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November 15, 2005

MEMORANDUM

D 318088
DP Barcode: ~~D310034~~

SUBJECT: Flazasulfuron (SL-160) in surface water-Report No. ECM0218W1-W3

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

TO: Hardip Singh (7507C)
OPP/Environmental Fate and Effects Division
Environmental Risk Branch

The EFED Environmental Fate and Effects Division has requested an Environmental Chemistry Method Evaluation on Flazasulfuron in surface water using the method submitted by ISK Biosciences Corporation in accordance with the registration of Flazasulfuron MRID No. 463944-10. The method 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. A statement of method acceptability is also included.

If you have questions concerning this report, please contact Charles Kennedy at (228) 688-2443 or Joseph Ferrario at (228) 688-3212.

- Attachments
- cc: Christian Byrne, QA Officer
BEAD/Environmental Chemistry Laboratory

 - Charles D. Kennedy
BEAD/Environmental Chemistry Laboratory

ENVIRONMENTAL CHEMISTRY METHOD REVIEW EVALUAION

Data Requirement: PMRA Data Code: NA
EPA DP Barcode: - D318088
OECD Data Point: NA
EPA Guideline: ECM Method Review

Test material:

Common name: Flazasulfuron
Chemical name: N-[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]-3-(trifluoromethyl)-2-pyridinesulfonamide
IUPAC: 1-(4,6-dimethoxypyrimidin-2-yl)-3-(3-trifluoromethyl-2-pyridylsulfonyl)urea

Primary Evaluator: Charles Kennedy Date: 11/03/05
Charles Kennedy, Chemist, EPA/OPP/BEAD/ECB
Peer Reviewer: Elizabeth Flynn Date: 11/03/05
Elizabeth Flynn, Chemist, EPA/OPP/BEAD/ECB
QA Officer: Christian Byrne Date: 11/03/05
Dr. Christian Byrne, EPA/OPP/BEAD/ECB

ANALYTICAL METHOD: Dr. Andreas Wais, June 8, 1999. Validation of an Analytical Method for the Determination of SL-160, DTPU, and TPSA in Surface Water, MRID No. 463944-10. Unpublished method created by RCC Ltd and submitted by ISK Biosciences Corporation. Study ID: 722417 Method Effective Date: June 8, 1999.

EXECUTIVE SUMMARY

The method is applicable for the quantitative determination of residues of SL-160 (determined as DTPP), DTPU, and TPSA in surface water.

The method was submitted to EPA by ISK Biosciences Corporation/Ishihara Sangyo Ltd, to support studies performed to seek registration for Flazasulfuron. The method was created by RCC Ltd in accordance with the good laboratory practice regulations set forth in Title 40, Part 160 of the Federal Regulations of the United States of America. An independent laboratory validation was not submitted with this method.

ENVIRONMENTAL CHEMISTRY METHOD REVIEW EVALUAION

Method Summary: Two target analytes are extracted from a 1000 mL alkalified surface water (DTPU, DTPP) followed by a third analyte being extracted from a separate 500 mL of surface water (TPSA). The alkalified water sample was extracted with dichloromethane. The organic phase was concentrated to dryness. The residue was dissolved in dichloromethane and cleaned-up on a silica gel column [elution of DTPU with dichloromethane/ethyl acetate (1+1 v/v)]. The eluate was concentrated to dryness. The residue was dissolved in bi-distilled water/acetonitrile and DTPU was quantified by HPLC with UV-detector. The aqueous phase remaining after the first partitioning step was acidified and extracted with dichloromethane. The organic phase was concentrated to dryness. The dried residue was dissolved in acetonitrile. After derivatization with sodium hydroxide (1 molar), the derivative was acidified and then extracted with dichloromethane. The organic phase was concentrated to dryness. The residue was dissolved in dichloromethane and cleaned-up on a silica gel column [elution of DTPP with dichloromethane/ethyl acetate (9+1 v/v)]. The eluate was concentrated to dryness. The residue was dissolved in bi-distilled water/acetonitrile and DTPP was quantified by HPLC with UV-detector. Target analyte TPSA was extracted from a 500 mL of surface water with ethyl acetate. The sample was further extracted with ethyl acetate by liquid-liquid partition followed by clean-up step on a silica gel column [elution with dichloromethane/ethyl acetate (95+5 v/v)]. The eluate was concentrated to dryness. The residue was dissolved in bi-distilled water and determined by HPLC with UV-detector.

