1.7
Metolachlor-OA	0.05 (LOQ)	10	93.4-109	98.8	4.7	4.8
	0.10	10	89.7-102	97.6	3.7	3.8
	0.50	10	97.9-108	102	3.1	3.1
	3.0	10	94.5-103	99.1	2.3	2.3
Mesotrione	0.05 (LOQ)	10	89.6-113	98.4	6.7	6.8
	0.10	10	91.0-103	97.9	3.9	4.0
	0.50	10	98.9-106	103	2.2	2.2
	3.0	10	99.3-105	101	1.8	1.8
	Surface (Reservoir) Water					
Atrazine	0.05 (LOQ)	10	92.0-104	97.2	4.4	4.5
	0.10	10	73.4-98.2	91.9	7.3	8.0
	0.50	10	90.6-98.3	94.2	2.3	2.4
	3.0	10	91.2-97.2	94.3	2.1	2.2
G-30033	0.05 (LOQ)	10	77.7-93.6	83.6	5.4	6.4
	0.10	10	75.1-92.5	81.7	6.4	7.8

122990 (Mesotrione), 080803 (Atrazine), 080807 (Simazine), 080808 (Propazine), 080801 (Ametryn), 080805 (Prometryn), and 108801 (*S*-Metolachlor)

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Analyte	Fortification Level (µg/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
	0.50	10	80.4-84.0	82.4	1.3	1.6
	3.0	10	80.7-83.9	82.5	1.1	1.3
G-28279	0.05 (LOQ)	10	66.5-103	89.1	9.8	11
	0.10	10	79.5-89.9	84.7	4.0	4.7
	0.50	10	80.3-85.5	82.8	1.9	2.3
	3.0	10	80.0-87.9	84.1	2.7	3.2
G-28273	0.50 (LOQ)	10	87.6-94.4	91.6	3.5	3.9
	3.0	10	93.3-100	96.7	2.1	2.2
Simazine	0.05 (LOQ)	10	81.5-97.6	89.3	4.8	5.4
	0.10	10	70.5-94.8	86.7	6.6	7.6
	0.50	10	84.0-94.0	88.8	3.4	3.8
	3.0	10	88.5-93.3	90.1	2.1	2.3
Propazine	0.05 (LOQ)	10	87.2-96.4	91.3	3.2	3.5
	0.10	10	70.1-96.8	89.2	7.5	8.4
	0.50	10	90.8-100	95.7	2.8	3.0
	3.0	10	94.7-99.3	96.7	1.7	1.7
Ametryn	0.05 (LOQ)	10	83.6-96.0	89.9	4.0	4.4
	0.10	10	88.2-97.4	93.0	2.7	2.9
	0.50	10	91.6-96.2	93.3	1.5	1.6
	3.0	10	94.0-97.9	95.8	1.2	1.2
Prometryn	0.05 (LOQ)	10	84.6-98.4	91.7	4.6	5.0
	0.10	10	86.1-98.4	94.4	3.5	3.7
	0.50	10	92.9-98.8	95.7	1.8	1.9
	3.0	10	95.9-102	98.9	1.8	1.9
GS-11354	0.05 (LOQ)	10	76.9-83.6	80.8	2.4	3.0
	0.10	10	77.7-84.2	81.4	2.0	2.5
	0.50	10	79.3-87.2	84.1	2.3	2.7
	3.0	10	84.0-86.7	85.4	1.1	1.3
GS-11355	0.05 (LOQ)	10	81.6-93.6	88.3	3.9	4.4
	0.10	10	75.6-82.6	80.3	2.1	2.7
	0.50	10	75.5-82.8	79.3	2.1	2.7
	3.0	10	76.7-80.7	79.2	1.4	1.8
GS-26831	0.05 (LOQ)	10	63.6-100	78.6	12	15
	0.10	10	66.2-86.6	76.5	6.9	9.0
	0.50	10	74.4-94.4	81.3	7.2	8.8
	3.0	10	76.7-89.3	82.3	3.6	4.4
<i>S</i> -Metolachlor	0.05 (LOQ)	10	99.8-117	111	6.5	5.9
	0.10	10	74.3-111	95.2	11	11
	0.50	10	92.7-105	100	3.7	3.7
	3.0	10	98.0-103	100	1.7	1.7
Metolachlor-ESA	0.05 (LOQ)	10	79.6-101	92.5	6.8	7.3
	0.10	10 ³	90.6-103	95	3	4
	0.50	10	92.3-100	96.5	2.5	2.5
	3.0	10	91.9-97.1	94.6	1.8	1.9
Metolachlor-OA	0.05 (LOQ)	10	80.3-105	94.5	6.8	7.2

Analyte	Fortification Level (µg/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
	0.10	10 ³	87.5-181	105	27	26
	0.50	10	95.5-109	102	5.0	4.9
	3.0	10	95.9-109	101	3.9	3.9
Mesotrione	0.05 (LOQ)	10	91.0-107	97.8	4.7	4.8
	0.10	10 ³	96.1-389	133	90	68
	0.50	10	101-109	105	2.5	2.4
	3.0	10	97.3-105	101	2.3	2.3
Treated (Finished) Water						
Atrazine	0.05 (LOQ)	10	101-114	107	4.0	3.8
	0.10	10 ³	68.7-111	101	13	13
	0.50	10	97.2-108	105	3.2	3.0
	3.0	10	99.2-106	102	2.2	2.1
G-30033	0.05 (LOQ)	10	84.9-107	96.4	6.3	6.5
	0.10	10 ³	39.9-105	94	19	21
	0.50	10	78.4-106	98.3	7.6	7.7
	3.0	10	90.5-96.0	93.2	1.7	1.8
G-28279	0.05 (LOQ)	10	82.0-123	102	10	9.9
	0.10	10 ³	56.2-113	99	16	16
	0.50	10	82.4-110	104	8.3	7.9
	3.0	10	100-105	102	1.8	1.8
G-28273	0.50 (LOQ)	10	74.5-105	92.1	8.8	9.6
	3.0	10	93.3-102	97.3	2.4	2.5
Simazine	0.05 (LOQ)	10	93.4-109	100	4.6	4.6
	0.10	10 ³	54.1-107	94	15	16
	0.50	10	90.7-106	100	4.3	4.3
	3.0	10	97.2-103	100	2.2	2.2
Propazine	0.05 (LOQ)	10	88.8-103	96.3	4.1	4.3
	0.10	10 ³	67.4-100	92	10	11
	0.50	10	94.8-105	99.2	3.4	3.4
	3.0	10	97.3-102	99.3	1.9	1.9
S-Metolachlor	0.05 (LOQ)	10	76.4-95.6	86.7	5.8	6.7
	0.10	10 ³	66.8-101	92	10	11
	0.50	10	94.4-104	100	2.9	2.9
	3.0	10	96.7-104	100	2.2	2.2
Metolachlor-ESA	0.05 (LOQ)	10	86.0-102	94.4	5.4	5.7
	0.10	10	88.4-105	97.3	5.0	5.1
	0.50	10	94.5-106	99.7	3.0	3.0
	3.0	10	94.6-99.8	96.8	1.7	1.7
Metolachlor-OA	0.05 (LOQ)	10	85.3-102	95.5	4.9	5.1
	0.10	10	93.1-103	99.3	3.3	3.3
	0.50	10	97.6-106	102	3.0	2.9
	3.0	10	92.7-101	97.5	2.6	2.7
ECM 2 – MRID 49960502 (Syngenta Method T001681-06)⁴						

Analyte	Fortification Level (µg/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
Water⁵						
Mesotrione	0.05 (LOQ)	3 ⁶	91.0-94.2	92.6	1.60	1.7
	0.50	3 ⁶	97.9-100.7	99.7	1.62	1.6
	5.0	3 ⁶	104.3-109.1	106.8	2.41	2.3
Deionized Water⁷						
Mesotrione	0.05 (LOQ)	13	70.0-99.3	83.2	7.86	9.45
	5.0	13	79.3-106.2	94.0	7.89	8.39

Data (recovery results were corrected when residues were quantified in the controls; p. 15 of MRID 47629802; p. 16 of MRID 49960502) were obtained from Tables 3-6, pp. 22-43 of MRID 47629802; Tables 3-4, pp. 21-22 of MRID 49960502; DER Attachment 2. Since the LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ.

1 Deionized water (Picopure purification system; pH 6.4, hardness 3.0 mg equivalent CaCO₃/L, 4.0 ppm total dissolved solids), ground (well; pH 7.1, hardness 43 mg equivalent CaCO₃/L, 108 ppm total dissolved solids), surface water (reservoir; pH 6.2, hardness 15 mg equivalent CaCO₃/L, 14 ppm total dissolved solids), and treated/finished water (pH 7.5, hardness 81 mg equivalent CaCO₃/L, 162 ppm total dissolved solids) were used in the study (pp. 15-16; Appendix 1, p. 70 of MRID 47629802). The deionized water was collected from Syngenta laboratory L-2021. The ground and treated water were collected from two separate residential water supplies: residential well in Summerfield, North Carolina, and residential tap in Belews Creek, North Carolina, respectively. The surface water was collected from a local municipality reservoir, a small lake in Kernersville, North Carolina. The water characterization was provided by Agvise Laboratories (Northwood, North Dakota).

2 Analytes were identified using one ion pair transition as follows: *m/z* 145.7→104.0 for G-28273, *m/z* 158.2→110.0 for GS-26831, *m/z* 174.2→96.2 for G-28279, *m/z* 186.1→96.0 for GS-11355, *m/z* 188.3→104.0 for G-30033, *m/z* 200.3→158.0 for GS-11354, *m/z* 202.1→132.1 for simazine, *m/z* 216.1→174.2 for atrazine, *m/z* 228.2→186.1 for ametryn, *m/z* 242.0→158.2 for prometryn, *m/z* 230.2→145.9 for propazine, *m/z* 284.2→176.3 for S-metolachlor, *m/z* 328.2→121.0 for metolachlor-ESA, *m/z* 278.1→206.3 for metolachlor-OA, and *m/z* 338.0→290.8 for mesotrione. The study author notes that the method was not designed to resolve the stereoisomers of racemic mixtures.

3 Mean, standard deviation, and RSD were reviewer-calculated (n = 10) since the study report statistics excluded one of the recovery values due to presumed laboratory error (n = 9). Rules of significant figures were followed.

