

Analytical method for fluindapyr [IR9792 (F9990)] and its metabolites 3-hydroxy-IR9792/F9990, 1-carboxy-IR9792/F9990 (sum of diastereomers), and pyrazole carboxamide in soil

Reports: ECM 1: EPA MRID No.: 50508176. Schreier, T. 2017. Terrestrial Field Dissipation of F9990 (IR9792) in New York, USA. FMC Tracking No.: 2014EFT-IFP1205. Study No.: PSM-14-02-02. Report prepared by Precision Study Management, Amarillo, Texas and SGS North America, Brookings, South Dakota (Analytical Phase); and sponsored and submitted by ISAGRO SpA, Milano, Italy, and FMC Corporation, Ewing, New Jersey; 253 pages. Final report issued December 31, 2017.

ECM 2: EPA MRID No.: 50508178. Schreier, T. 2018. Terrestrial Field Dissipation of F9990 (IR9792) in Nebraska, USA. FMC Tracking No.: 2014EFT-IFP1331. Study No.: PSM-14-02-04. Report prepared by Precision Study Management, Amarillo, Texas and SGS North America, Brookings, South Dakota (Analytical Phase); and sponsored and submitted by ISAGRO SpA, Milano, Italy, and FMC Corporation, Ewing, New Jersey; 253 pages. Final report issued January 3, 2018.

ILV: EPA MRID No. 50518199. Sahvorost, N. 2018. – Final Report. Independent Laboratory Validation of Analytical Method for the Determination of IR9792/F9990, 3-Hydroxy-IR9792/F9990, 1-Carboxy-IR9792/F9990 (sum of diastereomers), and Pyrazole Carboxamide in Soil. FMC Code No.: 2017AMT-IFP3870. Study Code No.: S17-07372. Report prepared by Eurofins Agrosience Services, Inc., Lancaster, Pennsylvania, sponsored and submitted by FMC Corporation, Ewing, New Jersey; 226 pages. Final report issued February 15, 2018.

Document No.: MRIDs 50518076 & 50518078 & 50518199

Guideline: 850.6100

Statements: ECM 1: The study was conducted in accordance with the USEPA FIFRA (40 CFR Part 160) and OECD Good Laboratory Practice (GLP) standards, with the exception of the collection of the trial and historical weather data, cultural practices, irrigation records, and pesticide history and maintenance, as well as the fact that the emails were not signed and dated (p. 3 of MRID 50518076). Signed and dated Data Confidentiality, GLP and Quality Assurance statements were provided (pp. 2-4). A certification of authenticity was included with the Quality Assurance statement.


ECM 2: The study was conducted in accordance with the USEPA FIFRA (40 CFR Part 160) and OECD Good Laboratory Practice (GLP) standards, with the exception of the collection of the trial and historical weather data, cultural practices, irrigation records, and pesticide history and maintenance, as well as the fact that the emails were not signed and dated (p. 3 of MRID 50518078). Signed and dated Data Confidentiality, GLP and Quality Assurance statements were provided (pp. 2-4). A certification of authenticity was included with the Quality Assurance statement.

ILV: The study was conducted in accordance with the USEPA FIFRA GLP standards (40 CFR Part 160; pp. 3, 6 of MRID 50518199). Signed and dated No Data Confidentiality, GLP and Quality Assurance statements were provided (pp. 2-4). A certification of authenticity was included with the Quality Assurance statement.

Classification: This analytical method is classified as Supplemental. ILV, ECM 1, and ECM 2 representative chromatograms did not support the specificity of the method for pyrazole carboxamide. ILV linearity was not satisfactory for 3-hydroxy-IR9792/F9990 in the NE loamy sand soil (Q), 1-carboxy-IR9792/F9990 diastereomer 1 in the NY silt loam soil (Q & C), and 1-carboxy-IR9792/F9990 diastereomer 2 in the NY silt loam soil (Q).


PC Code: 138008

EFED Final Reviewer: Patricia Engel
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Date: 4/21/2020

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

Executive Summary

The analytical method, Precision Study Management Study Nos. PSM-14-02-02 and PSM-14-02-04, is designed for the quantitative determination of fluindapyr and its three metabolites 3-hydroxy-IR9792/F9990, 1-carboxy-IR9792/F9990 (sum of diastereomers), and pyrazole carboxamide in soil at the LOQ of 0.005 mg/kg using LC/MS/MS. The LOQ for 1-carboxy-IR9792/F9990 was further defined as 0.00316 mg/kg and 0.00184 mg/kg for diastereomer 1 and 2, respectively, and were derived from the method LOQ for the sum of the diastereomers and the ratio of each of the diastereomers. Samples were fortified with both diastereomers; only quantification was performed separately. The method LOQ (0.005 mg/kg) is less than the lowest toxicological level of concern in soil for fluindapyr. Relative magnitude of the LOQ for fluindapyr metabolites relative to the lowest toxicological level of concern for each in soil is unknown.¹ The analytical phase report (containing method validation results) of ECM 1 and ECM 2 was identical and used the soils from ECM 1 and ECM 2. The ECM 1 and ECM 2 validated the method using characterized loamy sand and silt loam soil matrices collected from two fluindapyr terrestrial field dissipation studies performed by Precision Study Management;

¹ Toxicological levels of concern have not been established for metabolites.

the ILV validated the method for all analytes using the same two soil matrices which were used by the ECM 1 and ECM 2. In the ECM1 and ECM 2, only the quantitation ion transition was quantified; a confirmatory method is typically not required where GC/MS and/or LC/MS methods are used as the primary method. The ILV validated the method in ECM 1 and ECM 2 for all analytes at both fortification levels in both soils in the first trial with insignificant modifications of the use of a reciprocal shaker instead of a wrist-action shaker, the use of matrix-matched standards, and optimization of the analytical method parameters and equipment. All ECM 1, ECM 2, and ILV data was satisfactory regarding accuracy and precision. The ECM had not provided recovery results specifically for 1-carboxy-IR9792/F9990 (sum of diastereomers), but rather diastereomer 1 and 2 of 1-carboxy-IR9792/F9990 separately. Since acceptable results were found for the individual diastereomers of 1-carboxy-IR9792/F9990, the reviewer concluded that acceptable results would be found for the summation of the results of the individual diastereomers of 1-carboxy-IR9792/F9990. ILV linearity was not satisfactory for 3-hydroxy-IR9792/F9990 in the NE loamy sand soil (Q), 1-carboxy-IR9792/F9990 diastereomer 1 in the NY silt loam soil (Q & C), and 1-carboxy-IR9792/F9990 diastereomer 2 in the NY silt loam soil (Q); ECM linearity was satisfactory for all analytes. ILV, ECM 1, and ECM 2 representative chromatograms did not support the specificity of the method for pyrazole carboxamide due to very broad LOQ and 10×LOQ peaks (Q & C) with significant shouldering and poorly defined RT peaks.

