

## Analytical method for ipflufenquin and its metabolites QP-1-1 and QP-1-7 in soil and for ipflufenquin in spray pads

**Reports:** ECM: EPA MRID No.: 51022001. Moate, T.F. 2018. Validation of Method GPL-MTH-099 for the Determination of NF-180, QP-1-1, and QP-1-7 in Soils and Spray Application Targets by LC-MS/MS. Report prepared by Golden Pacific Laboratories, LLC (GPL), Fresno, California, sponsored by Nippon Soda Co., Ltd., Tokyo, Japan, and submitted by Nippon Soda Co., Ltd. (c/o Nisso America, Inc.), New York, New York (pp. 1-3); 173 pages. GPL Study No.: 160694. Final report issued February 16, 2018.

ILV: EPA MRID No.: 50920985. Garrigue, P. 2019. Independent Laboratory Validation of Residue Analytical Method for the Determination of NF-180, QP-1-1, and QP-1-7 in Soil and NF-180 in Sediment. Report prepared by SGS France – Laboratoire de Rouen, Saint Etienne du Rouvray, France, sponsored by Nippon Soda Co., Ltd., Tokyo, Japan, and Nippon Soda Co., Ltd. (c/o Nisso America, Inc.), New York, New York, and submitted by Nippon Soda Co., Ltd. (c/o Nisso America, Inc.), New York, New York (pp. 1, 3); 75 pages. GLP Study No.: BPL19-0009. Final report issued July 11, 2019.

**Document No.:** MRIDs 51022001 & 50920985

**Guideline:** 850.6100


**Statements:** ECM: The study was conducted in compliance with USEPA FIFRA Good Laboratory Practice (GLP) standards (40 CFR Part 160; p. 3 of MRID 51022001). Signed and dated Data Confidentiality, GLP and Quality Assurance statements were provided (pp. 2-4). The statement of authenticity was included with the QA statement.

ILV: The study was conducted in compliance with French GLP standards (Appendix II Article D 523-8; 2007), except for the characterization of the test system (p. 3; Appendix G, p. 75 of MRID 50920985). Signed and dated Data Confidentiality, GLP and Quality Assurance statements were provided (pp. 2-4; Appendix G, p. 75). The statement of authenticity was included with the QA and GLP statements (pp. 3-4).

**Classification:** This analytical method is classified as **Supplemental**. The method was not reproducible for ipflufenquin in spray pads since no ILV performance data was submitted. Only one soil matrix was included in the ILV; it could not be determined if the ILV was provided with the most difficult soil matrix with which to validate the method and if the ILV soil matrix covered the range of soils used in the five sites included in the terrestrial field dissipation studies.


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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 Joint Venture personnel. The CDM/CSS-Dynamac JV role does not include establishing Agency policies.*

## **Executive Summary**

The analytical method, GPL-MTH-099 Revision 1, is designed for the quantitative determination of ipflufenquin and its metabolites QP-1-1 and QP-1-7 in soil at the stated LOQ of 0.002 µg/g and of ipflufenquin in spray pads at the stated LOQ of 40 µg/sample using HPLC/MS/MS. The LOQ for soil analysis is less than the lowest toxicological level of concern in soil. The LOQ for spray pad analysis is less than the lowest toxicological level of concern in soil. For the soil method validation, the ECM used characterized sandy loam and silt loam soil matrices; the ILV used a different characterized sandy loam soil matrix. It could not be determined if the ILV was provided with the most difficult soil matrix with which to validate the method and if the ILV soil matrix covered the range of soils used in the five sites included in the terrestrial field dissipation studies. The ILV validated the method for ipflufenquin, QP-1-1 and QP-1-7 in the first trial with the substitution of 0.2-µm filters in the place of 0.45-µm filters and insignificant analytical instrument and equipment modifications. No updated ECM is required. All ILV and ECM data regarding repeatability, accuracy, precision, linearity, and specificity were satisfactory for ipflufenquin, QP-1-1, and QP-1-7 in tested soil matrices. For the spray pad method validation, the ECM used 15-cm Whatman #3 filter paper. All ECM data regarding repeatability, accuracy, precision, linearity and specificity were satisfactory for ipflufenquin; method was not reproducible since no ILV performance data was submitted. The ECM reported that the procedure for spray pads was not intended as a residue method.

