MEMORANDUM

SUBJECT: Transmittal of DERs for Method Analysis of Florasulam in Soil/Sediment and Water.

TO: Kathryn Montague, Team Leader
Herbicide branch
Registration Division (7505P)

FROM: Marietta Echeverria, Environmental Scientist
Environmental Risk Branch IV
Environmental Fate and Effects Division (7507P)

APPROVED
BY: Elizabeth Behl, Branch Chief
Environmental Risk Branch IV
Environmental Fate and Effects Division (7507P)

Attached please find the review of the Method Analysis for Florasulam in Soil/Sediment (MRID 46808205) and Water (MRIDs 46800801, 46808207). This review was completed by the BEAD Environmental Chemistry Lab in support of the registration of florasulam.

Note that both of these studies have been classified as unacceptable. The remaining studies associated with this data package (MRIDs 46808010, 46808012, 46808013, 46808014, 46808015, 46808016, 46808017, 46808026, 46808027) have been screened by the BEAD Environmental Chemistry Lab and deemed to be extraneous submissions.
MEMORANDUM


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

To: Cara Dzubow, Program Analyst
OPP/Environmental Fate and Effects Division
Information and Support Branch (7507C)

The Environmental Fate and Effects Division (EFED) has requested an Environmental Chemistry Method Review of the residues of XDE-520 and its 5-hydroxy metabolite in surface water using Method MRID No. 4680080-11 submitted by Dow Agrosciences, LLC in accordance with the registration of Florasulam. The method validation data was reviewed and the conclusions included in the attached Environmental Chemistry Method Review Report.

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 Shanda L Bennett at (228) 688 - 3251 or me at (228) 688-3212.

cc: Dr. Christian Byrne, QA Officer
BEAD/ECL

Elizabeth Flynt, Chemist
BEAD/ECL
ENVIRONMENTAL CHEMISTRY METHOD
REVIEW REPORT

Data Requirement:
PMRA Data Code: NA
EPA DP Barcode: 340787
OECD Data Point: NA
EPA Guideline: ECM 0234W1-W2

Test material:
Common name: Florasulam
Chemical name: N-(2,6-difluorophenyl)-8-fluoro-5-methoxy[1,2,4]triazolo[1,5-c] pyrimidine-2-sulfonamide
IUPAC Name: 2',6',8-trifluoro-5-methoxy[1,2,4]triazolo[1,5-c]pyrimidine-2-sulfonanilide
CAS Number: 145701-23-1

Primary Evaluator: Shanda Bennett, Chemist, EPA/OPP/BEAD/ECB
Date: 10/23/2007

Peer Reviewer: Elizabeth Flynn, EPA/OPP/BEAD/ECB
Date: 10/23/07

QA Officer: Dr. Christian Byrne, EPA/OPP/BEAD/ECB

ANALYTICAL METHOD: 468080-11, Butcher, S., Gibson, R., August 29, 1996. "Determination of the Residues of XDE-570 and Its 5-hydroxy Metabolite in Surface Water". The unpublished study was sponsored by Dow AgroSciences LLC, 9330 Zionville Road 308/2E, Indianapolis, Indiana 46268-1054. The study was performed by DowElanco Limited, Letcombe Laboratory, Letcombe Regis, Wantage, Oxon OX12 9JT UK. Pages 1-23.

EXECUTIVE SUMMARY

The method is applicable for the quantitative determination of the residues Florasulam (XDE-570) and its metabolite, 5-Hydroxy (XDE-570), in surface water.

The method was submitted to EPA by Dow AgroSciences LLC to support the registration of the herbicide - Florasulam. The method was created and reviewed by DowElanco Limited in Oxon OX12 9JT UK in accordance with OECD Principles of Good Laboratory Practice Standards. ECB finds this method unacceptable as submitted.