4 Samples were processed and analyzed as in Syngenta Method T001681-06; however, mesotrione was the only analyte for fortifications. Mesotrione was identified using one ion pair transition as follows: *m/z* 337.91→290.90.

5 Water description for Method Verification Set No. 2K7-SYN-MESO-MT01 was not reported (pp. 14-15, 17; Table 3, p. 21 of MRID 49960502). Water samples were described as “simulated samples” (p. 17). Water characterization was not provided.

6 RSDs were reviewer-calculated since the study report statistics did not include them. Rules of significant figures were followed.

7 Water description for Method Performance set determined by the reviewer based on Figures 4-5, pp. 90-91 of MRID 49960502 since it was not reported in the study report (pp. 14-15, 17 of MRID 49960502). Water characterization was not provided.

Table 3. Independent Validation Method Recoveries for Atrazine, Simazine, Propazine, G-30033, G-28279, G-28273, Ametryn, Prometryn, GS-11354, GS-11355, GS-26831, *S*-Metolachlor, Metolachlor-ESA, Metolachlor-OA and Mesotrione in Water^{1,2,3}

Analyte	Fortification Level (µg/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
Surface Water						
Atrazine	0.05 (LOQ)	5	100-108	104	3.2	3.1
	0.50	5	102-117	107	6.0	5.6
Simazine	0.05 (LOQ)	5	99-107	102	3.5	3.4
	0.50	5	106-119	111	5.7	5.1
Propazine	0.05 (LOQ)	5	83-90	87	2.6	3.0
	0.50	5	94-108	100	5.6	5.6
G-30033	0.05 (LOQ)	5	88-103	98	6.2	6.3
	0.50	5	98-111	105	5.1	4.9
G-28279	0.05 (LOQ)	5	83-101	91	6.9	7.6
	0.50	5	95-112	104	6.3	6.1
G-28273	0.50 (LOQ)	5	77-88	83	4.5	5.5
	5.0	5	88-107	97	8.3	8.6
Ametryn	0.05 (LOQ)	5	78-86	82	3.0	3.7
	0.50	5	81-90	85	3.3	3.8
Prometryn	0.05 (LOQ)	5	68-76	72	3.1	4.2
	0.50	5	71-77	73	2.3	3.2
GS-11354	0.05 (LOQ)	5	95-106	102	4.4	4.3
	0.50	5	100-109	104	4.0	3.8
GS-11355	0.05 (LOQ)	5	95-108	102	5.6	5.5
	0.50	5	104-110	107	2.4	2.2
GS-26831	0.05 (LOQ)	5	67-87	80	7.7	9.7
	0.50	5	94-117	107	9.2	8.6
<i>S</i> -Metolachlor	0.05 (LOQ)	5	77-86	81	3.7	4.6
	0.50	5	74-83	77	3.7	4.9
Metolachlor-ESA	0.05 (LOQ)	5	82-103	91	10	11
	0.50	5	96-104	101	3.0	2.9
Metolachlor-OA	0.05 (LOQ)	5	94-107	103	5.9	5.7
	0.50	5	92-109	99	6.6	6.6
Mesotrione	0.05 (LOQ)	5	92-113	104	9.5	9.2
	0.50	5	99-117	106	6.7	6.3
Ground Water						
Atrazine	0.05 (LOQ)	5	103-109	107	2.3	2.2
	0.50	5	101-111	105	3.8	3.6
Simazine	0.05 (LOQ)	5	104-113	108	4.1	3.8
	0.50	5	106-112	109	2.6	2.4
Propazine	0.05 (LOQ)	5	82-87	84	1.9	2.3
	0.50	5	93-103	98	3.6	3.7
G-30033	0.05 (LOQ)	5	99-106	103	2.7	2.7
	0.50	5	102-112	106	3.8	3.6
G-28279	0.05 (LOQ)	5	79-152	111	29	26
	0.50	5	99-111	103	4.9	4.8

Analyte	Fortification Level (µg/L)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%)	Relative Standard Deviation (%)
G-28273	0.50 (LOQ)	5	86-111	97	9.8	10
	5.0	5	97-110	105	4.8	4.5
Ametryn	0.05 (LOQ)	5	81-86	84	1.9	2.3
	0.50	5	84-92	88	2.9	3.3
Prometryn	0.05 (LOQ)	5	66-70	69	1.9	2.8
	0.50	5	71-78	74	3.0	4.0
GS-11354	0.05 (LOQ)	5	103-112	107	3.8	3.6
	0.50	5	105-113	109	3.6	3.4
GS-11355	0.05 (LOQ)	5	100-110	106	4.3	4.0
	0.50	5	101-115	109	5.2	4.8
GS-26831	0.05 (LOQ)	5	85-134	107	22	20
	0.50	5	97-112	105	5.7	5.4
<i>S</i> -Metolachlor	0.05 (LOQ)	5	65-71	68	2.6	3.8
	0.50	5	67-74	70	2.7	3.9
Metolachlor-ESA	0.05 (LOQ)	5	101-127	115	12	10
	0.50	5	100-107	103	2.7	2.6
Metolachlor-OA	0.05 (LOQ)	5	73-102	83	13	15
	0.50	5	95-106	100	4.5	4.5
Mesotrione	0.05 (LOQ)	5	93-100	97	2.9	3.0
	0.50	5	94-112	99	7.4	7.5

Data (recovery results were corrected when residues were quantified in the controls; Tables 2-3, pp. 44-73) were obtained from Tables 2-3, pp. 44-73 of MRID 49960503. Since the LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ.

1 The ILV was performed as a validation of ECM 1 (p. 14).

2 The surface (Sample ID: RIMV00312-0001 SURFACE; pH 7.3, hardness 27 mg equivalent CaCO₃/L, 58 ppm total dissolved solids) and ground water (Sample ID: RIMV00312-0002 GROUND; pH 7.5, hardness 59 mg equivalent CaCO₃/L, 122 ppm total dissolved solids) matrices used in the study were provided by the Sponsor and characterized by Agvise Laboratories (Northwood, North Dakota; p. 23; Appendix 8, pp. 764-765 of MRID 49960503). Water sources were not reported.

3 Analytes were identified using three ion pair transitions (primary, confirmatory 1, and confirmatory 2, respectively) as follows: *m/z* 216→174, *m/z* 216→104, and *m/z* 216→132 for atrazine, *m/z* 202→132, *m/z* 202→124, and *m/z* 202→104 for simazine, *m/z* 230→146 and *m/z* 230→188 for propazine (only two monitored ion transitions), *m/z* 188→104, *m/z* 188→146, and *m/z* 188→110 for G-30033, *m/z* 174→96, *m/z* 174→104, and *m/z* 174→146 for G-28279, *m/z* 146→104, *m/z* 146→110, and *m/z* 146→79 for G-28273, *m/z* 228→186, *m/z* 228→116, and *m/z* 228→138 for ametryn, *m/z* 242→158, *m/z* 242→200, and *m/z* 242→152 for prometryn, *m/z* 200→158, *m/z* 200→116, and *m/z* 200→110 for GS-11354, *m/z* 186→96, *m/z* 186→158, and *m/z* 186→91 for GS-11355, *m/z* 158→110, *m/z* 158→116, and *m/z* 158→85 for GS-26831, *m/z* 284→176, *m/z* 284→252, and *m/z* 284→212 for *S*-metolachlor, *m/z* 328→121, *m/z* 328→192, and *m/z* 328→135 for metolachlor-ESA, *m/z* 278→206, *m/z* 278→174, and *m/z* 278→158 for metolachlor-OA, and *m/z* 338→291, *m/z* 338→212, and *m/z* 338→248 for mesotrione. Quantification was performed using only one ion transition, the primary ion transition (p. 30; Figure 1, pp. 75-89 of MRID 49960503).

III. Method Characteristics

In the ECM 1 and ILV, LOQs in water were 0.50 µg/L for G-28273 and 0.05 µg/L for Atrazine, Simazine, Propazine, G-30033, G-28279, G-28273, Ametryn, Prometryn, GS-11354, GS-11355, GS-26831, S-Metolachlor, Metolachlor-ESA, Metolachlor-OA, and Mesotrione (pp. 13, 17 of MRID 47629802; pp. 9, 34, 39 of MRID 49960503). In ECM 1, the LOQ was defined based on the lowest fortification levels tested during the study. The LOQ was reported in the ILV based on the ECM 1. In the ECM 1, the LODs in water were 10 pg (equivalent to 0.2 pg/µL, 0.2 µg/L) for G-28273 and 1.0 pg (equivalent to 0.02 pg/µL, 0.02 µg/L) for Atrazine, Simazine, Propazine, G-30033, G-28279, G-28273, Ametryn, Prometryn, GS-11354, GS-11355, GS-26831, S-Metolachlor, Metolachlor-ESA, Metolachlor-OA, and Mesotrione. The LOD was defined in ECM 1 as the lowest-on-column injected quantity of analyte used to construct the calibration plot. The LODs were not reported in the ILV. In ECM 2, the LOQ for mesotrione in water was reported as 0.05 µg/L, based on ECM 1; the LOD was not reported (p. 17 of MRID 49960502). No LOQ calculations were reported in ECM 1, ECM 2, or ILV; no LOD calculations were reported in ECM 1.

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

122990 (Mesotrione), 080803 (Atrazine), 080807 (Simazine), 080808 (Propazine), 080801 (Ametryn), 080805 (Prometryn), and 108801 (S-Metolachlor) MRIDs 47629802/49960502/49960503

Table 4a. Method Characteristics for Atrazine, Simazine, Propazine, G-30033, G-28279, G-28273, Ametryn, Prometryn, GS-11354, GS-11355, GS-26831, S-Metolachlor, Metolachlor-ESA, Metolachlor-OA and Mesotrione in Deionized, Surface, and Ground Water

Analyte		Atrazine	Simazine	Propazine	G-30033	G-28279	G-28273	
Limit of Quantitation (LOQ)*		0.05 µg/L					0.50 µg/L	
Limit of Detection (LOD)	ECM 1	1.0 pg (equivalent to 0.02 pg/µL, 0.02 µg/L)					10 pg (equivalent to 0.2 pg/µL, 0.2 µg/L)	
	ECM 2	Not applicable						
	ILV	Not reported						
Linearity (calibration curve r and concentration range)	ECM 1	r = 0.9998	Reported as $r \geq 0.9993$ ($r^2 \geq 0.9986$; raw data not provided).					
		1.0-200 pg (0.020-0.5 ng/µL)					0.2-6 ng/µL ¹	
	ECM 2	Not applicable						
	ILV	r = 0.99990679	r = 0.99951614	r = 0.99980498	r = 0.99985553	r = 0.99952908	r = 0.99911086	
Repeatable	ECM 1 ²	Yes at LOQ, 2×LOQ, 10×LOQ, and 60×LOQ in deionized, surface, and ground water.		Yes at LOQ, 2×LOQ, 10×LOQ, and 60×LOQ in surface and ground water.	Yes at LOQ, 10×LOQ, and 60×LOQ in deionized water; No at 2×LOQ (RSD 22%).	Yes at LOQ, 2×LOQ, 10×LOQ, and 60×LOQ in deionized, surface, and ground water.	Yes at LOQ and 6×LOQ in deionized, surface, and ground water. No 10×LOQ samples prepared.	
		Not applicable						
	ILV ^{3,4}	Yes at LOQ and 10×LOQ in surface and ground water.				Yes at LOQ and 10×LOQ in surface water. Yes at 10×LOQ in ground water; No at LOQ (RSD 26%).	Yes at LOQ and 10×LOQ in surface and ground water.	