**Table 1. Analytical Method Summary**

Analyte(s) by Pesticide <sup>1</sup>	MRID		EPA Review	Matrix	Method Date (dd/mm/yyyy)	Registrant	Analysis	Limit of Quantitation (LOQ)
	Environmental Chemistry Method	Independent Laboratory Validation						
Ipflufenquin (NF-180)	51022001	50920985		Soil <sup>2,3</sup>	16/02/2018 (Validation)	Nippon Soda Co., Ltd. (c/o Nisso America Inc.)	LC/MS/MS	0.002 µg/g
QP-1-1					05/10/2017 (Original Method) <sup>6</sup>			
QP-1-7					05/10/2017 (Original Method) <sup>6</sup>			
Ipflufenquin (NF-180)		None submitted <sup>4</sup>		Spray pad <sup>5</sup>	05/10/2017 (Original Method) <sup>6</sup> No Validation was submitted <sup>4</sup>			40 µg/sample

1 Ipflufenquin = 2-[2-(7,8-Difluoro-2-methyl-3-quinolyloxy)-6-fluorophenyl]propan-2-ol; QP-1-1 = 7,8-Difluoro-3-(3-fluoro-2-isopropenylphenoxy)-2-methylquinoline; and QP-1-7 = (2-[2-(7,8-Difluoro-2-methyl-3-quinolyloxy)-6-fluorophenyl]-2-hydroxypropanoic acid.

2 In the ECM, sandy loam soil (77% sand, 15% silt, 8% clay; pH 8.3 in 1:1 soil:water ratio; 0.68% organic matter – Walkley Black; 1.14 g/cm<sup>3</sup> bulk density; 8.2 meq/100 g cation exchange capacity) obtained from California, and silt loam soil (16% sand, 58% silt, 26% clay; pH 6.9 in 1:1 soil:water ratio; 3.5% organic matter – Walkley Black; 1.01 g/cm<sup>3</sup> bulk density; 16.6 meq/100 g cation exchange capacity) obtained from Iowa were characterized by Agvise Laboratories, Northwood, North Dakota, and used in the study (USDA Soil Texture Classification; p. 16; Appendix E, pp. 92-93 of MRID 51022001).

3 In the ILV, sandy loam soil (Lufa Speyer 2.3; 59.6 ± 1.4% sand, 33.6 ± 0.5% silt, 6.8 ± 1.6% clay; pH 5.9 ± 0.6 in 0.01M CaCl<sub>2</sub>; 0.67 ± 0.03% organic carbon; 7.6 ± 0.8 meq/100 g cation exchange capacity) was characterized by Lufa Speyer, Speyer, Germany, and used in the study (USDA Soil Texture Classification; Appendix F, pp. 71-72 of MRID 50920985).

4 The ECM reported that the procedure for spray pads was not intended as a residue method (p. 25 of MRID 51002201).

5 In the ECM, 15-cm Whatman #3 filter paper was used (p. 17 of MRID 51022001).

6 Original Method was GPL-MTH-099 Revision 1 dated October 5, 2017 (Appendix B, p. 69 of MRID 51022001).

## I. Principle of the Method

Soil (20 g) in 250-mL HDPE Nalgene bottles was fortified with 0.2 mL of 0.2 or 2 µg/mL fortification solutions, if necessary (pp. 12, 15-17; Appendix B, pp. 75-76; Appendix C, pp. 85-86 of MRID 51022001). The soil samples were extracted twice using 100 mL then 50 mL of acetonitrile:water:acetic acid (80:20:5, v:v:v) with shaking (*ca.* 200 rpm) for 30 minutes. The sample was centrifuged for 5 minutes at 3000 rpm. The supernatant was isolated while filtering (Advantec 5A filter paper), and aliquots (5 mL) were diluted to 10 mL with acetonitrile:water (50:50, v:v). Aliquots of the diluted subsamples were filtered (0.45-µm PTFE filter) into an autosampler vial prior to LC-MS/MS analysis. Further dilutions with acetonitrile:water (50:50, v:v) were performed, if necessary.

The filter papers were placed into 1-L glass jars and fortified with 2 mL of 20 or 200 µg/mL fortification solutions, if necessary (p. 17; Appendix B, pp. 76-77 of MRID 51022001). The filter papers were extracted once using 500 mL of acetonitrile:water:acetic acid (80:20:5, v:v:v) with

shaking (*ca.* 200 rpm) for 30 minutes. The extract was isolated, and aliquots (0.1 mL) of the extract were filtered (0.45- $\mu$ m PTFE filter) and diluted with 10 mL of acetonitrile:water (50:50, v:v). An aliquot of the diluted extract was transferred into an autosampler vial prior to LC-MS/MS analysis. Further dilutions with acetonitrile:water (50:50, v:v) were performed, if necessary. The method noted that sample jars with spray pads from field samples should be rinsed three times with the extraction solvent prior to the addition of the remaining solvent to the sample jar.