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 | | | | | | |
| Fluindapyr (IR9792/F9990) | 50518076 ¹ & 50518078 ¹ | 50518099 | | Soil ^{2,3} | 31/12/2017 ⁴ & 31/08/2017 ⁵ (MRID 50518076) | FMC Corporation | LC/MS/MS | 0.005 mg/kg |
| 3-Hydroxy-IR9792/F9990 | | | | | | | | |
| Pyrazole carboxamide | | | | | | | | |
| 1-Carboxy-IR9792/F9990 (sum of diastereomers) | | | | | | | | 0.00316 mg/kg ⁷ |
| 1-Carboxy-IR9792/F9990 (diastereomer 1) ⁶ | | | | | | | | |
| 1-Carboxy-IR9792/F9990 (diastereomer 2) ⁶ | | | | | | | | |

- 1 The analytical phase report (containing method validation results) of ECM 1 (MRID 50518076) and ECM 2 (MRID 50518078) was identical with respect to the method procedure and method validation results for the soils from ECM 1 and ECM 2.
- 2 In the ECM 1 and ECM 2, Nebraska loamy sand soil (0-6"; 83% sand, 10% silt, 7% clay; pH 6.0 in 1:1 soil:water ratio; 0.90% organic carbon – Walkley Black) and New York silt loam soil (0-6"; 25% sand, 60% silt, 15% clay; pH 5.1 in 1:1 soil:water ratio; 2.5% organic carbon – Walkley Black) were used in the study (USDA soil texture classification; Appendix IV, Attachment 1, pp. 211-212 of MRID 50518076; Appendix IV, Attachment 1, p. 212 of MRID 50518078). The soil matrices were collected as part of two fluindapyr terrestrial field dissipation studies performed by Precision Study Management (Amarillo, Texas; p. 1 of MRID 50518076; p. 1 of MRID 50518078). The test systems were bare ground soil plots located near Brunswick, Nebraska, USA at the junction of North American Eco-regions 9.2, 9.3 and 9.4 and near North Rose, New York, USA in the North American Eco-region 8.1 (p. 16 of MRID 50518076; p. 16 of MRID 50518078). Site use for the past three years of the two sites were included in the study report.
- 3 In the ILV, Nebraska loamy sand soil (0-6"; SGS Soil ID 14-02-04 UTC-SC-1-CTR-6; 83% sand, 10% silt, 7% clay; pH 6.0 in 1:1 soil:water ratio; 0.90% organic carbon – Walkley Black) and New York silt loam soil (0-6"; SGS Soil ID 14-02-02 UTC-SC-1-CTR-6; 25% sand, 60% silt, 15% clay; pH 5.1 in 1:1 soil:water ratio; 2.5% organic carbon – Walkley Black) were used in the study (USDA soil texture classification; pp. 20-21 of MRID 50518199). The soil matrices were the same as those used in the ECM 1 and ECM 2.
- 4 Date for the terrestrial field dissipation report (p. 1 of MRID 50518076; p. 1 of MRID 50518078).
- 5 Date for the analytical phase report of the terrestrial field dissipation report (Appendix III, p. 68 of MRID 50518076; Appendix III, p. 67 of MRID 50518078).
- 6 Diastereomer 1 and 2 were termed diastereomer a and b in the ILV.
- 7 The individual LOQs for diastereomer 1 and 2 of 1-carboxy-IR9792/F9990 were derived from the method LOQ for the sum of the diastereomers and the ratio of each of the diastereomers. Samples were fortified with the 1.72:1 mixture of diastereomers at the method LOQ (0.005 mg/kg); only quantification was performed separately in the HPLC/MS/MS chromatograms.

I. Principle of the Method

Soil (5.0 ± 0.1 g) was weighed into a 50-mL centrifuge tube and fortified with 250 μ L of standard solution of fluindapyr or one of its metabolites in methanol (Appendix III, pp. 80-83 of MRID 50518076; Appendix III, pp. 79-83 50518078). The samples were extracted with 25 mL of acetone:water (9:1, v:v) via shaking on a wrist-action shaker for *ca.* 60 minutes. After centrifugation (4000 rpm for *ca.* 10 minutes), the supernatant was decanted into a 100-mL volumetric flask (filter paper may be used). The soil pellet was extracted once with 25 mL of acetone:water (1:1, v:v) and once with 25 mL of acetone:0.5N HCl (1:1, v:v) via sonication at *ca.* 40°C for 60 minutes then shaking on a wrist-action shaker for *ca.* 60 minutes. All supernatants were combined in the 100-mL volumetric flask. The volume of the extract was adjusted to 100 mL using acetone. A 50-mL aliquot was removed and centrifuged prior to the removal of a 5-mL aliquot. The 5-mL aliquot was evaporated under nitrogen until *ca.* 1-2 mL water remained. The volume was adjusted to 5-mL using methanol, and a portion was removed for HPLC/MS/MS analysis.

Samples were analyzed using either A) a Dionex Ultimate 3000 UHPLC coupled to a Sciex Triple Quadrupole API 4000 MS or B) a Shimadzu Nexera XR HPLC coupled to a Sciex Triple Quadrupole 6500+ MS (Appendix III, pp. 83-86 of MRID 50518076; Appendix III, pp. 83-86 50518078). The following LC conditions were used for both HPLC/MS Systems: Phenomenex Kinetex 2.6 μ C18 100A column (50 x 4.6 mm, column temperature 20°C), SecurityGuard Ultra Cartridge UHPLC C18 for 4.6 mm guard column, mobile phase of (A) 10mM ammonium acetate and 0.2% formic acid in water and (B) 0.2% formic acid in methanol [percent A:B (v:v) at 0-3.5 min. 90:10, 6.0 min. 60:40, 22.0-23.0 min. 20:80, 23.1-24.0 min. 90:10], and injection volume of 10 μ L. The following MS/MS conditions were used for the two diastereomers of 1-carboxy-IR9792/F9990 and pyrazole carboxamide: positive electrospray ionization mode and multiple reaction monitoring (MRM). The following MS/MS conditions were used for 3-hydroxy-IR9792/F9990: negative electrospray ionization mode and MRM. Analytes were identified with HPLC/MS/MS System A using two ion pair transitions as follows (primary and confirmatory, respectively): m/z 176.059 \rightarrow 136 and m/z 176.059 \rightarrow 156 for pyrazole carboxamide; m/z 382.1 \rightarrow 336.200 and m/z 382.1 \rightarrow 296.100 for 1-carboxy-IR9792/F9990 (diastereomer 1); m/z 382.1 \rightarrow 336.201 and m/z 382.1 \rightarrow 296.101 for 1-carboxy-IR9792/F9990 (diastereomers 2); m/z 366.235 \rightarrow 174.8 and m/z 366.235 \rightarrow 130.7 for 3-hydroxy-IR9792/F9990, and m/z 352.185 \rightarrow 332.1 and m/z 352.185 \rightarrow 256.1 for fluindapyr. Analytes were identified with HPLC/MS/MS System B using two ion pair transitions as follows (primary and confirmatory, respectively): m/z 176.0 \rightarrow 136.0 and m/z 176.0 \rightarrow 156.0 for pyrazole carboxamide; m/z 382.1 \rightarrow 336.1 and m/z 382.1 \rightarrow 296.1 for 1-carboxy-IR9792/F9990 (diastereomer 1); m/z 382.1 \rightarrow 336.1 and m/z 382.1 \rightarrow 296.1 for 1-carboxy-IR9792/F9990 (diastereomers 2); m/z 366.1 \rightarrow 175.0 and m/z 366.1 \rightarrow 131.0 for 3-hydroxy-IR9792/F9990, and m/z 352.1 \rightarrow 256.1 and m/z 352.1 \rightarrow 312.1 for fluindapyr. Approximate retention times with HPLC/MS/MS System A were 2.7, 11.80, 12.63, 17.63, and 18.78 minutes for pyrazole carboxamide, 1-carboxy-IR9792/F9990 (diastereomer 1), 1-carboxy-IR9792/F9990 (diastereomers 2), 3-hydroxy-IR9792/F9990, and fluindapyr, respectively. Approximate retention times with HPLC/MS/MS System B were 2.8, 11.8, 12.6, 17.8, and 18.9 minutes for pyrazole carboxamide, 1-carboxy-IR9792/F9990 (diastereomer 1), 1-carboxy-IR9792/F9990 (diastereomers 2), 3-hydroxy-IR9792/F9990, and fluindapyr,

respectively. Solvent-based calibration standards were used in the ECM (Appendix III, p. 81 of MRID 50518076; Appendix III, p. 80 of MRID 50518078).