122990 (Mesotrione), 080803 (Atrazine), 080807 (Simazine), 080808 (Propazine), 080801 (Ametryn), 080805 (Prometryn), and 108801 (S-Metolachlor)
 MRIDs 47629802/49960502/49960503

Analyte		Atrazine	Simazine	Propazine	G-30033	G-28279	G-28273
Reproducible		Yes at 0.05 µg/L (LLMV)* and 0.50 µg/L in surface and ground water.				Yes at 0.05 µg/L (LLMV) and 0.50 µg/L in surface water. Yes at 0.50 µg/L (LLMV) in ground water. No at 0.05 µg/L.	Yes at 0.50 µg/L (LLMV) in surface and ground water. No at 5.0 µg/L.
		Could not be determined for deionized water ; only one set of performance data was submitted.					
Specific	ECM 2	Not applicable					
	ECM 1	Representative chromatograms were only provided for the surface water matrix. Representative chromatograms were not provided for all fortifications, including 10×LOQ.					
		Yes, matrix interferences were <10% of the LOQ (based on peak area).	Yes, matrix interferences were <1% of the LOQ (based on peak area).		Yes, matrix interferences were <1% of the LOQ (based on peak area); however, baseline noise interfered with analyte peak integration. ⁵	Yes, matrix interferences were <3% of the LOQ (based on peak area); however, baseline noise interfered with analyte peak integration. Nearby contaminant (peak ht. = <i>ca.</i> analyte peak ht.) observed. ⁶	Yes, matrix interferences were <10% of the LOQ (based on peak area).
ILV	No , matrix interferences were <i>ca.</i> 33% of the LOQ (based on peak area) ⁷ in surface water and not observed in ground water.	Yes, matrix interferences were <i>ca.</i> 13% of the LOQ (based on peak area) in surface water and not observed in ground water. Baseline noise noted around analyte peak.	Yes, no matrix interferences were observed.	Yes, matrix interferences were <i>ca.</i> 28% of the LOQ (based on peak area) ⁷ in surface water and not observed in ground water; however, baseline noise interfered with analyte peak integration in	No , no matrix interferences were observed; however, baseline noise significantly interfered with analyte peak integration and analyte peak was not distinguishable from baseline noise. ⁹	No , no matrix interferences were observed; however, baseline noise interfered with analyte peak integration. Analyte peak was small compared to baseline noise and only distinguishable by RT. ¹⁰	

122990 (Mesotrione), 080803 (Atrazine), 080807 (Simazine), 080808 (Propazine), 080801 (Ametryn), 080805 (Prometryn), and 108801 (S-Metolachlor)
MRIDs 47629802/49960502/49960503

Analyte	Atrazine	Simazine	Propazine	G-30033	G-28279	G-28273
				surface water. ⁸		

Data were obtained from pp. 13, 17 (LOQ/LOD); pp. 13, 17 (linearity); Tables 3-6, pp. 22-43 (recovery results); Figure 2, pp. 52-66 (chromatograms); Figure 3, p. 67 (calibration curves) of MRID 47629802 (ECM 1); pp. 9, 34, 39 (LOQ/LOD); pp. 25-26 (linearity); Tables 2-3, pp. 44-73 (recovery results); Figures 1-3, pp. 75-356 (chromatograms); Figures 4-9, pp. 357-362 (calibration curves) of MRID 49960503; DER Attachment 2. Data from MRID 49960502 (ECM 2) not included since mesotrione was the only analyte for fortifications (pp. 14-16 of MRID 49960502).

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

1 The calibration range for G-28273 was reported as 0.2 ppb to 6 ppb in the ILV communications (Appendix 6, p. 657 of MRID 49960503).

2 MRID 47629802 = ECM 1 (Syngenta Method T001681-06). In the ECM 1, deionized water (Picopure purification system; pH 6.4, hardness 3.0 mg equivalent CaCO₃/L, 4.0 ppm total dissolved solids), ground (well; pH 7.1, hardness 43 mg equivalent CaCO₃/L, 108 ppm total dissolved solids), surface water (reservoir; pH 6.2, hardness 15 mg equivalent CaCO₃/L, 14 ppm total dissolved solids), and treated/finished water (pH 7.5, hardness 81 mg equivalent CaCO₃/L, 162 ppm total dissolved solids) were used in the study (pp. 15-16; Appendix 1, p. 70 of MRID 47629802). The deionized water was collected from Syngenta laboratory L-2021. The ground and treated water were collected from two separate residential water supplies: residential well in Summerfield, North Carolina, and residential tap in Belews Creek, North Carolina, respectively. The surface water was collected from a local municipality reservoir, a small lake in Kernersville, North Carolina. The water characterization was provided by Agvise Laboratories (Northwood, North Dakota).

3 In the ILV, the surface (Sample ID: RIMV00312-0001 SURFACE; pH 7.3, hardness 27 mg equivalent CaCO₃/L, 58 ppm total dissolved solids) and ground water (Sample ID: RIMV00312-0002 GROUND; pH 7.5, hardness 59 mg equivalent CaCO₃/L, 122 ppm total dissolved solids) matrices used in the study were provided by the Sponsor and characterized by Agvise Laboratories (Northwood, North Dakota; p. 23; Appendix 8, pp. 764-765 of MRID 49960503). Water sources were not reported.

4 The ILV validated the method for all analytes in surface and ground water matrices at both fortification levels after the second trial, with insignificant analytical instrument and parameter modifications (pp. 9, 14, 26-34, 38 of MRID 49960503). The first trial was unsuccessful due to inconsistent recoveries for various analytes [low recoveries (individual recoveries, 17-67%) for ametryn, prometryn, propazine, and S-metolachlor in surface water; Appendix 7, pp. 733-744]. The second trial was initiated after instrument maintenance and correcting matrix effects (suppression; p. 9). The ILV was performed as a validation of ECM 1 (p. 14). Deionized water and treated/finished water were not included as ILV test water matrices. Although communications regarding remedying the low recoveries occurred between the ILV study author and Syngenta Study Sponsor/Monitor (not part of ECM 1), details of the necessary analytical corrections were not reported, so it could not be determined if an Updated ECM should be submitted (Appendix 6, pp. 575, 650-654).

5 Based on Figure 2, p. 53, of MRID 47629802.

6 Based on Figure 2, p. 54, of MRID 47629802.

7 Based on Figure 1, pp. 90, 105 of MRID 49960503.

8 Based on Figure 1, pp. 93, 108, 123, of MRID 49960503.

9 Based on Figure 1, pp. 109, 124, and Figure 2, pp. 154, 169, of MRID 49960503.

10 Based on Figure 1, pp. 110, 125, and Figure 2, pp. 155, 170, of MRID 49960503.

122990 (Mesotrione), 080803 (Atrazine), 080807 (Simazine), 080808 (Propazine), 080801 (Ametryn), 080805 (Prometryn), and 108801 (S-Metolachlor) MRIDs 47629802/49960502/49960503

Table 4a (con't). Method Characteristics for Atrazine, Simazine, Propazine, G-30033, G-28279, G-28273, Ametryn, Prometryn, GS-11354, GS-11355, GS-26831, S-Metolachlor, Metolachlor-ESA, Metolachlor-OA and Mesotrione in Deionized, Surface, and Ground Water

Analyte		Ametryn	Prometryn	GS-11354	GS-11355	GS-26831
Limit of Quantitation (LOQ)*		0.05 µg/L				
Limit of Detection (LOD)	ECM 1	1.0 pg (equivalent to 0.02 pg/µL, 0.02 µg/L)				
	ECM 2	Not applicable				
	ILV	Not reported				
Linearity (calibration curve r and concentration range)	ECM 1	Reported as $r \geq 0.9993$ ($r^2 \geq 0.9986$); raw data not provided.				
		1.0-200 pg (0.020-0.5 ng/µL)				
	ECM 2	Not applicable				
	ILV	$r = 0.99969771$	$r = 0.99996211$	$r = 0.99986225$	$r = 0.99984802$	$r = 0.99954711$
		0.02-4.0 pg/µL				
Repeatable	ECM 1 ¹	Yes at LOQ, 2×LOQ, 10×LOQ, and 60×LOQ in deionized, surface, and ground water.				
	ECM 2	Not applicable				
	ILV ^{2,3}	Yes at LOQ and 10×LOQ in surface and ground water.	Yes at LOQ and 10×LOQ in surface water. Yes at 10×LOQ in ground water; No at LOQ (mean 69%).	Yes at LOQ and 10×LOQ in surface and ground water.		
Reproducible		Yes at 0.05 µg/L (LLMV)* and 0.50 µg/L in surface and ground water.	Yes at 0.05 µg/L (LLMV) and 0.50 µg/L in surface water. Yes at 0.50 µg/L (LLMV) in ground water. No at 0.05 µg/L.	Yes at 0.05 µg/L (LLMV) and 0.50 µg/L in surface and ground water.		
	Could not be determined for deionized water ; only one set of performance data was submitted.					