Samples are analyzed using a Sciex Triple Quad 6500+ mass spectrometer coupled with a Shimadzu LC-20AD HPLC (pp. 17-18 of MRID 51022001). The following LC conditions were used: Phenomenex Kinetex 2.6- $\mu$ m C18 100 Å column (3 mm x 100 mm; column temperature 40°C), gradient mobile phase of A) 0.1% acetic acid in acetonitrile and B) 0.1% acetic acid in water [time, percent A:B; 0.00-0.15 min. 30:70, 5.00-5.90 min. 95:5, 6.00-7.00 min. 30:70], injection volume of 10  $\mu$ L, MS/MS with Electrospray Ionization (ESI) source in positive polarity (source temperature 500°C). Two ion pair transitions were monitored for each analyte (quantitation and confirmation, respectively):  $m/z$  348.1 $\rightarrow$ 330.1 and  $m/z$  348.1 $\rightarrow$ 180.1 for ipflufenquin,  $m/z$  330.1 $\rightarrow$ 180.2 and  $m/z$  330.1 $\rightarrow$ 314.2 for QP-1-1, and  $m/z$  378 $\rightarrow$ 332 and  $m/z$  378 $\rightarrow$ 314.1 for QP-1-7. Retention times were 4.6 minutes for ipflufenquin, 5.6 minutes for QP-1-1, and 3.4 minutes for QP-1-7. The reviewer noted that the ECM did not include the guard column (Phenomenex SecurityGuard ULTRA UHPLC C18 for 3.0 mm) as was included in the original method GPL-MTH-099 Revision 1 (Appendix B, p. 77 of MRID 51022001).

The ILV performed the ECM method for ipflufenquin, QP-1-1, and QP-1-7 in soil as written, except for the use of 0.2- $\mu$ m filters instead of 0.45- $\mu$ m filters and insignificant analytical instrument and equipment modifications (pp. 11-13, 19-24 of MRID 50920985). The LC/MS/MS instrument was an API 5500 Q-trap mass spectrometer coupled with a Shimadzu LC-30AD HPLC System. The LC conditions were the same as those of the ECM, including the fact that a guard column was not utilized. Two ion pair transitions were monitored for each analyte (quantitation and confirmation, respectively):  $m/z$  348.0 $\rightarrow$ 330.0 and  $m/z$  348.0 $\rightarrow$ 180.0 for ipflufenquin,  $m/z$  330.0 $\rightarrow$ 180.0 and  $m/z$  330.0 $\rightarrow$ 314.0 for QP-1-1, and  $m/z$  378.0 $\rightarrow$ 332.0 and  $m/z$  378.0 $\rightarrow$ 314.0 for QP-1-7. Approximate retention times were 4.1 minutes for ipflufenquin, 5.2 minutes for QP-1-1, and 2.9 minutes for QP-1-7. No ILV was submitted for the ECM method for ipflufenquin on spray pads.

In the ECM and ILV, the Limit of Quantification (LOQ) was 0.002  $\mu$ g/g for all analytes in soil matrices (pp. 24-25 of MRID 51022001; p. 33 of MRID 50920985). The Limit of Detection (LOD) values were 0.0003  $\mu$ g/g in the ECM and 0.0005  $\mu$ g/g in the ILV for all analytes in soil matrices. In the ECM, the LOQ for spray pads was 40  $\mu$ g/sample; the LOD was not reported.

## II. Recovery Findings

ECM (MRID 51022001): Mean recoveries and relative standard deviations (RSDs) were within guidelines (mean 70-120%; RSD  $\leq$ 20%) for analysis of ipflufenquin and its metabolites QP-1-1 and QP-1-7 at fortification levels of 0.002  $\mu\text{g/g}$  (LOQ) and 0.02  $\mu\text{g/g}$  (10 $\times$ LOQ) in two soil matrices and for analysis of ipflufenquin at fortification levels of 40  $\mu\text{g/sample}$  (LOQ) and 400  $\mu\text{g/sample}$  (10 $\times$ LOQ) in spray pads (Tables 1-14, pp. 28-41). Two ion pair transitions were monitored, one quantitation and one confirmation; quantitation and confirmation recovery results were comparable. Sandy loam soil (77% sand, 15% silt, 8% clay; pH 8.3 in 1:1 soil:water ratio; 0.68% organic matter – Walkley Black; 1.14  $\text{g/cm}^3$  bulk density; 8.2 meq/100 g cation exchange capacity) obtained from California, and silt loam soil (16% sand, 58% silt, 26% clay; pH 6.9 in 1:1 soil:water ratio; 3.5% organic matter – Walkley Black; 1.01  $\text{g/cm}^3$  bulk density; 16.6 meq/100 g cation exchange capacity) obtained from Iowa were characterized by Agvise Laboratories, Northwood, North Dakota, and used in the study for the soil validation (USDA Soil Texture Classification; p. 16; Appendix E, pp. 92-93). For the spray pad validation, 15-cm Whatman #3 filter paper was used (p. 17). The ECM reported that the procedure for spray pads was not intended as a residue method (p. 25).