The independent laboratory performed the ECM as written, except for the use of a reciprocal shaker instead of a wrist-action shaker, the use of matrix-matched standards, and insignificant analytical method modifications for optimization (p. 21; Appendix A, pp. 34-38, 41 of MRID 50518199). Samples were analyzed using a Shimadzu Nexera X2 HPLC coupled to an Applied Biosystems Sciex API 4000 MS. All LC and MS parameters were the same as the ECM, except that a guard column was not used. Analytes were identified using two ion pair transitions as follows (primary and confirmatory, respectively): m/z 176→136 and m/z 176→156 for pyrazole carboxamide; m/z 382→336.200 and m/z 382→296.100 for 1-carboxy-IR9792/F9990 (diastereomer 1); m/z 382→336.201 and m/z 382→296.101 for 1-carboxy-IR9792/F9990 (diastereomers 2); m/z 366→175 and m/z 366→131 for 3-hydroxy-IR9792/F9990, and m/z 352→332 and m/z 352→357 for fluindapyr (these were similar to those of the ECM for HPLC/MS System A). Expected retention times were *ca.* 3.0, 11.9, 12.8, 18.0, and 19.0 minutes for pyrazole carboxamide, 1-carboxy-IR9792/F9990 (diastereomer 1), 1-carboxy-IR9792/F9990 (diastereomers 2), 3-hydroxy-IR9792/F9990, and fluindapyr, respectively. The ILV modifications did not warrant an updated ECM.

In the ECM 1, ECM 2, and ILV, Limit of Quantification (LOQ) for fluindapyr, pyrazole carboxamide, 1-carboxy-IR9792/F9990 (sum of diastereomers), and 3-hydroxy-IR9792/F9990 in soil was 0.005 mg/kg (Appendix III, p. 94 of MRID 50518076; Appendix III, p. 93 of MRID 50518078; pp. 27, 29 of MRID 50518199). In the ECM 1, ECM 2, and ILV, the LOQ for 1-carboxy-IR9792/F9990 was further defined as 0.00316 mg/kg and 0.00184 mg/kg for diastereomer 1 and 2, respectively (diastereomer 1 and 2 were termed diastereomer a and b in the ILV). The Limit of Detection (LOD) for all analytes in soil was 0.001 mg/kg (20% of the LOQ) in the ECM 1, ECM 2, and ILV. In the ECM 1, ECM 2, and ILV, the LOD for 1-carboxy-IR9792/F9990 was further defined as 0.000632 mg/kg and 0.000368 mg/kg for diastereomer 1 and 2, respectively.

II. Recovery Findings

ECM 1 (MRID 50518076) & ECM 2 (MRID 50518078): The analytical phase report (containing method validation results) of ECM 1 and ECM 2 was identical with respect to the method procedure and method validation results for the soils from ECM 1 and ECM 2. Mean recoveries and relative standard deviations (RSD) were within guideline requirements (mean 70-120%; RSD \leq 20%) for analysis of fluindapyr [IR9792(F9990)] and its two metabolites 3-hydroxy-IR9792/F9990 and pyrazole carboxamide in two soil matrices at fortification levels of 0.005 mg/kg (LOQ) and 0.05 mg/kg (10 \times LOQ; Appendix III, Tables 1-10, pp. 96-100 of MRID 50518076; Appendix III, Tables 1-10, pp. 95-99 of MRID 50518078). The two diastereomers of 1-carboxy-IR9792/F9990 were quantified separately, but not together. Mean recoveries and RSDs were within guidelines for analysis for 1-carboxy-IR9792/F9990 (diastereomer 1) in two soil matrices at fortification levels of 0.00316 mg/kg (LOQ) and 0.0316 mg/kg (10 \times LOQ), and mean recoveries and RSDs were within guidelines for analysis for 1-carboxy-IR9792/F9990 (diastereomer 2) in two soil matrices at fortification levels of 0.00184 mg/kg (LOQ) and 0.0184 mg/kg (10 \times LOQ). Analytes were identified using two ion pair transitions (primary and confirmatory) with HPLC/MS/MS System A or HPLC/MS/MS System B; however, recovery results were only reported for the primary/quantitation ion transition. A confirmatory method is not usually required when LC/MS or GC/MS is used as the primary method to generate study data. In the ECM 1 and ECM 2, Nebraska loamy sand soil (0-6"; 83% sand, 10% silt, 7% clay; pH 6.0 in 1:1 soil:water ratio; 0.90% organic carbon – Walkley Black) and New York silt loam soil (0-6"; 25% sand, 60% silt, 15% clay; pH 5.1 in 1:1 soil:water ratio; 2.5% organic carbon – Walkley Black) were used in the study (USDA soil texture classification; Appendix IV, Attachment 1, pp. 211-212 of MRID 50518076; Appendix IV, Attachment 1, p. 212 of MRID 50518078). The soil matrices were collected as part of two fluindapyr terrestrial field dissipation studies performed by Precision Study Management (Amarillo, Texas; p. 1 of MRID 50518076; p. 1 of MRID 50518078). The test systems were bare ground soil plots located near Brunswick, Nebraska, USA at the junction of North American Eco-regions 9.2, 9.3 and 9.4 and near North Rose, New York, USA in the North American Eco-region 8.1 (p. 16 of MRID 50518076; p. 16 of MRID 50518078). Site use for the past three years of the two sites were included in the study report.

ILV (MRID 50518199): Mean recoveries and RSDs were within guidelines for analysis for analysis of fluindapyr [IR9792(F9990)] and its three metabolites 3-hydroxy-IR9792/F9990, 1-carboxy-IR9792/F9990 (sum of diastereomers), and pyrazole carboxamide in two soil matrices at fortification levels of 0.005 mg/kg (LOQ) and 0.05 mg/kg (10 \times LOQ; pp. 24-27). The two diastereomers of 1-carboxy-IR9792/F9990 were quantified separately, as well as summed together. Mean recoveries and RSDs were within guidelines for analysis for 1-carboxy-IR9792/F9990 (diastereomer a) in two soil matrices at fortification levels of 0.00316 mg/kg (LOQ) and 0.0316 mg/kg (10 \times LOQ), and mean recoveries and RSDs were within guidelines for analysis for 1-carboxy-IR9792/F9990 (diastereomer b) in two soil matrices at fortification levels of 0.00184 mg/kg (LOQ) and 0.0184 mg/kg (10 \times LOQ). Diastereomer 1 and 2 were termed diastereomer a and b in the ILV. Analytes were identified and quantified using two ion transitions; quantitation ion and confirmation ion recovery results were comparable. Nebraska loamy sand soil (0-6"; SGS Soil ID 14-02-04 UTC-SC-1-CTR-6; 83% sand, 10% silt, 7% clay; pH 6.0 in 1:1 soil:water ratio; 0.90% organic carbon – Walkley Black) and New York silt loam

soil (0-6"; SGS Soil ID 14-02-02 UTC-SC-1-CTR-6; 25% sand, 60% silt, 15% clay; pH 5.1 in 1:1 soil:water ratio; 2.5% organic carbon – Walkley Black) were used in the study (USDA soil texture classification; pp. 20-21). The soil matrices were the same as those used in the ECM 1 and ECM 2. The method was validated for all analytes at both fortification levels in both soils in the first trial with insignificant modifications of the use of a reciprocal shaker instead of a wrist-action shaker, the use of matrix-matched standards, and optimization of the analytical method parameters and equipment (pp. 21, 28-29; Appendix A, pp. 36-38, 41).