122990 (Mesotrione), 080803 (Atrazine), 080807 (Simazine), 080808 (Propazine), 080801 (Ametryn), 080805 (Prometryn), and 108801 (S-Metolachlor)
 MRIDs 47629802/49960502/49960503

Analyte		Ametryn	Prometryn	GS-11354	GS-11355	GS-26831
Specific	ECM 2	Not applicable				
	ECM 1	Representative chromatograms were only provided for the surface water matrix. Representative chromatograms were not provided for all fortifications, including 10×LOQ.				
		Yes, matrix interferences were <1% of the LOQ (based on peak area).	Yes, matrix interferences were <1% of the LOQ (based on peak area); however, baseline noise interfered with analyte peak integration. Multiple contaminants (peak ht. ca. 25% of LOQ peak ht.) observed near analyte peak. ⁴	Yes, matrix interferences were <1% of the LOQ (based on peak area); however, significant baseline noise was observed at analyte peak RT.		
ILV	Yes, no matrix interferences were observed.	Yes, no matrix interferences were observed. Some baseline noise was observed near analyte peak.	No in surface water since baseline noise interfered with analyte peak integration. ⁵ Analyte peak very small compared to baseline noise. Yes in ground water. No matrix interferences were observed.	No , no matrix interferences were observed; however, baseline noise significantly interfered with analyte peak integration. ⁶ Analyte peak very small compared to baseline noise.		

Data were obtained from pp. 13, 17 (LOQ/LOD); pp. 13, 17 (linearity); Tables 3-6, pp. 22-43 (recovery results); Figure 2, pp. 52-66 (chromatograms); Figure 3, p. 67 (calibration curves) of MRID 47629802 (ECM 1); pp. 9, 34, 39 (LOQ/LOD); pp. 25-26 (linearity); Tables 2-3, pp. 44-73 (recovery results); Figures 1-3, pp. 75-356 (chromatograms); Figures 10-14, pp. 363-367 (calibration curves) of MRID 49960503; DER Attachment 2. Data from MRID 49960502 (ECM 2) not included since mesotrione was the only analyte for fortifications (pp. 14-16 of MRID 49960502).

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

1 MRID 47629802 = ECM 1 (Syngenta Method T001681-06). In the ECM 1, deionized water (Picopure purification system; pH 6.4, hardness 3.0 mg equivalent CaCO₃/L, 4.0 ppm total dissolved solids), ground (well; pH 7.1, hardness 43 mg equivalent CaCO₃/L, 108 ppm total dissolved solids), surface water (reservoir; pH 6.2, hardness 15 mg equivalent CaCO₃/L, 14 ppm total dissolved solids), and treated/finished water (pH 7.5, hardness 81 mg equivalent CaCO₃/L, 162 ppm total dissolved solids) were used in the study (pp. 15-16; Appendix 1, p. 70 of MRID 47629802). The deionized water was collected from Syngenta laboratory L-2021. The ground and treated water were collected from two separate residential water supplies: residential well in Summerfield, North Carolina, and residential tap in Belews Creek, North Carolina, respectively. The surface water was collected from a local municipality reservoir, a small lake in Kernersville, North Carolina. The water characterization was provided by Agvise Laboratories (Northwood, North Dakota).

2 In the ILV, the surface (Sample ID: RIMV00312-0001 SURFACE; pH 7.3, hardness 27 mg equivalent CaCO₃/L, 58 ppm total dissolved solids) and ground

122990 (Mesotrione), 080803 (Atrazine), 080807 (Simazine), 080808 (Propazine), 080801 (Ametryn), 080805 (Prometryn), and 108801 (S-Metolachlor) MRIDs 47629802/49960502/49960503

water (Sample ID: RIMV00312-0002 GROUND; pH 7.5, hardness 59 mg equivalent CaCO₃/L, 122 ppm total dissolved solids) matrices used in the study were provided by the Sponsor and characterized by Agvise Laboratories (Northwood, North Dakota; p. 23; Appendix 8, pp. 764-765 of MRID 49960503). Water sources were not reported.

- 3 The ILV validated the method for all analytes in surface and ground water matrices at both fortification levels after the second trial, with insignificant analytical instrument and parameter modifications (pp. 9, 14, 26-34, 38 of MRID 49960503). The first trial was unsuccessful due to inconsistent recoveries for various analytes [low recoveries (individual recoveries, 17-67%) for ametryn, prometryn, propazine, and S-metolachlor in surface water; Appendix 7, pp. 733-744]. The second trial was initiated after instrument maintenance and correcting matrix effects (suppression; p. 9). The ILV was performed as a validation of ECM 1 (p. 14). Deionized water and treated/finished water were not included as ILV test water matrices. Although communications regarding remedying the low recoveries occurred between the ILV study author and Syngenta Study Sponsor/Monitor (not part of ECM 1), details of the necessary analytical corrections were not reported, so it could not be determined if an Updated ECM should be submitted (Appendix 6, pp. 575, 650-654).
- 4 Based on Figure 2, p. 61, of MRID 47629802.
- 5 Based on Figure 1, pp. 114, 129, of MRID 49960503.
- 6 Based on Figure 1, pp. 115, 130, and Figure 2, pp. 160, 175, of MRID 49960503.

122990 (Mesotrione), 080803 (Atrazine), 080807 (Simazine), 080808 (Propazine), 080801 (Ametryn), 080805 (Prometryn), and 108801 (S-Metolachlor) MRIDs 47629802/49960502/49960503

Table 4a (con't). Method Characteristics for Atrazine, Simazine, Propazine, G-30033, G-28279, G-28273, Ametryn, Prometryn, GS-11354, GS-11355, GS-26831, S-Metolachlor, Metolachlor-ESA, Metolachlor-OA and Mesotrione in Deionized, Surface, and Ground Water

Analyte		S-Metolachlor	Metolachlor-ESA	Metolachlor-OA	Mesotrione
Limit of Quantitation (LOQ)*		0.05 µg/L			
Limit of Detection (LOD)	ECM 1	1.0 pg (equivalent to 0.02 pg/µL, 0.02 µg/L)			
	ECM 2	Not applicable			Not reported
	ILV	Not reported			
Linearity (calibration curve r and concentration range)	ECM 1	Reported as $r \geq 0.9993$ ($r^2 \geq 0.9986$); raw data not provided.			
		1.0-200 pg (0.020-0.5 ng/µL)			
	ECM 2	Not applicable			$r = 0.9940-0.9998$
		0.01-500 pg/µL			
ILV	$r = 0.99974964$	$r = 0.99969006$	$r = 0.99964934$	$r = 0.99905545$	
	0.02-4.0 pg/µL				
Repeatable	ECM 1 ¹	Yes at LOQ, 2×LOQ, 10×LOQ, and 60×LOQ in deionized, surface, and ground water.	Yes at LOQ, 2×LOQ, 10×LOQ, and 60×LOQ in deionized and ground water. Yes at LOQ, 10×LOQ, and 60×LOQ in surface water; No at 2×LOQ (RSD 26%).	Yes at LOQ, 2×LOQ, 10×LOQ, and 60×LOQ in deionized and ground water. Yes at LOQ, 10×LOQ, and 60×LOQ in surface water; No at 2×LOQ (mean 133% RSD 21%).	
	ECM 2 ²	Not applicable		Yes at LOQ, 10×LOQ, and 100×LOQ in unknown water, but $n = 3$. Yes at LOQ and 100×LOQ in deionized water.	
	ILV ^{3,4}	Yes at LOQ and 10×LOQ in surface water. Yes at 10×LOQ in ground water; No at LOQ (mean 68%).	Yes at LOQ and 10×LOQ in surface and ground water.		

122990 (Mesotrione), 080803 (Atrazine), 080807 (Simazine), 080808 (Propazine), 080801 (Ametryn), 080805 (Prometryn), and 108801 (S-Metolachlor) MRIDs 47629802/49960502/49960503

Analyte		S-Metolachlor	Metolachlor-ESA	Metolachlor-OA	Mesotrione
Reproducible	ECM 1/ILV	Yes at 0.05 µg/L (LLMV) and 0.50 µg/L in surface water.	Yes at 0.05 µg/L (LLMV) and 0.50 µg/L in surface and ground water.		
		Yes at 0.50 µg/L (LLMV) in ground water. No at 0.05 µg/L.	Could not be determined for deionized water; only one set of performance data was submitted.		
	ECM 1/ECM 2	Not applicable			Yes at 0.05 µg/L (LLMV) in deionized water. No at 0.50 µg/L.
	ECM 2/ILV	Not applicable			Yes at 0.05 µg/L (LLMV) and 0.50 µg/L, but different water matrices.
Specific	ECM 1	Representative chromatograms were only provided for the surface water matrix. Representative chromatograms were not provided for all fortifications, including 10×LOQ.			
		Yes, matrix interferences were <15% of the LOQ (based on peak area).	Yes, matrix interferences were <1% of the LOQ (based on peak area); however, analyte peak attenuation was choppy.	Yes, matrix interferences were <5% of the LOQ (based on peak area). Isomers were separated.	Yes, matrix interferences were <3% of the LOQ (based on peak area).
	ECM 2	Not applicable			Yes, matrix interferences were <i>ca.</i> 27% of the LOQ (based on peak area). ⁵
	ILV	The LOQ was fairly small compared to the height of the baseline noise in the majority of the chromatograms.			
	Yes, no matrix interferences were observed.	Yes, no matrix interferences were observed. Some baseline noise was observed near analyte peak.	No , no matrix interferences were observed; however, baseline noise interfered with analyte peak integration, and analyte peak very small compared to baseline noise. ⁶ Integration in surface water included two peaks (isomers), but only one peak was integrated in ground water.	Yes, no matrix interferences were observed. Some baseline noise was observed near analyte peak.	

Data were obtained from pp. 13, 17 (LOQ/LOD); pp. 13, 17 (linearity); Tables 3-6, pp. 22-43 (recovery results); Figure 2, pp. 52-66 (chromatograms); Figure 3, p. 67 (calibration curves) of MRID 47629802 (ECM 1); p. 17 (LOQ/LOD); pp. 15 (linearity); Tables 3-4, pp. 21-22 (recovery results); Figures 3-5, pp. 86-91

122990 (Mesotrione), 080803 (Atrazine), 080807 (Simazine), 080808 (Propazine), 080801 (Ametryn), 080805 (Prometryn), and 108801 (S-Metolachlor)
MRIDs 47629802/49960502/49960503

(chromatograms); Figure 2, p. 85 (calibration curves) of MRID 49960502 (ECM 2); pp. 9, 34, 39 (LOQ/LOD); pp. 25-26 (linearity); Tables 2-3, pp. 44-73 (recovery results); Figures 1-3, pp. 75-356 (chromatograms); Figures 15-18, pp. 368-371 (calibration curves) of MRID 49960503; DER Attachment 2.