ILV (MRID 50920985): Mean recoveries and RSDs were within guidelines for analysis of ipflufenquin and its metabolites QP-1-1 and QP-1-7 at fortification levels of 0.002  $\mu\text{g/g}$  (LOQ) and 0.02  $\mu\text{g/g}$  (10 $\times$ LOQ) in one soil matrix (Table 13, p. 33; DER Attachment 2). Two ion pair transitions were monitored, one quantitation and one confirmation; quantitation and confirmation recovery results were comparable. The sandy loam soil (Lufa Speyer 2.3; 59.6  $\pm$  1.4% sand, 33.6  $\pm$  0.5% silt, 6.8  $\pm$  1.6% clay; pH 5.9  $\pm$  0.6 in 0.01M  $\text{CaCl}_2$ ; 0.67  $\pm$  0.03% organic carbon; 7.6  $\pm$  0.8 meq/100 g cation exchange capacity) was characterized by Lufa Speyer, Speyer, Germany, and used in the study (USDA Soil Texture Classification; Appendix F, pp. 71-72). The method was validated for ipflufenquin, QP-1-1 and QP-1-7 in the first trial with the substitution of 0.2- $\mu\text{m}$  filters in the place of 0.45- $\mu\text{m}$  filters and insignificant analytical instrument and equipment modifications (pp. 11-13, 19-24, 35). No updated ECM is required. No samples were prepared for spray pad validation.

**Table 2. Initial Validation Method Recoveries for Ipflufenquin, QP-1-1, and QP-1-7 in Soil<sup>1,2</sup>**

Analyte	Fortification Level (µg/g or µg/sample)	Number of Tests <sup>4</sup>	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%) <sup>5</sup>	Relative Standard Deviation (%)
<b>CA Sandy Loam Soil<sup>3</sup></b>						
Quantitation Ion Transition						
Ipflufenquin (NF-180)	0.002 (LOQ)	5	86.1-90.1	88.0	1.78	2.02
	0.02	5	86.1-90.1	88.0	1.67	1.90
QP-1-1	0.002 (LOQ)	5	82.0-90.5	85.8	3.44	4.01
	0.02	5	85.5-88.5	86.7	1.15	1.33
QP-1-7	0.002 (LOQ)	5	91.0-94.5	92.4	1.29	1.40
	0.02	5	88.0-92.5	91.2	1.99	2.18
Confirmation Ion Transition						
Ipflufenquin (NF-180)	0.002 (LOQ)	5	84.2-95.5	90.3	4.87	5.39
	0.02	5	86.1-91.1	88.1	1.90	2.16
QP-1-1	0.002 (LOQ)	5	85.0-93.5	89.5	3.64	4.07
	0.02	5	87.5-91.5	89.6	1.43	1.60
QP-1-7	0.002 (LOQ)	5	89.0-101	95.9	4.49	4.68
	0.02	5	88.0-94.0	91.4	2.22	2.43
<b>IA Silt Loam Soil<sup>3</sup></b>						
Quantitation Ion Transition						
Ipflufenquin (NF-180)	0.002 (LOQ)	5	76.7-79.7	78.1	1.29	1.65
	0.02	5	79.2-80.2	79.8	0.418	0.524
QP-1-1	0.002 (LOQ)	5	74.5-82.0	78.5	3.37	4.29
	0.02	5	79.0-84.0	81.1	1.85	2.28
QP-1-7	0.002 (LOQ)	5	88.0-91.5	90.6	1.52	1.68
	0.02	5	90.5-93.5	91.9	1.29	1.40
Confirmation Ion Transition						
Ipflufenquin (NF-180)	0.002 (LOQ)	5	75.2-89.1	80.3	5.23	6.51
	0.02	5	78.7-83.2	80.8	1.85	2.29
QP-1-1	0.002 (LOQ)	5	73.5-84.0	78.5	4.12	5.25
	0.02	5	77.0-81.5	79.0	1.71	2.15
QP-1-7	0.002 (LOQ)	5	83.5-99.5	92.0	6.11	6.64
	0.02	5	90.5-93.0	91.9	0.962	1.05
<b>Spray Pad<sup>4</sup></b>						
Quantitation Ion Transition						
Ipflufenquin (NF-180)	40 (LOQ)	5	103-108	106	2.00	1.89
	400	5	105-110	108	1.92	1.78
Confirmation Ion Transition						
Ipflufenquin (NF-180)	40 (LOQ)	5	102-105	103	1.30	1.26
	400	5	99.2-110	106	4.36	4.11

Data (uncorrected recovery results; pp. 20-21) were obtained from Tables 1-14, pp. 28-41 of MRID 51022001.

1 Ipflufenquin = 2-[2-(7,8-Difluoro-2-methyl-3-quinolyloxy)-6-fluorophenyl]propan-2-ol; QP-1-1 = 7,8-Difluoro-3-(3-fluoro-2-isopropenylphenoxy)-2-methylquinoline; and QP-1-7 = (2-[2-(7,8-Difluoro-2-methyl-3-quinolyloxy)-6-fluorophenyl]-2-hydroxypropanoic acid.

2 Two ion pair transitions were monitored for each analyte (quantitation and confirmation, respectively): *m/z* 348.1→330.1 and *m/z* 348.1→180.1 for ipflufenquin, *m/z* 330.1→180.2 and *m/z* 330.1→314.2 for QP-1-1, and *m/z* 378→332 and *m/z* 378→314.1 for QP-1-7.