Table 2. Initial Validation Method Recoveries for Fluindapyr [IR9792 (F9990)] and Its Metabolites 3-Hydroxy-IR9792/F9990, 1-Carboxy-IR9792/F9990 (Sum of Diastereomers), and Pyrazole Carboxamide in Soil^{1,2}

| Analyte | Fortification Level (mg/kg) | Number of Tests | Recovery Range (%) | Mean Recovery (%) | Standard Deviation (%) | Relative Standard Deviation (%) |
|---|-----------------------------|-----------------|--------------------|-------------------|------------------------|---------------------------------|
| Nebraska Loamy Sand Soil | | | | | | |
| Quantitation Ion Transition | | | | | | |
| Fluindapyr [IR9792 (F9990)] | 0.005 | 5 | 84.44-92.43 | 88.68 | 3.65 | 4.11 |
| | 0.05 | 5 | 88.55-94.32 | 91.81 | 2.07 | 2.26 |
| 3-Hydroxy-IR9792/F9990 | 0.005 | 5 | 73.21-94.63 | 84.65 | 8.25 | 9.75 |
| | 0.05 | 5 | 90.23-97.10 | 94.31 | 2.66 | 2.82 |
| 1-Carboxy-IR9792/F9990 (Diastereomer 1) | 0.00316 | 5 | 81.67-90.01 | 85.79 | 3.10 | 3.62 |
| | 0.0316 | 5 | 72.88-93.20 | 80.49 | 8.20 | 10.19 |
| 1-Carboxy-IR9792/F9990 (Diastereomer 2) | 0.00184 | 5 | 78.39-86.25 | 82.66 | 3.07 | 3.72 |
| | 0.0184 | 5 | 72.86-95.11 | 82.40 | 8.27 | 10.04 |
| 1-Carboxy-IR9792/F9990 (Sum of Diastereomers) | 0.005 | 5 | Not summed | | | |
| | 0.05 | 5 | | | | |
| Pyrazole Carboxamide | 0.005 | 5 | 84.22-92.46 | 87.87 | 3.55 | 4.04 |
| | 0.05 | 5 | 89.37-99.10 | 92.72 | 3.72 | 4.01 |
| New York Silt Loam Soil | | | | | | |
| Quantitation Ion Transition | | | | | | |
| Fluindapyr [IR9792 (F9990)] | 0.005 | 5 | 85.12-92.21 | 88.87 | 3.08 | 3.47 |
| | 0.05 | 5 | 86.52-96.37 | 92.88 | 3.88 | 4.17 |
| 3-Hydroxy-IR9792/F9990 | 0.005 | 5 | 72.85-80.50 | 77.29 | 3.03 | 3.92 |
| | 0.05 | 5 | 75.82-87.82 | 82.32 | 4.94 | 5.93 |
| 1-Carboxy-IR9792/F9990 (Diastereomer 1) | 0.00316 | 5 | 74.13-86.03 | 81.46 | 6.46 | 7.93 |
| | 0.0316 | 5 | 86.92-100.57 | 93.83 | 5.04 | 5.37 |
| 1-Carboxy-IR9792/F9990 (Diastereomer 2) | 0.00184 | 5 | 73.99-93.19 | 84.00 | 9.41 | 11.20 |
| | 0.0184 | 5 | 84.09-97.37 | 90.18 | 4.77 | 5.29 |
| 1-Carboxy-IR9792/F9990 (Sum of Diastereomers) | 0.005 | 5 | Not summed | | | |
| | 0.05 | 5 | | | | |
| Pyrazole Carboxamide | 0.005 | 5 | 75.84-89.91 | 81.86 | 5.31 | 6.49 |
| | 0.05 | 5 | 98.50-106.49 | 100.91 | 3.34 | 3.21 |

Data (recovery results were corrected when residues were quantified in the controls; Appendix III, p. 91 of MRID 50518076; Appendix III, p. 90 of MRID 50518078) were obtained from Appendix III, Tables 1-10, pp. 96-100 of MRID 50518076; Appendix III, Tables 1-10, pp. 95-99 of MRID 50518078.

1 The Nebraska loamy sand soil (0-6"; 83% sand, 10% silt, 7% clay; pH 6.0 in 1:1 soil:water ratio; 0.90% organic carbon – Walkley Black) and New York silt loam soil (0-6"; 25% sand, 60% silt, 15% clay; pH 5.1 in 1:1 soil:water ratio; 2.5% organic carbon – Walkley Black) were used in the study (USDA soil texture classification; Appendix IV, Attachment 1, pp. 211-212 of MRID 50518076; Appendix IV, Attachment 1, p. 212 of MRID 50518078). The soil matrices were collected as part of two fluindapyr terrestrial field dissipation studies performed by Precision Study Management (Amarillo, Texas; p. 1 of MRID 50518076; p. 1 of MRID 50518078). The test systems were bare ground soil plots located near Brunswick, Nebraska, USA at the junction

of North American Eco-regions 9.2, 9.3 and 9.4 and near North Rose, New York, USA in the North American Eco-region 8.1 (p. 16 of MRID 50518076; p. 16 of MRID 50518078). Site use for the past three years of the two sites were included in the study report.

- 2 Analytes were identified using two ion pair transitions (primary and confirmatory) with HPLC/MS/MS System A or HPLC/MS/MS System B; however, recovery results were only reported for the primary/quantitation ion transition. A confirmatory method is not usually required when LC/MS or GC/MS is used as the primary method to generate study data. Analytes were identified with HPLC/MS/MS System A using two ion pair transitions as follows (primary and confirmatory, respectively): m/z 176.059→136 and m/z 176.059→156 for pyrazole carboxamide; m/z 382.1→336.200 and m/z 382.1→296.100 for 1-carboxy-IR9792/F9990 (diastereomer 1); m/z 382.1→336.201 and m/z 382.1→296.101 for 1-carboxy-IR9792/F9990 (diastereomers 2); m/z 366.235→174.8 and m/z 366.235→130.7 for 3-hydroxy-IR9792/F9990, and m/z 352.185→332.1 and m/z 352.185→256.1 for fluindapyr. Analytes were identified with HPLC/MS/MS System B using two ion pair transitions as follows (primary and confirmatory, respectively): m/z 176.0→136.0 and m/z 176.0→156.0 for pyrazole carboxamide; m/z 382.1→336.1 and m/z 382.1→296.1 for 1-carboxy-IR9792/F9990 (diastereomer 1); m/z 382.1→336.1 and m/z 382.1→296.1 for 1-carboxy-IR9792/F9990 (diastereomers 2); m/z 366.1→175.0 and m/z 366.1→131.0 for 3-hydroxy-IR9792/F9990, and m/z 352.1→256.1 and m/z 352.1→312.1 for fluindapyr.

Table 3. Independent Validation Method Recoveries for Fluindapyr [IR9792 (F9990)] and Its Metabolites 3-Hydroxy-IR9792/F9990, 1-Carboxy-IR9792/F9990 (Sum of Diastereomers), and Pyrazole Carboxamide in Soil^{1,2,3}