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

- 1 MRID 47629802 = ECM 1 (Syngenta Method T001681-06). In the ECM 1, deionized water (Picopure purification system; pH 6.4, hardness 3.0 mg equivalent CaCO₃/L, 4.0 ppm total dissolved solids), ground (well; pH 7.1, hardness 43 mg equivalent CaCO₃/L, 108 ppm total dissolved solids), surface water (reservoir; pH 6.2, hardness 15 mg equivalent CaCO₃/L, 14 ppm total dissolved solids), and treated/finished water (pH 7.5, hardness 81 mg equivalent CaCO₃/L, 162 ppm total dissolved solids) were used in the study (pp. 15-16; Appendix 1, p. 70 of MRID 47629802). The deionized water was collected from Syngenta laboratory L-2021. The ground and treated water were collected from two separate residential water supplies: residential well in Summerfield, North Carolina, and residential tap in Belews Creek, North Carolina, respectively. The surface water was collected from a local municipality reservoir, a small lake in Kernersville, North Carolina. The water characterization was provided by Agvise Laboratories (Northwood, North Dakota).
- 2 MRID 49960502 = ECM 2. Syngenta Method T001681-06 was used for sample analysis; however, mesotrione was the only analyte for fortifications (pp. 14-16 of MRID 49960502). ECM 2 referenced ECM 1 (p. 17). For the Method Verification set, water samples were only described as “simulated samples” (pp. 14-15, 17; Tables 3-4, pp. 21-22). For the Method Performance set, no water description was reported; the reviewer determined that deionized water was used based on Figures 4-5, pp. 90-91 of MRID 49960502. No water characterization was not provided.
- 3 In the ILV, the surface (Sample ID: RIMV00312-0001 SURFACE; pH 7.3, hardness 27 mg equivalent CaCO₃/L, 58 ppm total dissolved solids) and ground water (Sample ID: RIMV00312-0002 GROUND; pH 7.5, hardness 59 mg equivalent CaCO₃/L, 122 ppm total dissolved solids) matrices used in the study were provided by the Sponsor and characterized by Agvise Laboratories (Northwood, North Dakota; p. 23; Appendix 8, pp. 764-765 of MRID 49960503). Water sources were not reported.
- 4 The ILV validated the method for all analytes in surface and ground water matrices at both fortification levels after the second trial, with insignificant analytical instrument and parameter modifications (pp. 9, 14, 26-34, 38 of MRID 49960503). The first trial was unsuccessful due to inconsistent recoveries for various analytes [low recoveries (individual recoveries, 17-67%) for ametryn, prometryn, propazine, and S-metolachlor in surface water; Appendix 7, pp. 733-744]. The second trial was initiated after instrument maintenance and correcting matrix effects (suppression; p. 9). The ILV was performed as a validation of ECM 1 (p. 14). Deionized water and treated/finished water were not included as ILV test water matrices. Although communications regarding remedying the low recoveries occurred between the ILV study author and Syngenta Study Sponsor/Monitor (not part of ECM 1), details of the necessary analytical corrections were not reported, so it could not be determined if an Updated ECM should be submitted (Appendix 6, pp. 575, 650-654).
- 5 Based on Figures 4-5, pp. 90-91, of MRID 49960502.
- 6 Based on Figure 1, pp. 118, 133, and Figure 2, pp. 163, 178, of MRID 49960503. Linearity is satisfactory when $r \geq 0.995$.

Table 4b. Method Characteristics for Atrazine, Simazine, Propazine, G-30033, G-28279, G-28273, S-Metolachlor, Metolachlor-ESA, and Metolachlor-OA in Treated/Finished Water

Analyte		Atrazine	Simazine	Propazine	G-30033	G-28279
Limit of Quantitation (LOQ)*		0.05 µg/L				
Limit of Detection (LOD)	ECM 1	1.0 pg (equivalent to 0.02 pg/µL, 0.02 µg/L)				
	ILV	Not reported				
Linearity (calibration curve r and concentration range)	ECM 1	Reported as $r \geq 0.9993$ ($r^2 \geq 0.9986$); raw data not provided. 1.0-200 pg (0.020-0.5 ng/µL)				
	ILV	No samples prepared in treated/finished water.				
Repeatable	ECM 1 ¹	Yes at LOQ, 2×LOQ, 10×LOQ, and 60×LOQ in treated/finished water.			Yes at LOQ, 10×LOQ, and 60×LOQ in surface water; No at 2×LOQ (RSD 21%).	Yes at LOQ, 2×LOQ, 10×LOQ, and 60×LOQ in treated/finished water.
	ILV	No samples prepared in treated/finished water.				
Reproducible		Could not be determined ; only one set of performance data was submitted.				
Specific	ECM 1	No representative chromatograms were provided. Representative chromatograms were only provided for the surface water matrix.				
	ILV	No samples prepared in treated/finished water.				

Data were obtained from pp. 13, 17 (LOQ/LOD); pp. 13, 17 (linearity); Tables 3-6, pp. 22-43 (recovery results); Figure 2, pp. 52-66 (chromatograms); Figure 3, p. 67 (calibration curves) of MRID 47629802 (ECM 1); DER Attachment 2.

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

¹ MRID 47629802 = ECM 1 (Syngenta Method T001681-06). In the ECM 1, deionized water (Picopure purification system; pH 6.4, hardness 3.0 mg equivalent CaCO₃/L, 4.0 ppm total dissolved solids), ground (well; pH 7.1, hardness 43 mg equivalent CaCO₃/L, 108 ppm total dissolved solids), surface water (reservoir; pH 6.2, hardness 15 mg equivalent CaCO₃/L, 14 ppm total dissolved solids), and treated/finished water (pH 7.5, hardness 81 mg equivalent CaCO₃/L, 162 ppm total dissolved solids) were used in the study (pp. 15-16; Appendix 1, p. 70 of MRID 47629802). The deionized water was collected from Syngenta laboratory L-2021. The ground and treated water were collected from two separate residential water supplies: residential well in Summerfield, North Carolina, and residential tap in Belews Creek, North Carolina, respectively. The surface water was collected from a local municipality reservoir, a small lake in Kernersville, North Carolina. The water characterization was provided by Agvise Laboratories (Northwood, North Dakota).

Table 4b (con't). Method Characteristics for Atrazine, Simazine, Propazine, G-30033, G-28279, G-28273, S-Metolachlor, Metolachlor-ESA, and Metolachlor-OA in Treated/Finished Water

Analyte		G-28273	S-Metolachlor	Metolachlor-ESA	Metolachlor-OA
Limit of Quantitation (LOQ)*		0.50 µg/L	0.05 µg/L		
Limit of Detection (LOD)	ECM 1	10 pg (equivalent to 0.2 pg/µL, 0.2 µg/L)	1.0 pg (equivalent to 0.02 pg/µL, 0.02 µg/L)		
	ILV	Not reported			
Linearity (calibration curve r and concentration range)	ECM 1	Reported as $r \geq 0.9993$ ($r^2 \geq 0.9986$); raw data not provided.			
		0.2-6 ng/µL ¹	1.0-200 pg (0.020-0.5 ng/µL)		
	ILV	No samples prepared in treated/finished water.			
Repeatable	ECM 1 ²	Yes at LOQ and 6×LOQ in treated/finished water. No 10×LOQ samples prepared.	Yes at LOQ, 2×LOQ, 10×LOQ, and 60×LOQ in treated/finished water.		
	ILV	No samples prepared in treated/finished water.			
Reproducible		Could not be determined ; only one set of performance data was submitted.			
Specific	ECM 1	No representative chromatograms were provided. Representative chromatograms were only provided for the surface water matrix.			
	ILV	No samples prepared in treated/finished water.			

Data were obtained from pp. 13, 17 (LOQ/LOD); pp. 13, 17 (linearity); Tables 3-6, pp. 22-43 (recovery results); Figure 2, pp. 52-66 (chromatograms); Figure 3, p. 67 (calibration curves) of MRID 47629802 (ECM 1); DER Attachment 2.

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

1 The calibration range for G-28273 was reported as 0.2 ppb to 6 ppb in the ILV communications (Appendix 6, p. 657 of MRID 49960503).

2 MRID 47629802 = ECM 1 (Syngenta Method T001681-06). In the ECM 1, deionized water (Picopure purification system; pH 6.4, hardness 3.0 mg equivalent CaCO₃/L, 4.0 ppm total dissolved solids), ground (well; pH 7.1, hardness 43 mg equivalent CaCO₃/L, 108 ppm total dissolved solids), surface water (reservoir; pH 6.2, hardness 15 mg equivalent CaCO₃/L, 14 ppm total dissolved solids), and treated/finished water (pH 7.5, hardness 81 mg equivalent CaCO₃/L, 162 ppm total dissolved solids) were used in the study (pp. 15-16; Appendix 1, p. 70 of MRID 47629802). The deionized water was collected from Syngenta laboratory L-2021. The ground and treated water were collected from two separate residential water supplies: residential well in Summerfield, North Carolina, and residential tap in Belews Creek, North Carolina, respectively. The surface water was collected from a local municipality reservoir, a small lake in Kernersville, North Carolina. The water characterization was provided by Agvise Laboratories (Northwood, North Dakota).

IV. Method Deficiencies and Reviewer's Comments

1. The following EFED Directive accompanied MRIDs 47629802, 49960502, and 49960503: Please review for all a.i.s included in the study reports. 2/27/2020 Update: We would like to add MRID 49960502 to the multiresidue ECM and ILV 1681-06 method for water, which is the analytical method specific for mesotrione. We would like the contractor to review the multiresidue method, including a focus on mesotrione.

The reviewer included all three MRIDs in this method validation DER; however, the DER method summary (Tables 1 and 4) was split into two water categories: 1) deionized, surface, and ground water; and 2) treated/finished water. This split was based on the fact that 9 of the 15 analytes were validated in all four water matrices using Syngenta Method No. T001681-06 in ECM 1 (MRID 47629802) and 6 of the 15 analytes were validated in only 3 water matrices using Syngenta Method No. T001681-06 in ECM 1 (MRID 47629802).

Typically, method validation DERs are not prepared by the reviewer with a matrix-specific validation assessment, e.g. the reproducibility of performance data was based on acceptable analyte recoveries at similar fortification levels, as opposed to also including a stipulation of the use of similar ECM and ILV matrices; however, given the limitations of the method in treated/finished water, the reviewer added the stipulation of the use of similar ECM and ILV matrices for clarity.

