

Fenoxaprop-P-ethyl; EPA PC Code 129092

ENVIRONMENTAL CHEMISTRY METHOD REVIEW REPORT

Test Material: Fenoxaprop-P-ethyl

MRID: 48790001

Title: Bayer method FP-002-S11-03. An analytical method for the determination of fenoxaprop P-ethyl, AE F088406 and AE F054014 in soil using LC/MS/MS.

MRID: 48790003

Title: Independent laboratory validation of Bayer method 01056: Analytical method 01056 for the determination of fenoxaprop P-ethyl (AE F046360) and its metabolites AE F088406 and AE F054014 in soil using LC/MS/MS".

EPA PC Code: 129092

OCSPP Guideline: 850.6100

For Cambridge Environmental

Primary Reviewer: Dan Hunt

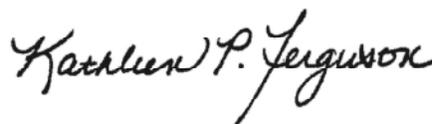
Signature:



Date: 1/11/13

Secondary Reviewer: Kathleen Ferguson

Signature:



Date: 1/11/13

QC/QA Manager: Joan Gaidos

Signature:



Date: 1/11/13

EPA MRID Number 48790001 (ECM); 48800003 (ILV)

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Data Requirement: EPA Guideline: 860.6100
OECD Data Point:

Page citations refer to MRID 48790001 (ECM) unless otherwise noted.
For MRID 48790003, the pages cited below appear in the bottom center of each page of the MRID.

Test material:

Common name: Fenoxaprop-P-ethyl
Chemical name:
IUPAC:

Primary Reviewer:  **Date:** 9/24/2013

[Chuck Peck, Environmental Engineer, EFED, ERB4]

ANALYTICAL METHOD: EPA MRID No. 48790001. Netzband, D. 2012. Bayer method FP-002-S11-03. An analytical method for the determination of fenoxaprop P-ethyl, AE F088406 and AE F054014 in soil using LC/MS/MS. Report prepared by Bayer CropScience, Stilwell, Kansas, sponsored and submitted by Bayer CropScience, Research Triangle Park, North Carolina; 17 pages. Final report issued March 27, 2012.

INDEPENDENT LABORATORY VALIDATION: EPA MRID No. 48790003. Pennell, M.F. 2012. Independent laboratory validation of Bayer method 01056: Analytical method 01056 for the determination of fenoxaprop P-ethyl (AE F046360) and its metabolites AE F088406 and AE F054014 in soil using LC/MS/MS. Report prepared by Critical Path Services, LLC, Garnet Valley, Pennsylvania, sponsored and submitted by Bayer CropScience, Research Triangle Park, North Carolina; 166 pages. Final report issued March 2, 2012.

EXECUTIVE SUMMARY

This method is designed for the quantitative determination of residues of fenoxaprop-P-ethyl and its metabolites AE F088406 and AE F054014 in soil using an external standardization method. The method was developed by Bayer CropScience. An independent laboratory validation (ILV), performed by Critical Path Services, LLC in accordance with USEPA GLP requirements, was submitted with the method.

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Method Summary: Soil is extracted twice by shaking with acetonitrile:water (80:20, v:v), followed by once with 10 g/L sodium chloride aqueous solution (p. 10). Extracts are combined, diluted with acetonitrile:water (80:20, v:v) and an aliquot mixed 1:1 with methanol:deionized water (70:30, v:v) prior to analysis for fenoxaprop-P-ethyl, AE F088406 and AE F054014 by LC/MS/MS (pp. 9-10; Appendix 1, p. 12). The ECM and ILV defined a limit of quantitation (LOQ) of 10 ng/g for all analytes in soil (p. 7; MRID 48790003, p. 12); a limit of detection (LOD) was not reported.

METHOD ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS

The original method, Bayer Method 01056 could not be independently validated (Trials 1 and 2 of the ILV); the revised method, Bayer Method FP-002-S11-02, was successfully validated on the first attempt (Trial 3 of the ILV). Data from Trials 1 and 2 are not reported in this report because they were not obtained using the method reported in the ECM.

The ECM provided by registrant titled Bayer Method FP-002-S11-03, dated March 27, 2012, appears identical to ILV validated Bayer Method FP-002-S11-02, dated January 12, 2012, except that Step 14 of Method FP-002-S11-03 indicates

“Decant the liquid into the same cylinder used in Step 5.6. Dilute the contents of the measuring cylinder to 80mL with acetonitrile/water solution (80/20). Stopper the cylinder and mix the contents.”

