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MEMORANDUM

SUBJECT: Flazasulfuron ECM0218S1-S5

FROM: Joseph Ferrario, Branch Chief
BEAD/Environmental Chemistry Laboratory

Joseph Ferrario 12/21/05

TO: Hardip Singh
Senior Gatekeeper Team/IO EFED/
Environmental Risk Branch IV (7507C)

The EFED/Environmental Fate and Effects Division has requested an Environmental Chemistry Method Evaluation on Flazasulfuron in soil using the method submitted by ISK Biosciences Corporation in accordance with the registration of Flazasulfuron MRID No. 462209-57. The method and independent laboratory validation data was reviewed and the conclusions included in the attached Environmental Chemistry Method Review Evaluation.

The following report includes an overview of the method and the method completeness, statements of adherence to EPA regulations, a presentation of results and a discussion of problems found in the registrant method and those discovered by the independent laboratory. A statement of method acceptability is also included.

If you have any questions concerning this report, please contact Elizabeth Flynt at (228) 688-2410 or me at (228) 688-3212.

Attachments
cc: Dr. Christian Byrne, QA Officer
BEAD/Environmental Chemistry Laboratory
Elizabeth C. Flynt
BEAD/ECL

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Flazasulfuron in soil/ECM02189S1-S5/71512/ISK Biosciences Corporation/
ENVIRONMENTAL CHEMISTRY METHOD REVIEW EVALUATION

Data Requirement: PMRA Data Code: NA
EPA DP Barcode: - D318316
OECD Data Point: NA
EPA Guideline: ECM Method Review

Test material:
Common name: Flazasulfuron
Chemical name: *N*-[[4,6-dimethoxypyrimidin-2-yl)-3-(3-trifluoromethyl-2-pyridylsulphonyl)urea
IUPAC name:

Primary Evaluator: Elizabeth Flynt **Date:**
Elizabeth Flynt, Chemist, EPA/OPP/BEAD/ECB

Peer Reviewer: Charles Kennedy **Date:** 10/26/05
Charles Kennedy, Chemist, EPA/OPP/BEAD/ECB

QA Officer: Christian Byrne **Date:** 11/03/05
Dr. Christian Byrne, EPA/OPP/BEAD/ECB

ANALYTICAL METHOD: 462209-57, Stockton, Megan T. Analytical Method for the Determination of SL-160 and Its Metabolites in Soil. Unpublished method created by ISK Biosciences Corporation, 7470 Auburn Road, Suite A, Concord, OH 44077 and submitted by same. Study ID:IB-2003-JLW-007-01-01, Method Effective Date: January 7, 2004.

EXECUTIVE SUMMARY

The method is applicable for the quantitative determination of residues of Flazasulfuron and 4 degradates in soil. The method was submitted to EPA to support studies performed to seek registration for Flazasulfuron. The method was created by ISK Biosciences Corporation in Concord, OH in accordance with EPA's Good Laboratory Practice Standards, Title 40 Code of Federal Regulations Part 160. An independent laboratory validation was submitted with this method. It was entitled, "Independent Laboratory Validation (ILV) of CCRL's Method (CCRL-MTH-045) for the Analysis of SL-160 and Its Metabolites (TPSA, DTPU, DTPP, and ADMP) in Soil". It was performed by EN-CAS Analytical Laboratories in Winston-Salem, NC 27107.

Method Summary: SL-160 and its metabolites are extracted from 50-g soil samples using 120-ml of acetonitrile and 30-ml of water. The samples are then shaken on the shaker for 30 minutes. After shaking, the samples are filtered through Buchner funnels into 500-ml flat bottoms and then evaporated to 10-20 ml using rotary evaporation. The sample residues are dissolved in water and extracted with methylene chloride. Methylene chloride extracts are dried using rotary evaporation. Once dried the samples are

reconstituted with acetonitrile, filtered and transferred to vials for LC/MS/MS analysis. SL-160 and its metabolites are determined using LC/MS/MS.

The limit of quantitation (LOQ) of the method is 0.00250 μg/g (ppm). The highest validated level in this method is 1.00 μg/g (ppm).

ECB was unable to verify precision/accuracy at the LOQ or 10 X LOQ because the registrant only used two replicates at each of the levels. The ILV used 5 replicates at each level. The precision/accuracy for the parent and all degradates with the exception of ADMP at the LOQ and 10 X LOQ for the ILV was within the acceptable range of 70% to 120 % with relative standard deviations less than 20%.

METHOD ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS

Under the conditions and parameters set in the *Ecological Effects Test Guidelines, OPPTS 850.7100, Data Reporting for Environmental Chemistry Methods;* "Public Draft." (U.S. Environmental Protection Agency. Office of Prevention, Pesticides, and Toxic Substances (7101). U.S. Government Printing Office: Washington, DC, 1996, EPA-712-C-96-348), this method was acceptable for all analytes with the exception of ADMP. The recoveries for this analyte were less than the prescribed range

COMPLIANCE

Signed and dated statements that this method was conducted in accordance with the requirements for Good Laboratory Practice Standards, 40 CFR 160 were present in the ILV. Also, a statement of non-confidentiality on the basis of the method falling within the scope of FIFRA Section 10 (d)(1)(A)(B), or (C) was signed and dated along with information on the Quality Assurance inspection dates and signatures was found in the ILV.

A. BACKGROUND INFORMATION

Flazasulfuron is a herbicide. It is effective against most broadleaf weeds, annual grass weeds, sedges in turf, citrus, vine, and sugarcane.