| Analyte | Fortification Level (mg/kg) | Number of Tests | Recovery Range (%) | Mean Recovery (%) | Standard Deviation (%) | Relative Standard Deviation (%) |
|---|-----------------------------|-----------------|--------------------|-------------------|------------------------|---------------------------------|
| Nebraska Loamy Sand Soil | | | | | | |
| Quantitation Ion Transition | | | | | | |
| Fluindapyr [IR9792 (F9990)] | 0.005 | 5 | 101-105 | 103 | 1.7 | 1.6 |
| | 0.05 | 5 | 98-104 | 101 | 2.5 | 2.5 |
| 3-Hydroxy-IR9792/F9990 | 0.005 | 5 | 100-106 | 103 | 2.9 | 2.8 |
| | 0.05 | 5 | 92-104 | 97 | 4.9 | 5.1 |
| 1-Carboxy-IR9792/F9990 (Diastereomer a) | 0.00316 | 5 | 99-108 | 103 | 4.3 | 4.2 |
| | 0.0316 | 5 | 94-108 | 102 | 5.1 | 5.0 |
| 1-Carboxy-IR9792/F9990 (Diastereomer b) | 0.00184 | 5 | 98-112 | 106 | 5.4 | 5.1 |
| | 0.0184 | 5 | 93-107 | 101 | 5.1 | 5.1 |
| 1-Carboxy-IR9792/F9990 (Sum of Diastereomers) | 0.005 | 5 | 98-109 | 104 | 4.6 | 4.4 |
| | 0.05 | 5 | 93-107 | 101 | 5.1 | 5.0 |
| Pyrazole Carboxamide | 0.005 | 5 | 98-107 | 103 | 3.7 | 3.6 |
| | 0.05 | 5 | 96-104 | 99 | 3.4 | 3.4 |
| Confirmation Ion Transition | | | | | | |
| Fluindapyr [IR9792 (F9990)] | 0.005 | 5 | 84-104 | 93 | 8.0 | 8.7 |
| | 0.05 | 5 | 98-105 | 101 | 3.2 | 3.1 |
| 3-Hydroxy-IR9792/F9990 | 0.005 | 5 | 77-108 | 97 | 13 | 13 |
| | 0.05 | 5 | 93-99 | 96 | 2.9 | 3.0 |
| 1-Carboxy-IR9792/F9990 (Diastereomer a) | 0.00316 | 5 | 90-109 | 100 | 8.1 | 8.1 |
| | 0.0316 | 5 | 95-106 | 101 | 4.2 | 4.2 |
| 1-Carboxy-IR9792/F9990 (Diastereomer b) | 0.00184 | 5 | 100-112 | 104 | 4.9 | 4.7 |
| | 0.0184 | 5 | 91-108 | 100 | 6.3 | 6.3 |
| 1-Carboxy-IR9792/F9990 (Sum of Diastereomers) | 0.005 | 5 | 95-106 | 101 | 5.9 | 5.8 |
| | 0.05 | 5 | 93-107 | 101 | 5.0 | 4.9 |
| Pyrazole Carboxamide | 0.005 | 5 | 100-107 | 104 | 2.6 | 2.5 |
| | 0.05 | 5 | 96-104 | 99 | 3.4 | 3.4 |
| New York Silt Loam Soil | | | | | | |
| Quantitation Ion Transition | | | | | | |
| Fluindapyr [IR9792 (F9990)] | 0.005 | 5 | 103-107 | 105 | 1.9 | 1.8 |
| | 0.05 | 5 | 100-106 | 102 | 3.4 | 3.3 |
| 3-Hydroxy-IR9792/F9990 | 0.005 | 5 | 92-110 | 98 | 7.2 | 7.3 |
| | 0.05 | 5 | 94-102 | 97 | 3.5 | 3.6 |
| 1-Carboxy-IR9792/F9990 (Diastereomer a) | 0.00316 | 5 | 90-99 | 96 | 3.4 | 3.5 |
| | 0.0316 | 5 | 92-99 | 96 | 3.2 | 3.4 |
| 1-Carboxy- | 0.00184 | 5 | 92-97 | 94 | 2.3 | 2.4 |

| Analyte | Fortification Level (mg/kg) | Number of Tests | Recovery Range (%) | Mean Recovery (%) | Standard Deviation (%) | Relative Standard Deviation (%) |
|---|-----------------------------|-----------------|--------------------|-------------------|------------------------|---------------------------------|
| IR9792/F9990 (Diastereomer b) | 0.0184 | 5 | 91-99 | 95 | 3.8 | 3.9 |
| 1-Carboxy-IR9792/F9990 (Sum of Diastereomers) | 0.005 | 5 | 92-98 | 95 | 2.4 | 2.5 |
| | 0.05 | 5 | 92-99 | 96 | 3.3 | 3.5 |
| Pyrazole Carboxamide | 0.005 | 5 | 103-106 | 04 | 1.0 | 0.9 |
| | 0.05 | 5 | 98-104 | 100 | 2.4 | 2.4 |
| Confirmation Ion Transition | | | | | | |
| Fluindapyr [IR9792 (F9990)] | 0.005 | 5 | 90-121 | 103 | 12 | 12 |
| | 0.05 | 5 | 94-109 | 102 | 6.0 | 5.9 |
| 3-Hydroxy-IR9792/F9990 | 0.005 | 5 | 78-108 | 92 | 12 | 13 |
| | 0.05 | 5 | 96-104 | 100 | 3.3 | 3.3 |
| 1-Carboxy-IR9792/F9990 (Diastereomer a) | 0.00316 | 5 | 94-107 | 99 | 4.8 | 4.8 |
| | 0.0316 | 5 | 94-98 | 96 | 2.3 | 2.4 |
| 1-Carboxy-IR9792/F9990 (Diastereomer b) | 0.00184 | 5 | 94-100 | 97 | 2.5 | 2.6 |
| | 0.0184 | 5 | 90-102 | 95 | 4.3 | 4.5 |
| 1-Carboxy-IR9792/F9990 (Sum of Diastereomers) | 0.005 | 5 | 95-103 | 98 | 3.0 | 3.0 |
| | 0.05 | 5 | 92-99 | 95 | 2.9 | 3.0 |
| Pyrazole Carboxamide | 0.005 | 5 | 97-107 | 102 | 3.5 | 3.4 |
| | 0.05 | 5 | 98-104 | 100 | 2.8 | 2.8 |

Data (uncorrected recovery results; Appendix A, pp. 38-40) were obtained from pp. 24-27 of MRID 50518199.

1 The Nebraska loamy sand soil (0-6"; SGS Soil ID 14-02-04 UTC-SC-1-CTR-6; 83% sand, 10% silt, 7% clay; pH 6.0 in 1:1 soil:water ratio; 0.90% organic carbon – Walkley Black) and New York silt loam soil (0-6"; SGS Soil ID 14-02-02 UTC-SC-1-CTR-6; 25% sand, 60% silt, 15% clay; pH 5.1 in 1:1 soil:water ratio; 2.5% organic carbon – Walkley Black) were used in the study (USDA soil texture classification; pp. 20-21). The soil matrices were the same as those used in the ECM 1 and ECM 2.

2 Analytes were identified using two ion pair transitions as follows (primary and confirmatory, respectively): m/z 176→136 and m/z 176→156 for pyrazole carboxamide; m/z 382→336.200 and m/z 382→296.100 for 1-carboxy-IR9792/F9990 (diastereomer 1); m/z 382→336.201 and m/z 382→296.101 for 1-carboxy-IR9792/F9990 (diastereomers 2); m/z 366→175 and m/z 366→131 for 3-hydroxy-IR9792/F9990, and m/z 352→332 and m/z 352→357 for fluindapyr (these were similar to those of the ECM for HPLC/MS System A).

3 Diastereomer 1 and 2 were termed diastereomer a and b in the ILV.

III. Method Characteristics

In the ECM 1, ECM 2, and ILV, the LOQ for fluindapyr, pyrazole carboxamide, 1-carboxy-IR9792/F9990 (sum of diastereomers), and 3-hydroxy-IR9792/F9990 in soil was 0.005 mg/kg (Appendix III, p. 94 of MRID 50518076; Appendix III, p. 93 of MRID 50518078; pp. 27, 29 of MRID 50518199). In the ECM 1, ECM 2, and ILV, the LOQ for 1-carboxy-IR9792/F9990 was further defined as 0.00316 mg/kg and 0.00184 mg/kg for diastereomer 1 and 2, respectively, based on the diastereomer ratio (diastereomer 1 and 2 were termed diastereomer a and b in the ILV). In the ILV, the LOQ was defined as the lowest analyte concentration at which the methodology had been successfully validated; no justification was provided in the ECM 1 or ECM 2. The Limit of Detection (LOD) for all analytes in soil was 0.001 mg/kg (20% of the LOQ) in the ECM 1, ECM 2, and ILV. In the ECM 1, ECM 2, and ILV, the LOD for 1-carboxy-IR9792/F9990 was further defined as 0.000632 mg/kg and 0.000368 mg/kg for diastereomer 1 and 2, respectively, based on the diastereomer ratio. In the ECM 1, ECM 2, and ILV, no calculations or comparisons of the LOQ or LOD to background noise were provided.