This step does not appear to have been included in the conduct of the ILV sample set, or in Bayer Method FP-002-S11-02. A discussion in Section 4.6, Communication with Study Sponsor, of the ILV report indicates the following

“The study sponsor asked the study director to measure the volume of the sample extract solutions to see how close they were to 80 mL. The results showed the volume was 60 mL for all of the samples (20 mL of the extraction solution was absorbed by the soil).”

As such, it is unclear if the omission of the dilution with acetonitrile/water had an impact on the results.

For the ECM, performance data, LOD, justification for selection of the LOQ concentration, and chromatograms were not provided.

For the ILV, LOD, and matrix characterization were not provided.

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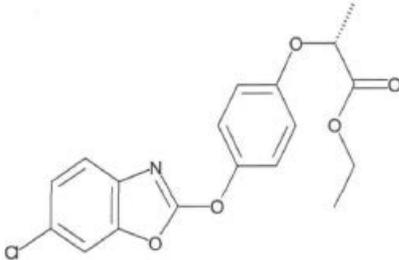
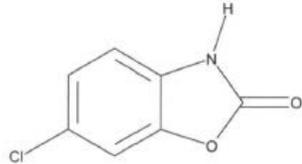
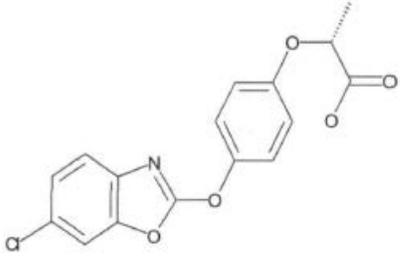
The Agency finds that this method meets the criteria for a scientifically valid method. The study is **unacceptable but upgradeable** for residues of fenoxaprop-P-ethyl and its products AE F088406 and AE F054014 in soil. If the deficiencies noted above are corrected, the study may be upgraded.

COMPLIANCE

This method was conducted according to OPPTS 860.1340 and is not an experimental study, therefore, USEPA GLP Standards 40 CFR, Part 160 do not apply (pp. 1, 3). Signed and dated statements of Data Confidentiality, GLP and Certificate of Authenticity were provided (pp. 2-4).

ENVIRONMENTAL CHEMISTRY METHOD REVIEW REPORT**A. BACKGROUND INFORMATION**

No background information was provided.

TABLE A.1. Test Compound Nomenclature	
Parameter	Value
Common name	Fenoxaprop-P-ethyl
Company experimental name	AE F046360.
IUPAC name	Not reported.
CAS Name	Ethyl (2R)-2-[4-[(6-chloro-2-benzoxazolyl)oxy]phenoxy]propanoate.
CAS #	71283-80-2.
Structure	
Common name	6-Chlorobenzoxazolone
Company experimental name	AE F054014.
IUPAC name	Not reported.
CAS Name	6-Chloro-2(3H)-benzoxazolone.
CAS #	19932-84-4.
Structure	
Common name	Fenoxaprop-P
Company experimental name	AE F088406.
IUPAC name	Not reported.
CAS Name	(2R)-2-[4-[(6-chloro-2-benzoxazolyl)oxy]phenoxy]propanoic acid.
CAS #	113158-40-0.
Structure	

Information obtained from Appendix 2, pp. 14-15 of the study report and MRID 48790003, pp. 7-8.

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Parameter	Value
Melting point/range (°C)	Not reported.
pH	Not reported.
Density (g/cm ³)	Not reported.
Water solubility at 20°C (mg/L)	Not reported.
Solvent solubility at 20°C (mg/L)	Not reported.
Vapor pressure at ___ °C (torr)	Not reported.
Dissociation constant (pK _a)	Not reported.
Octanol/water partition coefficient	Not reported.
UV/visible absorption spectrum (nm)	Not reported.

B. MATERIALS AND METHODS**B.1. Principle of Method**

Soil is extracted twice by shaking with acetonitrile:water (80:20, v:v), followed by once with 10 g/L sodium chloride aqueous solution (p. 10). Extracts are combined, diluted with acetonitrile:water (80:20, v:v) and an aliquot mixed 1:1 with methanol:deionized water (70:30, v:v) prior to analysis for fenoxaprop-P-ethyl, AE F088406 and AE F054014 by LC/MS/MS with electrospray ionization (pp. 7, 9-10; Appendix 1, pp. 12-13). For each analyte, two ion transitions are monitored for quantitation (primary) and confirmation (secondary, Appendix 1, p. 13).