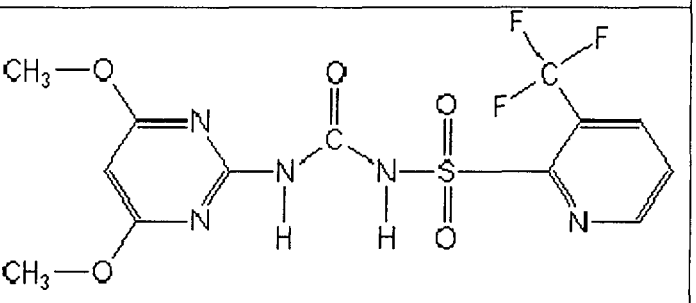
TABLE A.1. Test Compound Nomenclature	
Compound	
Common name	Flazasulfuron
Company experimental name	SL-160
IUPAC name	1-(4,6-dimethoxypyrimidin-2-yl)-3-(3-trifluoromethyl-2-pyridylsulphonyl)urea
CAS Name	*N*-[[4,6-dimethoxy-2-pyrimidinyl)amino]carbpmu;]3-(trifluoromethyl)-2-pyridinesulfonamide
CAS #	104040-78-0

TABLE A.2. Physicochemical Properties of the Technical Grade Test Compound

Parameter	**Value**
Melting point/range	147°C-150°C
pH	Not given
Density	Not given
Water solubility (___°C)	Not given
Solvent solubility (mg/L at 20°C)	acetone-22.7 g/l; methanol-4.2 g/l; acetonitrile 8.7 g/l; hexane 0.5 g/l
Vapour pressure at ___°C	Not given
Dissociation constant (pK_a)	Not given
Octanol/water partition coefficient Log(K_{ow})	Not given
UV/visible absorption spectrum	Not given

B. MATERIALS AND METHODS

B.1. Principle of Method

TABLE B.1.1.	**Summary Parameters for the Analytical Method Used for the Quantitation of Chemical Residues in Matrices Studied**
Method ID	ECM0218S1-S5
Analyte(s)	Flazasulfuron
Extraction solvent/technique	50 g soil samples extracted with acetonitrile/water

TABLE B.1.1.	Summary Parameters for the Analytical Method Used for the Quantitation of Chemical Residues in Matrices Studied
Cleanup strategies	Samples are filtered and evaporated to 10-20 ml. Samples are then reconstituted in ACN and filtered.
Instrument/Detector	Sciex API3000 LC/MS/MS with Shimadzu SCL-10A Controller, Perkin Elmer PE-200 Autosampler; Column: Phenomenix Prodigy 5 µ ODS (250 mm x 4.60 mm id)

C. RESULTS AND DISCUSSION

C.1. Recovery Results Summary

TABLE C.1.1. Average Recovery Results from Method Validation of Washington and North Dakota Soil

Compound	Spiking Level (µg/g)	Average Recoveries Obtained (%)	Relative Standard Deviation
SL-160	0.005	97.2, 96.6	Not able to calculate based on only two replicates at each level
	0.100	80.2, 83.2	
DTPU	0.005	101, 101	
	0.100	102, 97.2	
DTPP	0.005	97.2, 102	
	0.100	92.7, 94.5	
ADMP	0.005	82.2, 86.4	
	0.100	81.0, 74.4	
TPSA	0.005	103, 91.2	
	0.100	101, 106	

C.1.2. Method Characteristics

TABLE C.1.2. Method Characteristics

Analyte	Flazasulfuron
Limit of Quantitation	0.0025 µg/g
Limit of Detection (LOD)	Not given
Accuracy/Precision at LOQ (0.005 µg/g)	See chart above
Reliability of the Method/ [ILV]	An independent laboratory method validation [ILV], (MRID No. 462209-47), was conducted to verify the reliability of method for the determination of flazasulfuron residues and it's degradates in soil. The values obtained indicated that the registrant method is acceptable according to *OPPTS 850.7100 Guidelines* with the exception of ADMPwhich was not successfully validated by the independent laboratory.
Linearity	All method responses were linear (coefficient of determination for all compounds was greater than r^2=0.9965)

TABLE C.1.2. Method Characteristics	
Specificity	The method is specific for the determination of flazasulfuron and its degradates by virtue of the chromatographic separation and selective detection system used. According to recently published guidelines , when detection is performed by tandem mass spectrometry methods, confirmation of the presence of the analyte should require the observation of a precursor ion plus one structurally significant product ion observed at the same retention time. Further confirmation is not necessary due to the highly specific nature of the MS/MS transitions monitored.

C.2. Independent Laboratory Validation (ILV)

The ILV was conducted in accordance with the *OPPTS 850.7100 Guidelines.* No method modifications were made.

TABLE C.2.1. Average Recovery Results Obtained by an Independent Laboratory Validation of the Method for the Determination of Flazasulfuron in Soil

Matrix	Spiking Level (ug/g)	Average Recoveries Obtained (%)	Relative Standard Deviation
Soil			
SL-160	0.0025	85	4.8
	0.025	91	8.1
TPSA	0.0025	73	11
	0.025	77	9.4
DTPU	0.0025	91	5.3
	0.025	90	4.8
DTPP	0.0025	84	3.7
	0.025	83	2.7
ADMP	0.0025	53	17
	0.025	45	29

D. CONCLUSION

From a review of the method, Stockton, Megan, "Analytical Method for the Determination of SL-160 and Its Metabolites in Soil", ECB concludes that the method appears scientifically sound and capable of determining the residues of Flazasulfuron and its degradates with the exception of ADMP in soil at the limit of quantitation of 0.0025 ug/g and above.