Method Summary: Florasulam (XDE-570) and its 5-hydroxy XDE-570 metabolite were extracted from surface water using a polystyrene divinylbenzene solid phase extraction cartridge, eluting both analytes from the cartridge with a 50:50 (v/v) acetonitrile/aqueous acid. The eluate was partitioned with methyl-tertiary-butyl ether (MTBE). The ether extract is purified using an aminopropyl solid phase extraction cartridge eluting the analytes with formic acid/acetonitrile/MTBE mixture. The eluate was evaporated to
dryness. The residue is further purified by using a silica solid phase extraction cartridge eluting the analytes with a formic acid/acetonitrile/toluene mixture. The eluate is evaporated to dryness and the residue is reconstituted into a 20:80:1 (v/v/v) acetonitrile/water/acetic acid solution. XDE-570 and its metabolite are quantified by HPLC using UV absorbance detector set at 260 nm.

**METHOD ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS**


The registrant did not submit an Independent Laboratory Validation (ILV) with the original method to support the data. The ILV should be performed by an independent laboratory that is not affiliated with the sponsor.

It was proposed that a comparison study entitled, “Determination of XDE-570 Concentrations in Drinking Water Using Both LC/UV and Immunoassay Methods” be used in place of the missing ILV since the LC/UV method used is the same as the method under review. Upon further investigation it was determined that the methods are quite different. The proposed comparison study was numbered R95-142 and was conducted in 1995 and utilized SPE extraction, followed by clean-up with additional SPE, and ion-pairing and derivatization by methylation. The matrix was drinking water. It also did not analyze for the metabolite (5-hydroxy XDE-570). The method under review is MRID #468080-11. It was numbered R96-15 and was conducted in 1996 and utilized SPE extraction, followed by clean-up with additional SPE, without ion-pairing or derivatization by methylation. The matrix was surface water. There are significant differences between the two methods that would preclude a direct comparison between them.

Additionally, although the calibration curves that were submitted in the original registrant’s method did meet the acceptability requirements, it could not be verified by ECL due to the omission of the response factors and chromatograms at the LOQ (limit of quantitation), MDL (minimal detection limit) and 10 x LOQ level.

There are insufficient chromatograms and the associated peak height responses to verify the method. On page 13, under Calculations, there are no representative sample calculations to verify any of the values presented on Tables 4 or 6.
ENVIRONMENTAL CHEMISTRY METHOD
REVIEW REPORT

In addition, on page 21, the title of the last sample “Control Sample RV96-014-001 (diluted x 4)” is incorrect. The fortification of 5-hydroxy XDE-570 was 2.00 µg/L and not 0.20 µg/L. See Table 6, page 18.

Finally, ECL recommends a minor clarification pertaining to page 11, section 6.6 of the Sample and Fortified Sample Analysis portion of the method. The method states, “include a reagent blank and procedural recovery in each analytical batch”. ECL would like for the registrant to clarify by changing the term “procedural recovery” to “procedural recovery control”.

COMPLIANCE

Signed and dated statements that this method was conducted in accordance with the requirements for Good Laboratory Practice Standards, 40 CFR 160 were not presented in the method. However, a statement was noted that this method was conducted in compliance with OECD Principles of Good Laboratory Practice Standards. 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

Florasulam, N-(2,6-difluorophenyl)-8-fluoro-5-methoxy[1,2,4]triazolo[1,5-c]pyrimidine-2-sulfonamide is a herbicide that is used to control various broadleaf weeds in cereals and corn.

<table>
<thead>
<tr>
<th>TABLE A.1. Test Compound Nomenclature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compound</td>
</tr>
<tr>
<td>Florasulam (XDE-570)</td>
</tr>
<tr>
<td>NA</td>
</tr>
</tbody>
</table>