- 3 Sandy loam soil (77% sand, 15% silt, 8% clay; pH 8.3 in 1:1 soil:water ratio; 0.68% organic matter – Walkley Black; 1.14 g/cm<sup>3</sup> bulk density; 8.2 meq/100 g cation exchange capacity) obtained from California, and silt loam soil (16% sand, 58% silt, 26% clay; pH 6.9 in 1:1 soil:water ratio; 3.5% organic matter – Walkley Black; 1.01 g/cm<sup>3</sup> bulk density; 16.6 meq/100 g cation exchange capacity) obtained from Iowa were characterized by Agvise Laboratories, Northwood, North Dakota, and used in the study (USDA Soil Texture Classification; p. 16; Appendix E, pp. 92-93 of MRID 51022001). The soil texture was verified by the reviewer using USDA-NRCS technical support tools.
- 4 15-cm Whatman #3 filter paper was used (p. 17 of MRID 51022001). Nominal LOQ and 10×LOQ reported; actual concentrations were 39.9 µg/sample and 399 µg/sample (Tables 13-14, pp. 40-41 of MRID 51022001).

**Table 3. Independent Validation Method Recoveries for Ipflufenquin, QP-1-1, and QP-1-7 in Soil<sup>1,2,3</sup>**

Analyte	Fortification Level (µg/g or µg/sample)	Number of Tests	Recovery Range (%)	Mean Recovery (%)	Standard Deviation (%) <sup>4</sup>	Relative Standard Deviation (%)
<b>Speyer 2.3 Sandy Loam Soil</b>						
Quantitation ion transition						
Ipflufenquin (NF-180)	0.002 (LOQ)	5	92-96	94	2	1.6
	0.02	5	88-97	94	4	4.1
QP-1-1	0.002 (LOQ)	5	91-103	98	5	4.6
	0.02	5	97-107	100	4	4.2
QP-1-7	0.002 (LOQ)	5	89-93	91	2	1.9
	0.02	5	93-95	94	1	0.9
Confirmation ion transition						
Ipflufenquin (NF-180)	0.002 (LOQ)	5	93-101	96	3	3.0
	0.02	5	90-97	94	3	2.9
QP-1-1	0.002 (LOQ)	5	95-110	104	6	5.6
	0.02	5	91-101	97	4	4.4
QP-1-7	0.002 (LOQ)	5	89-93	91	2	1.8
	0.02	5	91-95	93	2	1.9
<b>Spray Pads</b>						
Ipflufenquin (NF-180)	40 (LOQ)	5	Not performed			
	400	5				

Data (uncorrected recovery results; p. 25) were obtained from Table 13, p. 33 of MRID 50920985 and DER Attachment 2.

1 Ipflufenquin = 2-[2-(7,8-Difluoro-2-methyl-3-quinolyloxy)-6-fluorophenyl]propan-2-ol; QP-1-1 = 7,8-Difluoro-3-(3-fluoro-2-isopropenylphenoxy)-2-methylquinoline; and QP-1-7 = (2-[2-(7,8-Difluoro-2-methyl-3-quinolyloxy)-6-fluorophenyl]-2-hydroxypropanoic acid.

2 Two ion pair transitions were monitored for each analyte (quantitation and confirmation, respectively): *m/z* 348.0→330.0 and *m/z* 348.0→180.0 for ipflufenquin, *m/z* 330.0→180.0 and *m/z* 330.0→314.0 for QP-1-1, and *m/z* 378.0→332.0 and *m/z* 378.0→314.0 for QP-1-7.

3 The sandy loam soil (Lufa Speyer 2.3; 59.6 ± 1.4% sand, 33.6 ± 0.5% silt, 6.8 ± 1.6% clay; pH 5.9 ± 0.6 in 0.01M CaCl<sub>2</sub>; 0.67 ± 0.03% organic carbon; 7.6 ± 0.8 meq/100 g cation exchange capacity) was characterized by Lufa Speyer, Speyer, Germany, and used in the study (USDA Soil Texture Classification; Appendix F, pp. 71-72 of MRID 50920985). The soil texture was verified by the reviewer using USDA-NRCS technical support tools.

4 Standard deviations were reviewer-calculated using the data in the study report since the study author did not report these values (see DER Attachment 2). Rules of significant figures were followed.