Table 4. Method Characteristics for Fluindapyr [IR9792 (F9990)] and Its Metabolites 3-Hydroxy-IR9792/F9990, 1-Carboxy-IR9792/F9990 (Sum of Diastereomers), and Pyrazole Carboxamide in Soil.*

| Analyte | | Fluindapyr [IR9792 (F9990)] | 3-Hydroxy- IR9792/F9990 | 1-Carboxy- IR9792/F9990 (Diastereomer 1 or Diastereomer a) | 1-Carboxy- IR9792/F9990 (Diastereomer 2 or Diastereomer b) | 1-Carboxy- IR9792/F9990 (Sum of Diastereomers) | Pyrazole Carboxamide | |
|--|--------------------|--|--|---|---|---|---|--|
| Limit of Quantitation (LOQ) | ECM | 0.005 mg/kg | | 0.00316 mg/kg | 0.00184 mg/kg | 0.005 mg/kg | | |
| | ILV | | | | | | | |
| Limit of Detection (LOD) | ECM | 0.001 mg/kg (20% of the LOQ) | | 0.000632 mg/kg (20% of the LOQ) | 0.000368 mg/kg (20% of the LOQ) | 0.001 mg/kg (20% of the LOQ) | | |
| | ILV | | | | | | | |
| Linearity (calibration curve r^2 and concentration range) ¹ | ECM ² | NY soil | $r^2 = 0.9997$ (Q) | $r^2 = 0.9998$ (Q) | $r^2 = 0.9998$ (Q) | $r^2 = 0.9992$ (Q) | Not summed | $r^2 = 0.9993$ (Q) |
| | | NE soil | $r^2 = 0.9984$ (Q) | $r^2 = 0.9970$ (Q) | $r^2 = 0.9988$ (Q) | $r^2 = 0.9986$ (Q) | | $r^2 = 0.9992$ (Q) |
| | | Range | 0.1-25 ng/mL | | | | | 0.1-25 ng/mL |
| | ILV | NE soil | $r^2 = 0.9998$ (Q) $r^2 = 0.9982$ (C) | $r^2 = 0.9990$ (Q) $r^2 = 0.9998$ (C) | $r^2 = 0.9940$ (Q) $r^2 = 0.9944$ (C) | $r^2 = 0.9946$ (Q) $r^2 = 0.9952$ (C) | Not used for quantification | $r^2 = 0.9998$ (Q & C) $r^2 = 0.9986$ (Q) $r^2 = 0.9990$ (C) |
| | | NY soil | $r^2 = 0.9992$ (Q) $r^2 = 0.9988$ (C) | $r^2 = 0.9980$ (Q) $r^2 = 0.9946$ (C) | $r^2 = 0.9984$ (Q) $r^2 = 0.9986$ (C) | $r^2 = 0.9982$ (Q) $r^2 = 0.9988$ (C) | | |
| | | Range | 0.1-10 ng/mL | | 0.0632-6.32 ng/mL | 0.0368-3.68 ng/mL | | |
| Repeatable | ECM ³ | Yes at LOQ and 10×LOQ (characterized loamy sand and silt loam soil matrices) | | | | Not summed | Yes at LOQ and 10×LOQ (characterized loamy sand and silt loam soil matrices) | |
| | ILV ^{4,5} | Yes at LOQ and 10×LOQ (characterized loamy sand and silt loam soil matrices) | | | | | | |
| Reproducible | | Yes at LOQ and 10×LOQ ⁶ | | | | | | |
| Specific | ECM | Yes, matrix interferences were <10% of the LOQ (based on peak area). | | | | Not used for quantification | No , matrix interferences were <5% of the LOQ (based on peak area); however, LOQ and 10×LOQ peaks (Q & C) were very broad with significant | |

| Analyte | Fluindapyr [IR9792 (F9990)] | 3-Hydroxy- IR9792/F9990 | 1-Carboxy- IR9792/F9990 (Diastereomer 1 or Diastereomer a) | 1-Carboxy- IR9792/F9990 (Diastereomer 2 or Diastereomer b) | 1-Carboxy- IR9792/F9990 (Sum of Diastereomers) | Pyrazole Carboxamide |
|---------|---|--|--|--|---|---|
| | | | | | | shouldering. ⁷ |
| ILV | Yes, matrix interferences were <5% of the LOQ (based on peak area). Some baseline interference was noted in the C ion at the LOQ. | Yes, matrix interferences were <10% of the LOQ (based on peak area). Some baseline interference was noted in the Q ion at the LOQ. | Yes, matrix interferences were <10% of the LOQ (based on peak area). Some baseline interference was noted in the Q ion at the LOQ. | Yes, matrix interferences were <12% of the LOQ (based on peak area). | Not used for quantification | No , matrix interferences were <5% of the LOQ (based on peak area); however, LOQ and 10×LOQ peaks (Q & C) were very broad with significant shouldering and poorly defined RT peaks. ⁸ |

Data were obtained from Appendix III, p. 94 (LOQ/LOD); Appendix III, Tables 1-10, pp. 96-100 (recovery results); Appendix III, Figure 1, p. 138, Figure 10, p. 142, Figure 19, p. 147, Figure 28, p. 151, Figure 37, p. 156 (NY calibration curves); Appendix III, Figures, 2-44, pp. 138-159 (NY chromatograms) of MRID 50518076 (ECM 1); Appendix III, p. 93 (LOQ/LOD); Appendix III, Tables 1-10, pp. 95-99 (recovery results); Appendix III, Figure 1, p. 138, Figure 10, p. 142, Figure 19, p. 147, Figure 28, p. 151, Figure 37, p. 156 (NE calibration curves); Appendix III, Figures, 2-44, pp. 138-159 (NE chromatograms) of MRID 50518078 (ECM 2); pp. 27, 29 (LOQ/LOD); pp. 24-27 (recovery results); Appendix D, Figures 5-6, pp. 95-114 (calibration curves); Appendix D, Figures 7-66, pp. 115-205 (chromatograms) of MRID 50518199; DER Attachment 2. NY = New York; NE = Nebraska. Q = Quantitation ion transition; C = Confirmation ion transition.

* The analytical phase report (containing method validation results) of ECM 1 (MRID 50518076) and ECM 2 (MRID 50518078) was identical with respect to the method procedure and method validation results for the soils from ECM 1 and ECM 2; therefore, in Table 4, “ECM” encompassed both ECM 1 and ECM 2.

1 ECM 1, ECM 2, and ILV coefficient of determination (r²) values are reviewer-generated from reported correlation coefficient (r) values [1/x weighting; Appendix III, Figure 1, p. 138, Figure 10, p. 142, Figure 19, p. 147, Figure 28, p. 151, Figure 37, p. 156 of MRID 50518076 (ECM 1); Appendix III, Figure 1, p. 138, Figure 10, p. 142, Figure 19, p. 147, Figure 28, p. 151, Figure 37, p. 156 of MRID 50518078 (ECM 2); Appendix D, Figures 5-6, pp. 95-114 of MRID 50518199; DER Attachment 2). Solvent-based calibration standards were used in the ECM 1 and ECM 2 (Appendix III, p. 81 of MRID 50518076; Appendix III, p. 80 of MRID 50518078). Matrix-matched standards were used in the ILV (pp. 34-35 of MRID 50518199). Although the r value was reported to five significant figures in the ECM, the reviewer only reported the r² value to four significant figures.