Mesotrione was made a focus of the DER by placing it first in Table 1 and including ECM 2 (MRID 49960502) in the DER.

2. Deionized, surface, and ground water: While Syngenta Method No. T001681-06 was validated by the original laboratory (ECM 1; MRID 47629802) for the 15 analytes in deionized, surface, and ground water, the ILV validated Syngenta Method No. T001681-06 for the 15 analytes in only surface and ground water. Deionized water was not included in the ILV (MRID 49960503); however, deionized water was included in the ECM 2 (MRID 49960502) for the validation of Syngenta Method No. T001681-06 with mesotrione. The reviewer considered ECM 2 to be a possible "ILV" for ECM 1 validation of mesotrione in deionized water since the performing laboratories differed (p. 1 of MRID 47629802; p. 1 of MRID 49960502). ECM 2 referenced ECM 1 (p. 17 of MRID 49960502).
3. Treated/finished water: In the ECM 1, it was stated that "this method may not be applicable for the listed thiomethyl-containing compounds in some treated (finished) water due to their inherent chemical instability in the presence of various types of oxidizing agents used for water treatment (e.g., chlorination)" (p. 7 of MRID 47629802). In the original laboratory validation, Syngenta Method No. T001681-06 in treated/finished water was only implemented with the following analytes: atrazine, simazine, propazine, G-30033, G-28279, G-28273, S-metolachlor, metolachlor-ESA, and metolachlor-OA (Table 10, p. 47).

In ECM 2, levels of mesotrione were evaluated in raw and treated/finished water from several Community Water Systems (CWS) using Syngenta Method No. T001681-06 (pp. 14, 17 of MRID 49960502). Prior to analysis of CWS water samples, method verifications were conducted; however, the test water matrices for the method validations was deionized water and undescribed water (“simulated samples”; p. 17). The report also noted that the selected CWSs are sourced by surface water (p. 14). Therefore, while the treated/finished water samples from CWSs were subjected to Syngenta Method No. T001681-06 to quantify mesotrione, no method validation in treated/finished water was included in the study report. See Reviewer’s Comment #19 for more detailed results of CWS analytical results.

4. Since the reported method LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ (p. 17 of MRID 47629802; p. 17 of MRID 49960502; pp. 9, 34, 39 of MRID 49960503). The lowest concentration tested with sufficiently accurate and precise recoveries is the LLMV.

Surface and ground water: Based on the performance data submitted by MRIDs 47629802 (ECM 1) and 49960503 (ILV), the LLMV was equivalent to the reported method LOQ (0.05 µg/L) for atrazine, simazine, propazine, G-30033, ametryn, GS-11354, GS-11355, GS-26831, metolachlor-ESA, metolachlor-OA and mesotrione in surface and ground water. The LLMV was also equivalent to the reported method LOQ (0.5 µg/L) for G-28273 in surface and ground water. The LLMV was equivalent to the reported method LOQ (0.05 µg/L) for G-28279, prometryn, and *S*-metolachlor in surface water; however, the LLMV for G-28279, prometryn, and *S*-metolachlor in ground water was 0.5 µg/L (reported method LOQ = 0.05 µg/L).

Deionized water: Based on the performance data submitted by MRID 47629802 (ECM 1), the LLMV was equivalent to the reported LOQ (0.05 µg/L) for atrazine, simazine, propazine, G-30033, G-28279, ametryn, prometryn, GS-11354, GS-11355, GS-26831, *S*-metolachlor, metolachlor-ESA, and metolachlor-OA in deionized water. The LLMV was also equivalent to the reported LOQ (0.5 µg/L) for G-28273 in deionized water. Based on the performance data submitted by MRIDs 47629802 (ECM 1) and 49960502 (ECM 2), the LLMV was equivalent to the reported LOQ (0.05 µg/L) for mesotrione in deionized water.

Treated/finished water: Based on the performance data submitted by MRID 47629802 (ECM 1), the LLMV was equivalent to the reported LOQ (0.05 µg/L) for atrazine, simazine, propazine, G-30033, G-28279, G-28273, *S*-metolachlor, metolachlor-ESA, and metolachlor-OA in treated/finished water. The LLMV was also equivalent to the reported LOQ (0.5 µg/L) for G-28273 in treated/finished water.

5. In ECM 1, no samples were prepared at the 10×LOQ fortification (5.0 µg/L) for the analysis of G-28273 in the four water matrices (Tables 3-6, pp. 22-43 of MRID

47629802). The reproducibility for the 10×LOQ analysis of G-28273 was not supported by the data.

In ECM 2, no samples were prepared at the 10×LOQ fortification (0.05 µg/L) for the analysis of mesotrione in deionized water (p. 17; Table 4, p. 22 of MRID 49960502).

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

6. Performance data was not acceptable for the following analyses: (ILV) the LOQ (0.05 µg/L) analyses in ground water of G-28279 (RSD 26%), prometryn (mean 69%), and S-metolachlor (mean 68%; Tables 2-3, pp. 44-73 of MRID 49960503); and (ECM 1) mesotrione in surface water at 0.10 µg/L (mean 133% RSD 68%), metolachlor-OA in surface water at 0.10 µg/L (RSD 26%), and G-30033 at 0.10 µg/L in deionized water (RSD 22%) and in treated water (RSD 21%; Tables 3-6, pp. 22-43 of MRID 47629802). Guideline 850.6100 criteria for precision and accuracy is that mean recoveries for replicates at each spiking level are between 70% and 120% and relative standard deviations (RSD) are ≤20% at the stated LOQ and at higher concentrations.
7. The specificity of the method for G-28279, G-28273, GS-26831 and metolachlor-OA in surface and ground water and for atrazine and GS-11355 in surface water was not supported by ILV representative chromatograms. For G-28279 in surface and ground water, baseline noise significantly interfered with analyte peak integration and analyte peak was not distinguishable from baseline noise (Figure 1, pp. 109, 124, and Figure 2, pp. 154, 169, of MRID 49960503). For G-28273 in surface and ground water, baseline noise interfered with analyte peak integration, and analyte peak was small compared to baseline noise and only distinguishable by RT (Figure 1, pp. 110, 125, and Figure 2, pp. 155, 170). For the following analyses, baseline noise significantly interfered with analyte peak integration, and analyte peak very small compared to baseline noise: GS-26831 in surface and ground water (Figure 1, pp. 115, 130, and Figure 2, pp. 160, 175), metolachlor-OA in surface and ground water (Figure 1, pp. 118, 133, and Figure 2, pp. 163, 178), and GS-11355 in surface water (Figure 1, pp. 114, 129) Additionally, metolachlor-OA peak integration in surface water included two peaks (isomers), but only one peak was integrated in ground water. For atrazine in surface water, matrix interferences were *ca.* 33% of the LOQ (based on peak area; Figure 1, pp. 90, 105). Although the matrix interferences were below the method LOD reported in the ECM 1 (0.02 µg/L, 40% of the LOQ), matrix interferences should not exceed 30% of the LOQ.

The reviewer believed that ILV specificity data suggested that matrix-matched standards and/or a more rigorous samples processing procedure may be necessary. Solvent-based calibration standards were used in the ILV (pp. 25-26, 30-31 of MRID 49960503).

8. The ILV required two trials to validate ECM 1 (p. 9 of MRID 49960503). The first trial was unsuccessful due to inconsistent recoveries for various analytes [low recoveries (individual recoveries, 17-67%) for ametryn, prometryn, propazine, and *S*-metolachlor in

surface water; Appendix 7, pp. 733-744]. The second trial was initiated after instrument maintenance and correcting matrix effects (suppression; p. 9). Although communications regarding remedying the low recoveries occurred between the ILV study author and Syngenta Study Sponsor/Monitor (not part of ECM 1), details of the necessary analytical corrections were not reported, so it could not be determined if an Updated ECM should be submitted (Appendix 6, pp. 575, 650-654). See Reviewer's Comment #17 for discussion of ILV communications.

The reviewer noted that solvent-based calibration standards were used in the ECM 1, ECM 2, and ILV (pp. 13-14 of MRID 47629802; p. 15 of MRID 49960502pp. 25-26, 30-31 of MRID 49960503). Matrix effects were not studied in any MRID, and the reason for the omission of comparison of matrix-matched standards was not reported.

9. In ECM 2, an insufficient number of samples (n = 3) was prepared for each fortification of mesotrione in the Method Verification set (p. 17; Table 3, p. 21 of MRID 49960502). OCSPP guidelines state that a minimum of five spiked replicates were analyzed at each concentration (*i.e.*, minimally, the LOQ and 10× LOQ) for each analyte.
10. The ECM 2 linearity was not satisfactory for two of 13 sample sets of the Method Performance Set of mesotrione in deionized water ($r = 0.9940$ and 0.9946 ; Table 4, p. 22 of MRID 49960502). Linearity is satisfactory when $r \geq 0.995$.

The ECM 1 linearity was satisfactory [reported as $r \geq 0.9993$ ($r^2 \geq 0.9986$)]; however, individual correlation coefficients were not provided for any analyte, except atrazine (pp. 13, 17; Figure 3, p. 67 of MRID 47629802).

11. ECM 1 did not provide full support for the specificity of the method because chromatograms were only provided for the surface water matrix (one of the four matrices) and chromatograms were not provided for all fortifications tested, including 10×LOQ for analytes (Figure 2, pp. 52-66 of MRID 47629802). Representative chromatograms for all fortifications/matrices should be provided for review.
12. The ECM 2 water matrix for the Method Verification Set No. 2K7-SYN-MESO-MT01 was not characterized (pp. 14-15, 17; Table 3, p. 21 of MRID 49960502). Water samples were only described as “simulated samples” (p. 17).
13. The method LOD was 1.0 pg (equivalent to 0.02 pg/μL, 0.02 μg/L) for all analytes, except G-28273 (method LOD = 10 pg; p. 17 of MRID 47629802). The following matrix interferences were observed at <LOD, but >50% of the LOD: (ILV) G-30033 in surface water [matrix interferences were *ca.* 28% of the LOQ (based on peak area; Figure 1, pp. 93, 108 of MRID 49960503)]; and (ECM 2) 7 in deionized water [matrix interferences were *ca.* 27% of the LOQ (based on peak area; Figures 4-5, pp. 90-91 of MRID 49960502)].
14. The following chromatographic concerns were noted in the ECM 1 chromatograms: 1)

for G-28279 in surface and ground water, baseline noise interfered with analyte peak integration, and nearby contaminant (peak ht. = *ca.* analyte peak ht.) was noted (Figure 2, p. 54, of MRID 47629802); and 2) for GS-11355, multiple contaminants (peak ht. *ca.* 25% of LOQ peak ht.) observed near analyte peak (Figure 2, p. 61).