### III. Method Characteristics

In the ECM and ILV, the LOQ was 0.002 µg/g for all analytes in soil matrices (pp. 24-25 of MRID 51022001; p. 33 of MRID 50920985). In the ECM, the LOQ was determined as the lowest fortification level at which acceptable recovery data was obtained and was equal to the lowest validated concentration. In the ILV, the LOQ was equal to the lowest validated concentration. The reported LOD values were 0.0003 µg/g in the ECM and 0.0005 µg/g in the ILV for all analytes in soil matrices. In the ILV, the LOD was set to at least 30% of the LOQ. In the ECM, the LOD values for ipflufenquin, QP-1-1, and QP-1-7 were calculated as 0.0001-0.0003 µg/g, based on the following equation:

$$\text{LOD}_{\text{calc}} = (t_{0.99} \times s)$$

Where,  $t_{0.99}$  is the one-tailed t-test value at the 99% confidence interval for n-1 degrees of freedom (where n is the number of replicates) and s is the standard deviation of the analyte recovery measurements at the target LOQ. No calculations or comparisons to background levels were reported to justify the LOQ for the method in the ECM or ILV; no calculations or comparisons to background levels were reported to justify the LOD for the method in the ILV.

In the ECM, the LOQ for spray pads was 40 µg/sample; the LOD was not reported since the procedure was not intended as a residue method (pp. 24-25 of MRID 51022001). In the ECM, the LOQ was determined as the lowest fortification level at which acceptable recovery data was obtained and was equal to the lowest validated concentration. Spray pad application validation was not performed by the ILV, and no LOQ or LOD was reported.



**Table 4a. Method Characteristics Ipflufenquin, QP-1-1, and QP-1-7 in Soil**

Test Material <sup>1</sup>		Ipflufenquin	QP-1-1	QP-1-7
Limit of Quantitation (LOQ)	ECM	0.002 µg/g		
	ILV			
Limit of Detection (LOD)	ECM	0.0003 µg/g (calculated)		
	ILV	0.0005 µg/g (at least 30% of the LOQ)		
Linearity (calibration curve r and concentration range)	ECM	r = 0.9999 (Q, CA) r = 0.9998 (C, CA) r = 1.0000 (Q, IA) r = 0.9999 (C, IA)	r = 0.9998 (Q, CA) r = 0.9999 (C, CA) r = 0.9999 (Q & C, IA)	r = 0.9999 (Q, CA) r = 1.0000 (C, CA) r = 1.0000 (Q, IA) r = 0.9999 (C, IA)
		0.0253-5.05 ng/mL	0.0250-5.00 ng/mL	
	ILV	r = 0.9999 (Q & C)	r = 0.9994 (Q) r = 0.9997 (C)	r = 0.9998 (Q) r = 1.0000 (C)
		0.02509-5.019 ng/mL	0.02512-5.024 ng/mL	0.02515-5.029 ng/mL
Repeatable	ECM <sup>2</sup>	Yes at LOQ and 10×LOQ in two characterized soil matrices.		
	ILV <sup>3,4</sup>	Yes at LOQ and 10×LOQ in one characterized soil matrix.		
Reproducible		Yes at LOQ and 10×LOQ.		
Specific	ECM	Yes, no matrix interferences were observed. Some non-interfering contaminants were noted at the LOQ.	Yes, no matrix interferences were observed.	Yes, no matrix interferences were observed. Minor peak tailing was observed.
	ILV	Yes, matrix interferences were <3% of the LOQ (based on peak area). Some minor baseline noise interference and non-interfering contaminants were noted at the LOQ. Minor peak tailing was observed at 10×LOQ.		

Data were obtained from pp. 24-25 (LOQ/LOD); Tables 1-12, pp. 28-39 (recovery results); Appendix F, pp. 95-100, 104-109 (calibration coefficients); Appendix G, Figures 1-48, pp. 119-166 (chromatograms) of MRID 51022001; p. 33 (LOQ/LOD); Table 13, p. 33 (recovery results); Appendix C, Figures 4-9, pp. 40-45 (calibration curves); Appendix C, Figures 10-39, pp. 46-60 (chromatograms) of MRID 50920985. Q = quantitation ion transition; C = confirmation ion transition. CA = California sandy loam soil; IA = Iowa silt loam soil.

1 Ipflufenquin = 2-[2-(7,8-Difluoro-2-methyl-3-quinolyloxy)-6-fluorophenyl]propan-2-ol; QP-1-1 = 7,8-Difluoro-3-(3-fluoro-2-isopropenylphenoxy)-2-methylquinoline; and QP-1-7 = (2-[2-(7,8-Difluoro-2-methyl-3-quinolyloxy)-6-fluorophenyl]-2-hydroxypropanoic acid.

2 In the ECM, sandy loam soil (77% sand, 15% silt, 8% clay; pH 8.3 in 1:1 soil:water ratio; 0.68% organic matter – Walkley Black; 1.14 g/cm<sup>3</sup> bulk density; 8.2 meq/100 g cation exchange capacity) obtained from California, and silt loam soil (16% sand, 58% silt, 26% clay; pH 6.9 in 1:1 soil:water ratio; 3.5% organic matter – Walkley Black; 1.01 g/cm<sup>3</sup> bulk density; 16.6 meq/100 g cation exchange capacity) obtained from Iowa were characterized by Agvise Laboratories, Northwood, North Dakota, and used in the study (USDA Soil Texture Classification; p. 16; Appendix E, pp. 92-93 of MRID 51022001).