The limit of detection (LOD) in surface water for DTPU is 0.2 µg/L, DTPP 0.025 µg/L, and TPSA 2.0 µL. The limit of quantitation (LOQ) for surface water for DTPU is 1.0 µg/L, DTPP 0.05 µg/L, and TPSA 10.0 µg/L.

METHOD ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS

There are several minor problems/deficiencies with this method. The method review revealed a general explanation approach on steps involving reagent mixtures, fortifications, and method extraction/clean-up information. The registrant stated claims of Limits of Detection, Limit of Quantification, and 10 x Limit of Quantification (DTPP, DTPU, TPSA) are supported with a data table but chromatograms at the MDL (DTPU, TSPA) 10 x LOQ (DTPP, DTPU, TPSA) are not included with the data package. The lack of an ILV accompanying the registrant method further complicates a true evaluation of the capabilities this method.

Although the registrant method as written could have been used to perform the Environmental Fate studies, it was not validated by an independent validation laboratory. ECB has concerns that even though the elements of the method are presented in the method, they are not laid out in a organized matter. Independent lab evaluation should be approached with caution using the information as presented. Under the conditions and

ENVIRONMENTAL CHEMISTRY METHOD REVIEW EVALUAION

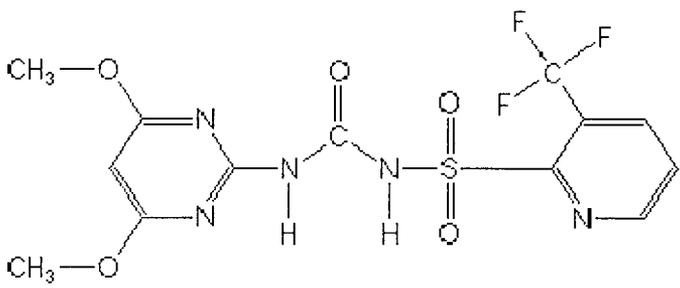
parameters set in the *Ecologic Effects Tests Guidelines, OPPTS 850.7100, Data Reporting for Environmental Chemistry Methods*; "Public Draft." (U.S. Environmental Protection Agency. Office of Prevention, Pesticides, and Toxic Substances (7101). U.S. Government Printing Office: Washington, DC, 1996, EPA-712-C-96-348), this method was acceptable for all analytes.

COMPLIANCE

Signed and dated statements that this method was conducted in accordance with the requirements for Good Laboratory Practice, 40 CFR 160 were presented in this method. 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.

A. BACKGROUND INFORMATION

Flazasulfuron 1-(4,6-dimethoxypyrimidin-2-yl)-3-(3-trifluoromethyl-2-pyridylsulphonyl)urea is an selective herbicide under development by Ishihara Sangyo Kaisha, Ltd. in Osaka, Japan. It is used as a preemergence or postemergence for most broadleaf weeds, annual grass weeds, sedges in turf, citrus, vine and sugarcane.