15. No reagent blanks were prepared in ECM 1 and ECM 2.
16. Sample recoveries of the ECM 1, ECM 2, and ILV were corrected for residues quantified in the controls (p. 15 of MRID 47629802; p. 16 of MRID 49960502; Tables 2-3, pp. 44-73 of MRID 49960503).
17. ECM 1/ILV Communication: The ILV study author provided an email communication log between Shawna Rees (Brown) (Morse Labs/ABC Laboratories ILV study author), Myra Manuli (Syngenta Study Sponsor/Monitor), Clark Chickering (role not reported), Kevin Clark (Senior Director), Emily Vogl (role not reported), Kim Douglas (role not reported), Elizabeth Hansen (Report Specialist II), Nick Giovanini (role not reported), Heather Reynolds (QA auditor, ABC), "Morse Lab", Twyla Roth (role not reported), Yuk Wong (Associate Chemist), Minaxi (Mina) Bhatt (Associate Chemist), Stan Shaffer (Senior Scientific Advisor), Seth Nasca (Chemist), Wendy Moore (Administrative Supervisor), Kerri Chapin (role not reported), Bob Plastridge (role not reported), and Alex Schulthesis (role not reported), Tim McDonald (Former ILV Study Monitor), and Peggy Bruton (role not reported; pp. 1, 5, 14-15, 38; Appendix 6, pp. 575-731 of MRID 49960503). These communications included protocol and method approval/clarification, acquisition of analytical standards and control samples, questions regarding preparation of reagents and recommended filters, trial outcome communication, SOP deviation exchange and signings, and ILV first and second trial results. No ECM 1 laboratory personnel were listed in ILV correspondence records (pp. 1, 4; Appendix 1, pp. 70-71 of MRID 47629802).

The roles/titles of Clark Chickering (ABC Laboratories, Inc.), Emily Vogl (ABC Laboratories, Inc.), Kim Douglas (Syngenta), and Nick Giovanini (ABC Laboratories, Inc.), Twyla Roth (ABC Laboratories, Inc.), Kerri Chapin (ABC Laboratories, Inc.), Bob Plastridge (ABC Laboratories, Inc.), Alex Schulthesis (Syngenta), and Peggy Bruton (Syngenta) should have been reported.

Shawna Rees (Brown) (Morse Labs/ABC Laboratories ILV study author) and Myra Manuli (Syngenta Study Sponsor/Monitor) had technical communications via telephone and email regarding remedying the low recoveries (<70%) for ametryn, prometryn, propazine, and S-metolachlor in surface water obtained from Trial 1 analyses for surface and ground water (Appendix 6, pp. 575, 650-654 of MRID 49960503).

ECM 2/ILV Communication: The ILV (Morse Labs/ABC Laboratories, Inc.) was performed as a validation of ECM 1 (p. 14 of MRID 49960503). No communication with the ECM 2 (ADPEN Laboratories, LLC) laboratory personnel was reported in the ILV or ECM 2.

ECM 1/ECM 2 Communication: ECM 1 (Syngenta) and ECM 2 (ADPEN Laboratories, LLC) were performed at different laboratories. The Study Monitor (Sunmao Chen) and ADPEN laboratory personnel for the ECM 2 were not those employed in ECM 1 (pp. 1, 4; Appendix 1, pp. 70-71 of MRID 47629802; pp. 1-7 of MRID 49960502). No communication between ECM 1 and ECM 2 laboratory personnel was reported in either study report.

18. 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. 13, 17 of MRID 47629802; p. 17 of MRID 49960502; pp. 9, 34, 39 of MRID 49960503). In ECM 1, the LOQ was defined based on the lowest fortification levels tested during the study. The ECM 1 study authors reported that the method LOQ was actually an LLMV, and an LOQ could be calculated using the Root Mean Square Error Method but was not in this study. The LOQ was reported in the ECM 2 and ILV based on the ECM 1. The LOD was defined in ECM 1 as the lowest-on-column injected quantity of analyte used to construct the calibration plot. The LODs were not reported in the ILV and ECM 2. No LOQ calculations were reported in ECM 1, ECM 2, or ILV; no LOD calculations were reported in ECM 1. Detection limits should not be based on the arbitrarily selected lowest concentration in the spiked samples. Since the LOQ was not based on scientifically acceptable procedures defined in 40 CFR Part 136, the reported LOQ is the lowest level of method validation (LLMV) rather than an LOQ.
19. In ECM 2, levels of mesotrione were evaluated in raw and treated/finished water from 59 Community Water Systems (CWS) from 7 states using Syngenta Method No. T001681-06 (pp. 14, 17 of MRID 49960502). Raw water samples were analyzed for levels of mesotrione. If mesotrione levels were $>0.05 \mu\text{g/L}$ in the raw water samples, then the corresponding finished water samples were analyzed for levels of mesotrione. In summary, low levels of mesotrione residues detected in some of the raw surface water samples [Winterset Water Treatment Plant, Iowa – up to $0.76 \mu\text{g/L}$; Creston, Iowa – up to $0.07 \mu\text{g/L}$; Flora Water Treatment, Illinois – up to $1.48 \mu\text{g/L}$; Evansville, Illinois – up to $0.38 \mu\text{g/L}$; Kaskaskia Water District, Illinois – up to $0.45 \mu\text{g/L}$; Aqua Illinois, Inc., Illinois – up to $0.23 \mu\text{g/L}$; Wayne City, Illinois – up to $0.15 \mu\text{g/L}$; Fort Wayne, Indiana – up to $0.41 \mu\text{g/L}$; Logansport, Indiana – up to $0.15 \mu\text{g/L}$; Westport Water Company – up to $0.69 \mu\text{g/L}$; Bedford Water Department, Indiana – up to $0.13 \mu\text{g/L}$; Mitchell Water Plant, Indiana – up to $0.21 \mu\text{g/L}$; Eagle Creek Water Treatment Plant, Indiana – up to $0.12 \mu\text{g/L}$; Winslow Water Works, Indiana – up to $0.08 \mu\text{g/L}$; Defiance, Ohio – up to $0.53 \mu\text{g/L}$; Versailles Water Works, Indiana – up to $0.09 \mu\text{g/L}$; Stucker Fork Treatment Plant, Indiana – up to $1.08 \mu\text{g/L}$; Baxter Springs Water Treatment Plant, Kansas – up to $0.06 \mu\text{g/L}$; Burlington City Water Works, Kansas – up to $0.08 \mu\text{g/L}$; Lacygne, Kansas – up to $0.11 \mu\text{g/L}$; Osawatomie, Kansas – up to $0.23 \mu\text{g/L}$; Chanute, Kansas – up to $0.18 \mu\text{g/L}$; Osage Co. RWD#3, Kansas – up to $0.12 \mu\text{g/L}$; Webster Co. Water District, Kentucky – up to $0.25 \mu\text{g/L}$; Hannibal Water Treatment Plant, Missouri – up to $0.18 \mu\text{g/L}$; Monroe City, Missouri – up to $0.18 \mu\text{g/L}$; Shelbina, Missouri – up to $0.12 \mu\text{g/L}$ (Salt River) and $0.08 \mu\text{g/L}$ (Shelbina Lake); Vandalia Water Treatment Plant, Missouri –

up to 0.07 µg/L; Wyaconda Water Treatment Plant, Missouri – up to 0.12 µg/L; Mcclure Water Treatment Plant, Ohio – up to 0.25 µg/L; Napoleon, Ohio – up to 0.23 µg/L; Monroeville, Ohio – up to 0.56 µg/L; Newark Water Works, Ohio – up to 0.28 µg/L; Piqua, Ohio – up to 0.33 µg/L (Swift Run); Bowling Green Water Treatment Plant, Ohio – up to 0.48 µg/L; and Upper Sandusky, Ohio – up to <0.05 µg/L], but no detections of mesotrione above the limit of quantitation (0.05 µg/L) was measured from any of the corresponding finished water samples (p. 17; Tables 5-64, pp. 23-82).

20. In the ECM 1, the study author reported that the method was not designed to resolve the stereoisomers of racemic mixtures (p. 14; Table 2, p. 21 of MRID 47629802). Additionally, the Syngenta Method T001681-06 method was reported to be “an extension and improvement” to the direct aqueous injection ESI-LC/MS/MS method reported previously by Huang, S.-B., *et al.* 2006, Perez, R., *et al.* 2005, and Reed, R.L. 2006 (pp. 7, 68 of MRID 47629802).
21. The ILV listed Protocol/SOP/Method Deviations/Memos to the Study File (pp. 38-39 of MRID 49960503). No method deviations were generated, and no other deviation negatively affected the integrity of the study.
22. In the ILV, a pre-validation evaluation was performed with the two water matrices to ensure that the test matrices were free of interferences that would affect analyte response (pp. 32-33 of MIRD 49960503). All analytes were not detected in the two ILV water matrices, except for atrazine (0.0136 µg/L) and G-30033 (0.00665 µg/L) in surface water.
23. It was reported for the ILV that each sample set of 13 samples required *ca.* 3 hours with LC/MS/MS performed overnight (p. 38 of MRID 49960503).

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

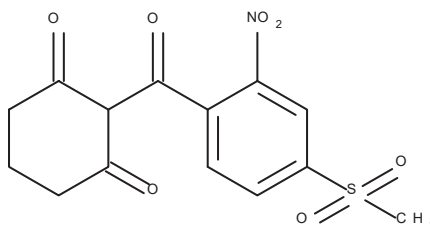
Mesotrione (ZA-1296)

IUPAC Name: 2-(4-Mesyl-2-nitrobenzoyl)cyclohexane-1,3-dione
2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione

CAS Name: 2-[4-(Methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione

CAS Number: 104206-82-8

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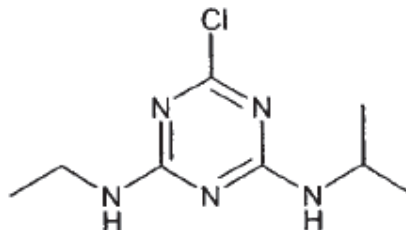
Atrazine (G-30027)

IUPAC Name: 2-Chloro-4-ethylamino-6-isopropylamino-s-triazine
6-Chloro-N²-ethyl-N⁴-isopropyl-1,3,5-triazine-2,4-diamine

CAS Name: 6-Chloro-N-ethyl-N'-(1-methylethyl)-1,3,5-triazine-2,4-diamine
6-Chloro-N-ethyl-N'-isopropyl-1,3,5-triazine-2,4-diamine
1,3,5-Triazine-2,4-diamine, 6-chloro-N-ethyl-N'-(1-methylethyl)-.