3 In the ILV, sandy loam soil (Lufa Speyer 2.3; 59.6 ± 1.4% sand, 33.6 ± 0.5% silt, 6.8 ± 1.6% clay; pH 5.9 ± 0.6 in 0.01M CaCl<sub>2</sub>; 0.67 ± 0.03% organic carbon; 7.6 ± 0.8 meq/100 g cation exchange capacity) was characterized by Lufa Speyer, Speyer, Germany, and used in the study (USDA Soil Texture Classification; Appendix F, pp. 71-72 of MRID 50920985).

4 The ILV validated the method for ipflufenquin, QP-1-1 and QP-1-7 in the first trial with the substitution of 0.2-µm filters in the place of 0.45-µm filters and insignificant analytical instrument and equipment modifications (pp. 11-13, 19-24, 35 of MRID 50920985). No updated ECM is required.

**Table 4b. Method Characteristics Ipflufenquin in Spray Pads**

Test Material <sup>1</sup>		Ipflufenquin
Limit of Quantitation (LOQ)	ECM	40 µg/sample
	ILV	<b>Not reported</b>
Limit of Detection (LOD)	ECM	<b>Not reported<sup>2</sup></b>
	ILV	<b>Not reported</b>
Linearity (calibration curve r and concentration range)	ECM	r = 0.9996 (Q) r = 0.9999 (C)
		0.0253-5.05 ng/mL
Repeatable	ILV	<b>No samples prepared</b>
	ECM <sup>3</sup>	Yes at LOQ and 10×LOQ in one filter paper type.
Reproducible	ILV	<b>No samples prepared</b>
	ECM	<b>Could not be determined;</b> only one set of performance data was submitted.
Specific	ECM	Yes, no matrix interferences were observed.
	ILV	<b>No samples prepared</b>

Data were obtained from pp. 24-25 (LOQ/LOD); Tables 13-14, pp. 40-41 (recovery results); Appendix F, pp. 113-114 (calibration coefficients); Appendix G, Figures 49-52, pp. 167-170 (chromatograms) of MRID 51022001. Q = quantitation ion transition; C = confirmation ion transition.

1 Ipflufenquin = 2-[2-(7,8-Difluoro-2-methyl-3-quinolyloxy)-6-fluorophenyl]propan-2-ol; QP-1-1 = 7,8-Difluoro-3-(3-fluoro-2-isopropenylphenoxy)-2-methylquinoline; and QP-1-7 = (2-[2-(7,8-Difluoro-2-methyl-3-quinolyloxy)-6-fluorophenyl]-2-hydroxypropanoic acid.

2 The ECM reported that a LOD was not reported since the procedure for spray pads was not intended as a residue method (p. 25 of MRID 51002201).

3 In the ECM, 15-cm Whatman #3 filter paper was used (p. 17 of MRID 51022001).

#### IV. Method Deficiencies and Reviewer's Comments

- The method was not reproducible for ipflufenquin in spray pads since no ILV performance data was submitted. The ECM reported that the procedure for spray pads was not intended as a residue method (p. 25 of MRID 51002201).
- It could not be determined if the ILV was provided with the most difficult soil matrix with which to validate the method and if the ILV soil matrix covered the range of soils used in the terrestrial field dissipation (TFD) studies since only one soil matrix was included in the ILV: sandy loam soil (Lufa Speyer 2.3; 59.6 ± 1.4% sand, 33.6 ± 0.5% silt, 6.8 ± 1.6% clay; pH 5.9 ± 0.6 in 0.01M CaCl<sub>2</sub>; 0.67 ± 0.03% organic carbon; 7.6 ± 0.8 meq/100 g cation exchange capacity; USDA Soil Texture Classification; Appendix F, pp. 71-72 of MRID 50920985). OCSPP guidelines state that "For a given sample matrix, the registrant should select the most difficult analytical sample condition from the study (e.g., high organic content versus low organic content in a soil matrix) to analyze from the study to demonstrate how well the method performs". The organic content of the ILV soil matrix was low, and more than one soil should

be included to encompass the range of soils used in the TFD studies. The submitted ipflufenquin TFD study (MRID 50920948) contained five test sites: NAFTA Regions 10 (California; sandy loam, loamy sand, sand), 2 (Georgia; sand, loamy sand, sandy loam, sandy clay loam), 5 (Iowa; silt loam, clay loam, silty clay loam), 11 (Idaho; loam, sandy loam), and 1 (New York; sandy loam, loam, silt loam); (Ecoregions 11.1, 8.3, 9.2, 10.1, and & 8.1, respectively; p. 11; Tables 4a-4e, pp. 64-68 of MRID 50920948).