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TABLE B.1. Summary Parameters for the Analytical Method Used for the Quantitation of Chemical Residues in Matrices Studied																																																											
Parameter	Value																																																										
Method ID	Bayer Method FP-002-S11-03 (p. 1)																																																										
Analyte(s)	Fenoxaprop-P-ethyl, AE F088406 and AE F054014 (p. 7).																																																										
Extraction solvent/technique	Soil (20 ± 0.2 g) is extracted twice by shaking for 20 minutes with 30 mL of acetonitrile:water (80:20, v:v) on a mechanical shaker, then centrifuged for 3 minutes at 2000 rpm. The soil is then extracted once with 20 mL of 10 g/L sodium chloride aqueous solution, with mechanical shaking and centrifuging. Extracts are combined, diluted to 80 mL with acetonitrile:water (80:20, v:v) and an aliquot (0.75 mL) mixed with 0.75 mL of methanol:deionized water (70:30, v:v; pp. 9-10).																																																										
Cleanup strategies	None.																																																										
Instrument/Detector	<p><u>ECM</u>: ABSciex API 4000 LC/MS/MS with a Phenomenex® Luna C18(2)-HST column (50 x 2.00 mm; 2.5 µm particle size) and electrospray ionization (p. 7; App. 1, p. 12). HPLC retention times are <i>ca.</i> 5.2 minutes for fenoxaprop-P-ethyl, <i>ca.</i> 5.1 minutes for AE F088406 and <i>ca.</i> 3.4 minutes for AE F054014 (App. 1, p. 13). Mobile Phase A: 10:90 (v/v) methanol:water (containing 10 mM ammonium formate and 120 µL/L formic acid) Mobile Phase B: 90:10 (v/v) methanol:water (containing 10 mM ammonium formate and 120 µL/L formic acid)</p> <table border="1"> <thead> <tr> <th>Time (min)</th> <th>Flowrate (mL/min)</th> <th>A (%)</th> <th>B (%)</th> </tr> </thead> <tbody> <tr> <td>0</td> <td>0.5</td> <td>95</td> <td>5</td> </tr> <tr> <td>0.5</td> <td>0.5</td> <td>95</td> <td>5</td> </tr> <tr> <td>2.5</td> <td>0.5</td> <td>5</td> <td>95</td> </tr> <tr> <td>6.0</td> <td>0.5</td> <td>5</td> <td>95</td> </tr> <tr> <td>7.0</td> <td>0.5</td> <td>5</td> <td>95</td> </tr> <tr> <td>7.1</td> <td>0.5</td> <td>95</td> <td>5</td> </tr> <tr> <td>8.0</td> <td>Stop</td> <td></td> <td></td> </tr> </tbody> </table> <p><u>ILV</u>: Same as ECM, except with slight modifications of instrument operating conditions (MRID 48790003, pp. 14, 17; Table 11, p. 34). HPLC retention times of <i>ca.</i> 6.37 minutes for fenoxaprop-P-ethyl, <i>ca.</i> 5.37 minutes for AE F088406 and <i>ca.</i> 4.67 minutes for AE F054014 (MRID 48790003, p. 18). Mobile Phase A: 10:90 (v/v) methanol:water (containing 10 mM ammonium formate and 120 µL/L formic acid) Mobile Phase B: 90:10 (v/v) methanol:water (containing 10 mM ammonium formate and 120 µL/L formic acid)</p> <table border="1"> <thead> <tr> <th>Time (min)</th> <th>Flowrate (mL/min)</th> <th>A (%)</th> <th>B (%)</th> </tr> </thead> <tbody> <tr> <td>0</td> <td>0.5</td> <td>95</td> <td>5</td> </tr> <tr> <td>4.0</td> <td>0.5</td> <td>5</td> <td>95</td> </tr> <tr> <td>7.0</td> <td>0.5</td> <td>5</td> <td>95</td> </tr> <tr> <td>7.1</td> <td>0.5</td> <td>95</td> <td>5</td> </tr> <tr> <td>10.5</td> <td>Stop</td> <td></td> <td></td> </tr> </tbody> </table>			Time (min)	Flowrate (mL/min)	A (%)	B (%)	0	0.5	95	5	0.5	0.5	95	5	2.5	0.5	5	95	6.0	0.5	5	95	7.0	0.5	5	95	7.1	0.5	95	5	8.0	Stop			Time (min)	Flowrate (mL/min)	A (%)	B (%)	0	0.5	95	5	4.0	0.5	5	95	7.0	0.5	5	95	7.1	0.5	95	5	10.5	Stop		
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Information obtained from pp. 1, 7, 9-10; Appendix 1, pp. 12-13 of the study report and MRID 48790003, pp. 14, 17-18; Table 11, p. 34.