CAS Number: 1912-24-9

SMILES String: Not found



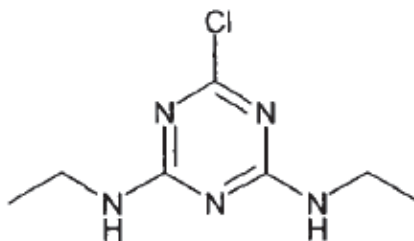
Simazine (G-27692)

IUPAC Name: 2-Chloro-4,6-bis(ethylamino)-s-triazine
6-Chloro- N^2,N^4 -diethyl-1,3,5-triazine-2,4-diamine

CAS Name: 6-Chloro- N,N' -diethyl-1,3,5-triazine-2,4-diamine
1,3,5-Triazine-2,4-diamine, 6-chloro- N,N' -diethyl-

CAS Number: 122-34-9

SMILES String: Not found



Propazine (G-30028)

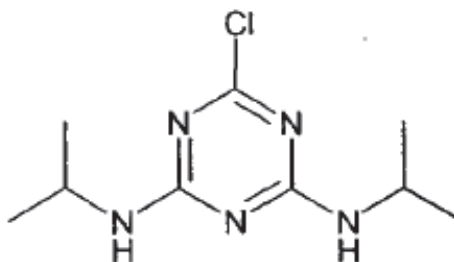
IUPAC Name: 2-Chloro-4,6-bis(isopropylamino)-s-triazine
6-Chloro- N^2,N^4 -diisopropyl-1,3,5-triazine-2,4-diamine

CAS Name: 6-Chloro- N,N' -bis(1-methylethyl)-1,3,5-triazine-2,4-diamine
6-Chloro- N,N' -diisopropyl-1,3,5-triazine-2,4-diamine

Chemical Name: 1,3,5-Triazine-2,4-diamine, 6-chloro- N,N' -bis(1-methylethyl)-

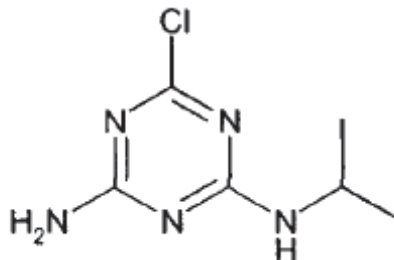
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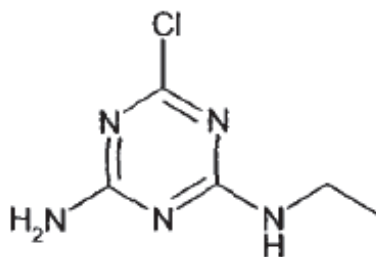
G-30033

IUPAC Name: 2-Amino-4-chloro-6-(isopropylamino)-s-triazin
CAS Name: 6-Chloro-N-(1-methylethyl)-1,3,5-triazine-2,4-diamine
CAS Number: 6190-65-4
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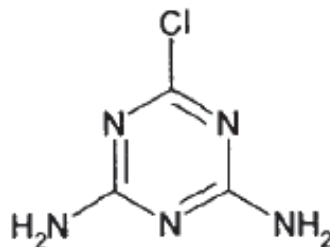
G-28279

IUPAC Name: Not reported
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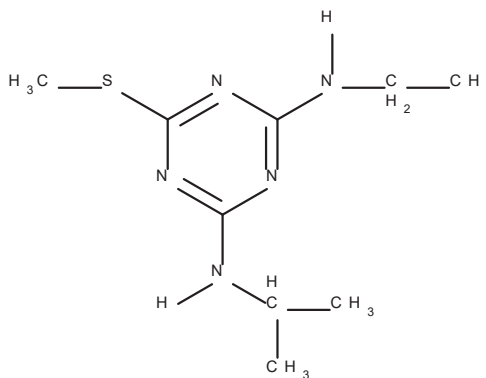
G-28273

IUPAC Name: Not reported
CAS Name: 6-Chloro-1,3,5-triazine-2,4-diamine
CAS Number: 3397-62-4
SMILES String: Not found



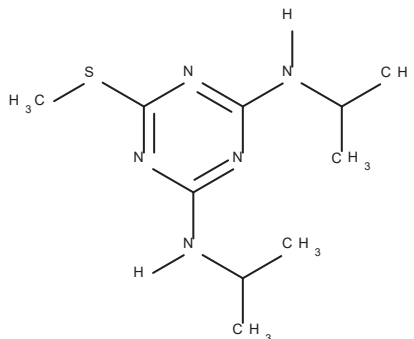
Ametryn (G-34162)

IUPAC Name: N²-ethyl-N⁴-isopropyl-6-methylthio-1,3,5-triazine-2,4-diamine
N-Ethyl-N'-isopropyl-6-methylsulfanyl-[1,3,5]triazine-2,4-diamine
CAS Name: N-ethyl-N'-(1-methylethyl)-6-(methylthio)-1,3,5-triazine-2,4-diamine
CAS Number: 834-12-8
SMILES String: CCNc1nc(NC(C)C)nc(SC)n1



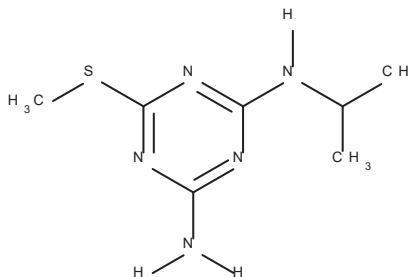
Prometryn (G-34161)

IUPAC Name: 2,4-Bis(isopropylamino)-6-methylthio-s-triazine
N²,N⁴-diisopropyl-6-methylthio-1,3,5-triazine-2,4-diamine
CAS Name: N,N'-bis(1-methylethyl)-6-(methylthio)-1,3,5-triazine-2,4-diamine
CAS Number: 7287-19-6
SMILES String: CSc1nc(NC(C)C)nc(NC(C)C)n1



GS-11354

IUPAC Name: N-Isopropyl-6-methylsulfanyl-[1,3,5]triazine-2,4-diamine
N²-isopropyl-6-methylsulfanyl-1,3,5-triazine-2,4-diamine
CAS Name: N-(1-methylethyl)-6-(methylthio)-1,3,5-triazine-2,4-diamine
CAS Number: 4147-57-3
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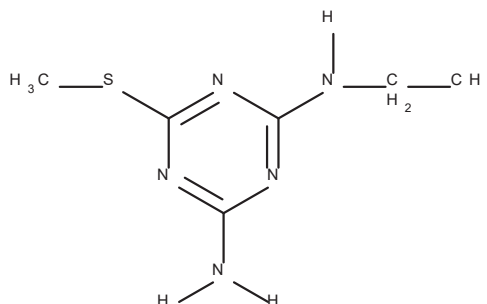
GS-11355

IUPAC Name: N4-ethyl-6-methylsulfanyl-1,3,5-triazine-2,4-diamine

CAS Name: N-Ethyl-6-(methylthio)-1,3,5-triazine-2,4-diamine

CAS Number: 4147-58-4

SMILES String: [H]N([H])c1nc(nc(n1)SC)N([H])CC



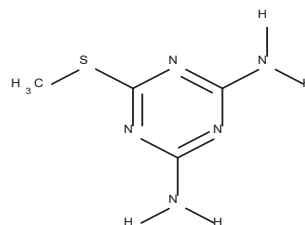
GS-26831

IUPAC Name: 6-Methylsulfanyl-1,3,5-triazine-2,4-diamine

CAS Name: 6-(Methylthio)-1,3,5-triazine-2,4-diamine

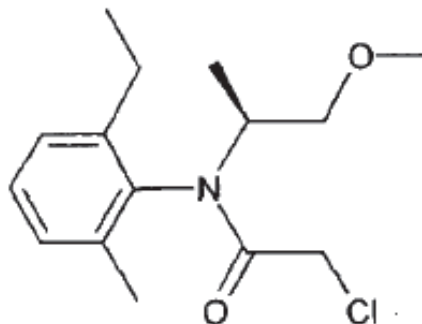
CAS Number: 5397-01-3

SMILES String: CSc1nc(nc(n1)N)N
[H]N([H])c1nc(nc(n1)SC)N([H])[H]



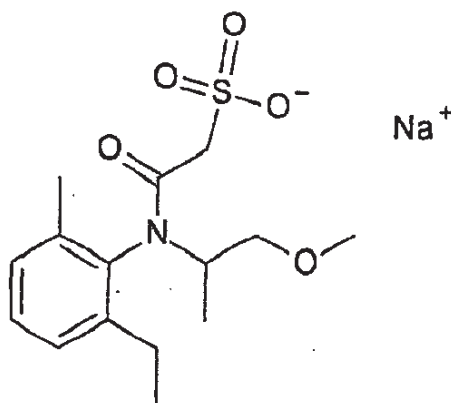
***S*-Metolachlor (CGA-77102)**

IUPAC Name: (S)-2-ethyl-6-methyl-N-(2-methoxy-1-methylethyl)-chloroacetanilide
CAS Name: (S)-2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)-acetamide
CAS Number: 87392-12-9
SMILES String: Not found



Metolachlor-ESA (Metolachlor-ethanesulfonic acid; CGA-354743)

IUPAC Name: Not reported
CAS Name: 2-[(2-ethyl-6-methylphenyl)(2-methoxyl-methylethyl)amino]-2-oxo-ethanesulfonic acid, sodium salt
CAS Number: 171118-09-5
SMILES String: Not found



122990 (Mesotrione), 080803 (Atrazine), 080807 (Simazine), 080808 (Propazine), 080801 (Ametryn), 080805 (Prometryn), and 108801 (S-Metolachlor)

MRIDs 47629802/49960502/49960503

Metolachlor-OA (Metolachlor-oxanillic acid)

IUPAC Name: Not reported

CAS Name: [(2-Ethyl-6-methylphenyl)(2-methoxy-1-methylethyl)amino]oxoacetic acid

CAS Number: 152019-73-3

SMILES String: Not found