TABLE A.1. Test Compound Nomenclature	
Compound	 <p>Chemical Structure</p>
Common name	Flazasulfuron
Company experimental name	SL-160
IUPAC name	1-(4,6-dimethoxypyrimidin-2-yl)-3-(3-trifluoromethyl-2-pyridylsulphonyl)urea
CAS Name	None given
CAS #	104040-78-0

ENVIRONMENTAL CHEMISTRY METHOD REVIEW EVALUAION

Parameter	Value	
Melting point/range	147-150°C (white powder)	
pH	Information not available	
Density	Information not available	
Water solubility (20 °C)	pH 5 buffer: 27mg/L at 25°C, pH 7 buffer: 2100 mg/L at 25°C (in acetonitrile 8.7 g/kg at 25°C)	
Solvent solubility (mg/ml at 20 °C)	<u>Solvent</u>	<u>Solubility (g/L)</u>
	Acetone	22.7
	Methanol	4.2
	Acetonitrile	8.7
Hexane	0.5	
Vapour pressure at ___ °C	Information not available	
Dissociation constant (pK _a)	Information not available	
Octanol/water partition coefficient	Information not available	
UV/visible absorption spectrum	Information not available	

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

The analytical methods for determination of Flazasulfuron (determined as DTPP) as well as its metabolites DTPU and TPSA in surface water were developed within this study. The three targeted analytes are extracted from surface water by solvent, evaporated, reconstituted and cleaned up by silica gel columns. The eluates are evaporated and reconstituted in bi-distilled water/acetonitrile (DTPP, DTPU) and bi-distilled water (TPSA) before quantification by HPLC with UV detectors.

	Summary Parameters for the Analytical Method Used for the Quantitation of Chemical Residues in Matrices Studied
Method ID	ECM0218W1-W3
Analyte(s)	SL-160 (as DTPP), DTPU, and TPSA
Extraction solvent/technique	Liquid/liquid extraction from surface water with dichloromethane, (DTPP, DTPU) and ethyl acetate (TPSA).
Cleanup strategies	Silica Gel column
Instrument/Detector	Merck-Hitachi HPLC system with a Merck-Hitachi AS-2000 sampling unit, Merck-Hitachi D-2500 integrator and Merck-Hitachi L-4000 UV-detector.

C. RESULTS AND DISCUSSION

C.1. Recovery Results Summary

TABLE C.1.1. Recovery Results from Method Validation of [matrices]			
Matrix	Spiking Level µg/L	Average Recovery Obtained (%)	Relative Standard Deviation
Surface Water			
SL-160 (as DTPP)*2 nd Amendment values	0.05	77.5	4.5
SL-160 (as DTPP)	0.1	87.3	13.3
	1.0	93.9	2.4
DTPU	1.0	97.0	2.8
	10.0	100.6	2.0
TPSA	10.0	94.9	3.7
	100.0	98.2	3.4

C.1.2. Method Characteristics

TABLE C.1.2. Method Characteristics	
Analyte	SL-160 (as DTPP), DTPU, TPSA
Limit of Quantitation	0.05µg/L*, 0.1µg/L, 1.0 µg/L, 10.0 µg/L
Limit of Detection (LOD)	0.025µg/L*, 0.05 µg/L, 0.2 µg/L, 2.0 µg/L
Accuracy/Precision at LOQ	See chart above
Reliability of the Method/ [ILV]	ILV not Available
Linearity	All method responses were linear (coefficient of determination for all compounds was greater than $r^2 = 0.9986$).
Specificity	The methods allow the determination SL-160 (determined as DTPP), DTPU, and TPSA in surface water. There was no interference with other substances observed at the retention time of the three test items above the limit of detection. Furthermore, the peak identity was confirmed by HPLC-DAD.

C.2. Independent Laboratory Validation (ILV)

TABLE C.2.1. A Independent Laboratory Validation of the Method was not available for the Determination of Flazasulfuron in Surface Water			
Compound	Spiking Level (ug/L)	Average Recoveries Obtained (%)	Relative Standard Deviation
	N/A	N/A	N/A

D. CONCLUSION

From a review of the method, “Validation of an Analytical Method for the Determination of SL-160, DTPU, and TPSA in Surface Water”, ECB suggests that the registrant submit a more organized written form of the method so it can be easily followed and reproduced by an outside laboratory. ECB also recommends an independent laboratory validation be performed on this method.