C. RESULTS AND DISCUSSION**C.1. Recovery Results Summary**

Analyte	Spiking Level (µg a.i.)	Mean Recoveries Obtained (%)	Relative Standard Deviation
Fenoxaprop-P-ethyl	--	--	--
	--	--	--
AE F088406	--	--	--
	--	--	--
AE F054014	--	--	--
	--	--	--

-- = Not reported.

C.1.1. Method Characteristics

Parameter	Value
Analyte(s)	Fenoxaprop-P-ethyl, AE F088406 and AE F054014 (p. 7).
Limit of Quantitation (LOQ)	0.01 mg/kg (p. 7)
Limit of Detection (LOD)	Not reported.
Accuracy/Precision at LOQ	<u>ECM</u> : Performance data were not reported.
Reliability of the Method/[ILV]	Acceptance criteria were met at the LOQ and 10 x LOQ for all analytes in soil (both primary and confirmation ions), with matrix spike recoveries ranging between 70% to 120% and relative standard deviation of ≤20% (MRID 48790003, Appendix 1A, pp. 68-70; Appendix 1B, pp. 77-79). Time required per validation sample set was reported as 11 hours (MRID 48790003, p. 20).
Linearity	<u>ECM</u> : No information provided. <u>ILV</u> : Linear regression; $r^2 = 0.998$ for fenoxaprop-P-ethyl; $r^2 = 0.9996-0.9998$ for AE F088406; $r^2 = 0.998$ for AE F054014 (weighted 1/x; reported in MRID 48790003, Appendix 1A, pp. 68-70; Appendix 1B, pp. 77-79).
Specificity	<u>ECM</u> : Could not be evaluated because only an example chromatogram, in water, was provided (Appendix 3, p. 16). <u>ILV</u> : Matrix blank controls showed some interferences at the retention times of fenoxaprop-P-ethyl in the methanol:water blank, reagent blank and matrix control (MRID 48790003, pp. 38, 41, 42,

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TABLE C.2. Method Characteristics	
Parameter	Value
	68, 77) and AE F088406 in matrix control (MRID 48790003, p. 69); however, interferences were <1% of LOQ. AE F054014 had no interferences at the expected retention times in reagent blanks and matrix controls (MRID 48790003, pp. 54, 57, and 58).

Information obtained from p. 7; Appendix 3, p. 16 of the study report; MRID 48790003, p. 20; Appendix 1A, pp. 68-70; Appendix 1B, pp. 77-79.

C.2. Independent Laboratory Validation (ILV)

The ILV was conducted according to OPPTS 850.7100 and 860.1340 (MRID 48790003, p. 1). Signed and dated statements of Data Confidentiality, GLP (40 CFR, Part 160), Quality Assurance and Certification of Authenticity were provided (MRID 48790003, pp. 2-5).

TABLE C.3. Recovery Results of the Method Obtained by an Independent Laboratory Validation for the Determination of Fenoxaprop-P-ethyl in Soil (n = 5)¹				
Analyte	Spiking Level (mg a.i./kg)	Ion Monitored	Mean Recoveries Obtained (%)	Relative Standard Deviation
Fenoxaprop-P-ethyl	0.01 (LOQ)	288.1	88	4.1
		77.1	88	2.3
	0.1	288.1	91	1.4
		77.1	92	2.1
AE F088406	0.01 (LOQ)	259.9	95	2.0
		151.9	95	3.5
	0.1	259.9	91	1.2
		151.9	91	1.7
AE F054014	0.01 (LOQ)	131.9	96	3.8
		76.0	93	3.4
	0.1	131.9	102	2.1
		76.0	104	2.2

Information obtained from MRID 48790003, Appendix 1A, pp. 68-70; Appendix 1B, pp. 77-79.

¹ Soil was not characterized.

D. CONCLUSION

This method is designed for the quantitative determination of residues of fenoxaprop-P-ethyl and its products AE F088406 and AE F054014 in soil. The Agency finds that this method meets the criteria for a scientifically valid method. The study is **unacceptable but upgradeable** for residues of fenoxaprop-P-ethyl and its products AE F088406 and AE F054014 in soil. The ILV demonstrated acceptable performance data at the LOQ and

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10 x LOQ. The ECM did not provide any method validation data and the matrix was not characterized in the ILV.

EPA MRID Number 48790001 (ECM); 48800003 (ILV)