2 Only the quantitation ion transition was quantified in the ECM; a confirmatory method is typically not required where GC/MS and/or LC/MS methods are used as the primary method.

3 In the ECM 1 and ECM 2, Nebraska loamy sand soil (0-6”; 83% sand, 10% silt, 7% clay; pH 6.0 in 1:1 soil:water ratio; 0.90% organic carbon – Walkley Black) and New York silt loam soil (0-6”; 25% sand, 60% silt, 15% clay; pH 5.1 in 1:1 soil:water ratio; 2.5% organic carbon – Walkley Black) were used in the study (USDA soil texture classification; Appendix IV, Attachment 1, pp. 211-212 of MRID 50518076; Appendix IV, Attachment 1, p. 212 of MRID

- 50518078). The soil matrices were collected as part of two fluindapyr terrestrial field dissipation studies performed by Precision Study Management (Amarillo, Texas; p. 1 of MRID 50518076; p. 1 of MRID 50518078). The test systems were bare ground soil plots located near Brunswick, Nebraska, USA at the junction of North American Eco-regions 9.2, 9.3 and 9.4 and near North Rose, New York, USA in the North American Eco-region 8.1 (p. 16 of MRID 50518076; p. 16 of MRID 50518078). Site use for the past three years of the two sites were included in the study report.
- 4 In the ILV, Nebraska loamy sand soil (0-6"; SGS Soil ID 14-02-04 UTC-SC-1-CTR-6; 83% sand, 10% silt, 7% clay; pH 6.0 in 1:1 soil:water ratio; 0.90% organic carbon – Walkley Black) and New York silt loam soil (0-6"; SGS Soil ID 14-02-02 UTC-SC-1-CTR-6; 25% sand, 60% silt, 15% clay; pH 5.1 in 1:1 soil:water ratio; 2.5% organic carbon – Walkley Black) were used in the study (USDA soil texture classification; pp. 20-21 of MRID 50518199). The soil matrices were the same as those used in the ECM 1 and ECM 2.
 - 5 The ILV validated the method in ECM 1 and ECM 2 for all analytes at both fortification levels in both soils in the first trial with insignificant modifications of the use of a reciprocal shaker instead of a wrist-action shaker, the use of matrix-matched standards, and optimization of the analytical method parameters and equipment (pp. 21, 28-29; Appendix A, pp. 36-38, 41 of MRID 50518199).
 - 6 The method was determined to be reproducible for all analytes, including 1-carboxy-IR9792/F9990 (sum of diastereomers), even though the ECM had not provided recovery results specifically for 1-carboxy-IR9792/F9990 (sum of diastereomers), but rather diastereomer 1 and 2 of 1-carboxy-IR9792/F9990 separately. The individual LOQs for diastereomer 1 and 2 of 1-carboxy-IR9792/F9990 were derived from the method LOQ for the sum of the diastereomers and the ratio of each of the diastereomers. Samples were fortified with the 1.72:1 mixture of diastereomers at the method LOQ (0.005 mg/kg); only quantification was performed separately in the HPLC/MS/MS chromatograms; only quantification was performed separately. Since acceptable results were found for the individual diastereomers of 1-carboxy-IR9792/F9990, the reviewer concluded that acceptable results would be found for the summation of the results of the individual diastereomers of 1-carboxy-IR9792/F9990.
 - 7 Based on Appendix III, Figures, 41-44, pp. 158-159 (NY chromatograms) of MRID 50518076 (ECM 1); Appendix III, Figures, 41-44, pp. 158-159 (NE chromatograms) of MRID 50518078 (ECM 2).
 - 8 Based on Appendix D, Figures 35-36, pp. 157-160 and Figures 65-66, pp. 202-205 of MRID 50518199. Linearity is satisfactory when $r^2 \geq 0.995$.

IV. Method Deficiencies and Reviewer's Comments

1. The method was determined to be reproducible for all analytes, including 1-carboxy-IR9792/F9990 (sum of diastereomers), even though the ECM had not provided recovery results specifically for 1-carboxy-IR9792/F9990 (sum of diastereomers), but rather diastereomer 1 and 2 of 1-carboxy-IR9792/F9990 separately. The individual LOQs for diastereomer 1 and 2 of 1-carboxy-IR9792/F9990 were derived from the method LOQ for the sum of the diastereomers (0.005 mg/kg) and the ratio of each of the diastereomers (1.72:1; Appendix III, pp. 79, 94 of MRID 50518076; Appendix III, pp. 78, 93 of MRID 50518078). Samples were fortified with the 1.72:1 mixture of diastereomers at the method LOQ (0.005 mg/kg); only quantification was performed separately in the HPLC/MS/MS chromatograms. Since acceptable results were found for the individual diastereomers of 1-carboxy-IR9792/F9990, the reviewer concluded that acceptable results would be found for the summation of the results of the individual diastereomers of 1-carboxy-IR9792/F9990.
2. The ILV, ECM 1, and ECM 2 representative chromatograms did not support the specificity of the method for pyrazole carboxamide. In the ILV representative chromatograms, LOQ and 10×LOQ peaks (Q & C) were very broad with significant shouldering and poorly defined RT peaks (Appendix D, Figures 35-36, pp. 157-160 and Figures 65-66, pp. 202-205 of MRID 50518199). In the ECM representative chromatograms, LOQ and 10×LOQ peaks (Q & C) were very broad with significant shouldering [Appendix III, Figures, 41-44, pp. 158-159 (NY chromatograms) of MRID 50518076 (ECM 1); Appendix III, Figures, 41-44, pp. 158-159 (NE chromatograms) of MRID 50518078 (ECM 2)]. The ILV study author did not comment on the peak shape of pyrazole carboxamide (p. 22 of MRID 50518199). The ILV study author considered the lack of significant matrix interference to be indicative of specificity.
3. The ILV linearity was not satisfactory for 3-hydroxy-IR9792/F9990 in the NY silt loam soil [$r^2 = 0.9946$ (Q)], 1-carboxy-IR9792/F9990 diastereomer a in the NE loamy sand soil [$r^2 = 0.9940$ (Q), 0.9944 (C)], and 1-carboxy-IR9792/F9990 diastereomer b in the NE loamy sand soil [$r^2 = 0.9946$ (Q); Appendix D, Figures 5-6, pp. 95-114 of MRID 50518199; DER Attachment 2]. Linearity is satisfactory when $r^2 \geq 0.995$. Diastereomer 1 and 2 were termed diastereomer a and b in the ILV.
4. The matrix effects were determined to be significant in the ILV, except for 3-hydroxy-IR9792/F9990 in silt loam soil from New York (matrix suppression observed); however, matrix-matched standards were used for all analytes/soils/fortifications (pp. 13, 22-23 of MRID 50518199). Solvent standards were used in the ECM 1 and ECM 2 (Appendix III, p. 81 of MRID 50518076; Appendix III, p. 80 of MRID 50518078). ECM 1 and ECM 2 recovery results were acceptable for 3-hydroxy-IR9792/F9990 in silt loam soil from New York (LOQ: 77.29% mean 3.92% RSD; 10LOQ: 82.32% mean 5.93% RSD; Appendix III, Tables 1-10, pp. 96-100 of MRID 50518076; Appendix III, Tables 1-10, pp. 95-99 of MRID 50518078).
5. The ECM 1, ECM 2, and ILV soil matrices were fully characterized, and the ILV soil