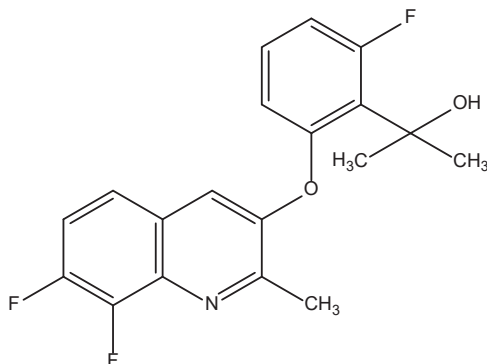
3. The determinations of LOD and LOQ in the ECM and ILV were not based on scientifically acceptable procedures as defined in 40 CFR Part 136 (pp. 24-25 of MRID 51022001; p. 33 of MRID 50920985). In the ECM, the LOQ was determined as the lowest fortification level at which acceptable recovery data was obtained and was equal to the lowest validated concentration. In the ILV, the LOQ was equal to the lowest validated concentration. In the ILV, the LOD was set to at least 30% of the LOQ. In the ECM, the LOD values for ipflufenquin, QP-1-1, and QP-1-7 in soil were calculated based on the following equation:  $LOD_{calc} = (t_{0.99} \times s)$ , where  $t_{0.99}$  is the one-tailed t-test value at the 99% confidence interval for n-1 degrees of freedom (where n is the number of replicates) and s is the standard deviation of the analyte recovery measurements at the target LOQ. The LOD for spray pads was not reported since the procedure was not intended as a residue method. No calculations or comparisons to background levels were reported to justify the LOQ for the method in the ECM or ILV; no calculations or comparisons to background levels were reported to justify the LOD for the method in the ILV. Spray pad application validation was not performed by the ILV, and no LOQ or LOD was reported. Detection limits should not be based on arbitrary values.
4. Matrix effects of the test soil matrices were studied in the ECM and ILV and found to be insignificant (<20%; pp. 25-26; Table 18, p. 43 of MRID 51022001; p. 32 of MRID 50920985). Solvent-based calibration standards were used for quantification of the residues (Appendix B, p. 74 of MRID 51022001). Matrix effects were not studied in the ECM for spray pads samples (p. 26).
5. The stability of the sample extracts was investigated by the ECM (p. 25; Tables 15-17, pp. 42-43 of MRID 51022001). The final sample extracts were found to be stable for up to 28 days with frozen storage (recovery within 20% of original for all analytes).
6. The original method for the ECM, GPL-MTH-099 Revision 1, was provided in Appendix B of the ECM (Appendix B, pp. 69-83 of MRID 51022001).
7. In the ECM, one set of 13 samples (soil or spray pad) required *ca.* 6 hours (sample processing) and *ca.* 1-2 hours (data processing) with LC/MS analysis performed overnight (p. 19 of MRID 51022001). In the ILV, the total time required to perform the method (extraction and analysis) with one sample set (30 samples, 1 control and 2 fortifications) was *ca.* 24 hours (p. 24 of MRID 50920985).

## **V. References**

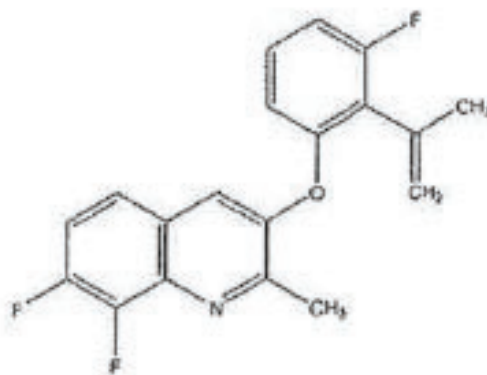
- U.S. Environmental Protection Agency. 2012. Ecological Effects Test Guidelines, OCSPP 850.6100, Environmental Chemistry Methods and Associated Independent Laboratory Validation. Office of Chemical Safety and Pollution Prevention, Washington, DC. EPA 712-C-001.
- 40 CFR Part 136. Appendix B. Definition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

**Attachment 1: Chemical Names and Structures****Ipflufenoquin (NF-180)**

**IUPAC Name:** 2-[2-(7,8-Difluoro-2-methyl-3-quinolyloxy)-6-fluorophenyl]propan-2-ol  
**CAS Name:** 2-[(7,8-Difluoro-2-methyl-3-quinolinyloxy)-6-fluoro- $\alpha,\alpha$ -dimethylbenzenemethanol  
**CAS Number:** 1314008-27-9  
**SMILES String:** FC1=C(F)C=CC2=C1N=C(C)C(OC3=C(C(C)(C)O)C(F)=CC=C3)=C2

**QP-1-1**

**IUPAC Name:** 7,8-Difluoro-3-(3-fluoro-2-isopropenylphenoxy)-2-methylquinoline  
**CAS Name:** Not reported  
**CAS Number:** Not reported  
**SMILES String:** Not found



## QP-1-7

**IUPAC Name:** 2-[2-(7,8-Difluoro-2-methyl-3-quinolyloxy)-6-fluorophenyl]-2-hydroxypropanoic acid  
**CAS Name:** Not reported  
**CAS Number:** Not reported  
**SMILES String:** Not found