- matrices were the same as those used in the ECM 1 and ECM 2. The soil matrices were collected as part of two fluindapyr terrestrial field dissipation studies performed by Precision Study Management (Amarillo, Texas; p. 1 of MRID 50518076; p. 1 of MRID 50518078). The two soil matrices differed in % organic carbon 0.90% versus 2.5% (Walkley Black; pp. 20-21 of MRID 50518199).
6. In the ILV, a study plan deviation was issued which describes the deviations from the target calibration range and reporting of the representative chromatograms of standard solutions at or below the level of LOD (p. 28 of MRID 50518199). The calibration curves covered the range of 40% instead of 20% of the LOQ and at least +20% of the highest analyte concentration level in a sample extract in the ILV. Concerning the reporting of the representative chromatograms of standard solutions at or below the level of LOD, no standards were prepared at or below the LOD level in the ILV.
 7. In the ECM, only the quantitation ion transition was quantified; a confirmatory method is typically not required where GC/MS and/or LC/MS methods are used as the primary method.
 8. The estimations of the LOQ and LOD in ECM 1, ECM 2, and ILV were not based on scientifically acceptable procedures as defined in 40 CFR Part 136 (Appendix III, p. 94 of MRID 50518076; Appendix III, p. 93 of MRID 50518078; pp. 27, 29 of MRID 50518199). In the ILV, the LOQ was defined as the lowest analyte concentration at which the methodology had been successfully validated; no justification was provided in the ECM 1 or ECM 2. Further work could have been done to explore the actual LOQ. This means that concentrations can be reliably quantified at the LOQ (i.e., LLMV), but whether lower concentrations may also be reliably quantified is uncertain. The LOD for all analytes in soil was 20% of the LOQ in the ECM 1, ECM 2, and ILV. In the ECM 1, ECM 2, and ILV, the LOQ and LOD for 1-carboxy-IR9792/F9990 was further defined based on the diastereomer ratio. In the ECM 1, ECM 2, and ILV, no calculations or comparisons of the LOQ or LOD to background noise were provided.
 9. The Analytical Reports of ECM 1 and ECM 2 contained results of terrestrial field dissipation concurrent fortifications, field sample results, and application pad verification (See Appendix III of MRID 50518076 and Appendix III of MRID 50518078 for more information).
 10. The ILV study author reported that no communication occurred with the method developers or others familiar with the method (pp. 17, 22, 29 of MRID 50518199).
 11. In the ILV, the storage stability of the intermediate stock and fortification solutions, as well as calibration solutions, were determined to be stable for up to 30 days under refrigeration (2-8°C; pp. 27-28 of MRID 50518199). The storage stability of the final 10×LOQ soil extracts were determined to be stable for up to 9 days under refrigeration (4-10°C); the mean found residues of the re-analyzed extracts were within ± 20 % of the original result.

12. The time frame required to complete the method was not reported in the ILV.

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.

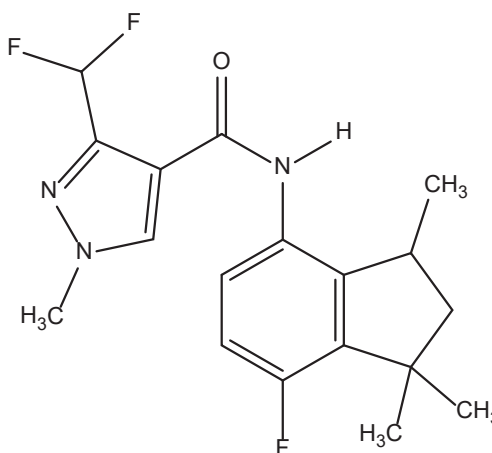
Attachment 1: Chemical Names and Structures**Fluindapyr (IR9792; F9990)**

IUPAC Name: 3-(Difluoromethyl)-N-[(3RS)-7-fluoro-2,3-dihydro-1,1,3-trimethyl-1H-inden-4-yl]-1-methyl-1H-pyrazole-4-carboxamide

CAS Name: 3-(Difluoromethyl)-N-(7-fluoro-2,3-dihydro-1,1,3-trimethyl-1H-inden-4-yl)-1-methyl-1H-pyrazole-4-carboxamide

CAS Number: 1383809-87-7

SMILES String: FC1=CC=C(N([H])C(C2=CN(C)N=C2C(F)F)=O)C3=C1C(C)(C)CC3C



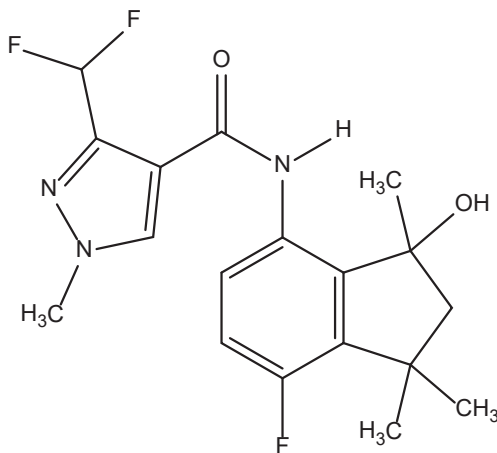
3-Hydroxy-IR9792/F9990

IUPAC Name: 3-(Difluoromethyl)-N-(7-fluoro-3-hydroxy-1,1,3-trimethyl-2,3-dihydro-1H-inden-4-yl)-1-methyl-1H-pyrazole-4-carboxamide

CAS Name: Not reported

CAS Number: Not reported

SMILES String: FC1=CC=C(N([H])C(C2=CN(C)N=C2C(F)F)=O)C3=C1C(C)(C)CC3(O)C



1-Carboxy-IR9792/F9990 (sum of diastereomers)

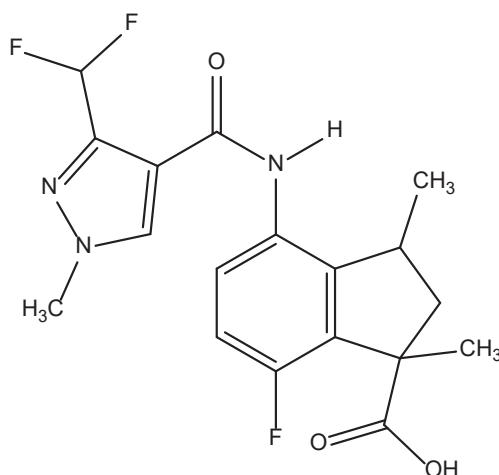
IUPAC Name: (1R,3S)-4-(3-(Difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamido)-7-fluoro-1,3-dimethyl-2,3-dihydro-1H-indene-1-carboxylic acid
And

(1R,3R)-4-(3-(Difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamido)-7-fluoro-1,3-dimethyl-2,3-dihydro-1H-indene-1-carboxylic acid

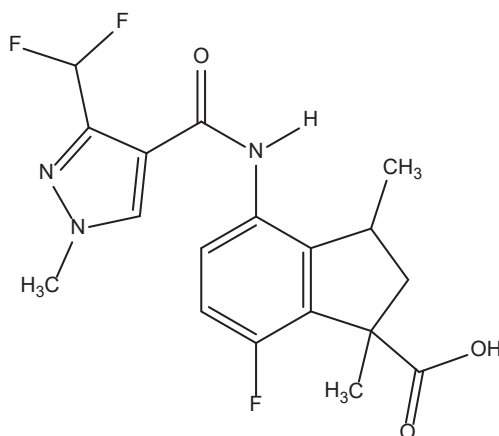
CAS Name: Not reported

CAS Number: Not reported

SMILES String: FC1=CC=C(N([H])C(C2=CN(C)N=C2C(F)F)=O)C3=C1C(C(O)=O)(C)C3C



trans-1-Carboxy-IR9792/F9990



cis-1-Carboxy-IR9792/F9990

Pyrazole Carboxamide (Pyr-amide)**IUPAC Name:** 3-(Difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamide**CAS Name:** Not reported**CAS Number:** 925689-10-7**SMILES String:** NC(C1=CN(C)N=C1C(F)F)=O