DP Barcode 340787 / MRID No.468080-11
Florasulam (XDE-570) and its 5-hydroxy metabolite is extracted from surface water using a polystyrene divinylbenzene solid phase extraction cartridge, eluting both analytes from the cartridge with a 50:50 (v/v) acetonitrile/aqueous acid. The eluate is partitioned with methyl-tertiary-butyl ether (MTBE). The ether extract is purified using an aminopropyl solid phase extraction cartridge eluting the analytes with a formic acid/acetonitrile/MTBE mixture. The eluate is evaporated to dryness. The residue is further purified by using a silica solid phase extraction cartridge. The analytes are eluted with a formic acid/acetonitrile/toluene mixture. The eluate is evaporated to dryness and the residue is reconstituted with a 20:80:1 (v/v/v) acetonitrile/water/acetic acid solution. XDE-570 and its metabolite are quantified by HPLC using UV absorbance detector set at 260 nm.
### Summary Parameters for the Analytical Method Used for the Quantitation of Chemical Residues in Matrices Studied

<table>
<thead>
<tr>
<th>Method ID</th>
<th>ECM0234W1-W2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analyte(s)</td>
<td>Florasulam (XDE-570), 5-Hydroxy (metabolite)</td>
</tr>
</tbody>
</table>

**Extraction solvent/technique**

The specified volume of fortification solution was added to each 500 mL of surface water, acidified with sulfuric acid, capped and mixed well. Florasulam (XDE-570) and its 5-Hydroxy metabolite were extracted from surface water using a polystyrene divinylbenzene solid phase extraction cartridge, eluting both analytes from the cartridge with a 50:50 (v/v) acetonitrile/aqueous acid. The eluate was partitioned with methyl-tertiary-butyl ether (MTBE).

**Cleanup strategies**

The ether extract is purified using an aminopropyl solid phase extraction cartridge eluting the analytes with formic acid/acetonitrile/MTBE mixture. The eluate was evaporated to dryness. The residue is further purified by using a silica solid phase extraction cartridge eluting the analytes with a formic acid/acetonitrile/toluene mixture. The eluate is evaporated to dryness and the residue is reconstituted into a 20:80:1 (v/v/v) acetonitrile/water/acetic acid solution. XDE-570 and its metabolite are quantified by HPLC using UV absorbance detector set at 260 nm.

**Instrument/Detector**

Milton Roy spectroMonitor 3100 UV detector Varian UK Ltd 9010 solvent delivery system Perkin-Elmer ISS100 autosampler

### RESULTS AND DISCUSSION

#### C.1. Recovery Results Summary

<table>
<thead>
<tr>
<th>Matrix</th>
<th>Spiking Level (µg/L)</th>
<th>Avg. % Recoveries</th>
<th>Relative Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Florasulam (XDE-570)</td>
<td>0.10</td>
<td>87</td>
<td>10.1</td>
</tr>
<tr>
<td></td>
<td>0.25</td>
<td>94</td>
<td>4.4</td>
</tr>
<tr>
<td></td>
<td>0.50</td>
<td>101</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td>1.00</td>
<td>98</td>
<td>2.9</td>
</tr>
<tr>
<td>5-Hydroxy XDE-570</td>
<td>0.20</td>
<td>96</td>
<td>10.1</td>
</tr>
<tr>
<td></td>
<td>0.50</td>
<td>86</td>
<td>8.0</td>
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<td></td>
<td>1.00</td>
<td>93</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td>2.00</td>
<td>89</td>
<td>4.8</td>
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</table>
C.1.2. Method Characteristics

<table>
<thead>
<tr>
<th>Method Characteristics</th>
<th>Florasulam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limit of Quantitation (LOQ)</td>
<td>0.10 µg/L for XDE-570&lt;br&gt;0.20 µg/L for 5-Hydroxy XDE-570</td>
</tr>
<tr>
<td>Limit of Detection (LOD)</td>
<td>0.02 µg/L for XDE-570&lt;br&gt;0.04 µg/L for 5-Hydroxy XDE-570</td>
</tr>
<tr>
<td>Accuracy/Precision at LOQ</td>
<td>XDE-570 – 81% to 108% (mean 94%)&lt;br&gt;5-Hydroxy XDE-570 – 78% - 110% (mean 92%)</td>
</tr>
<tr>
<td>Reliability of the Method/ [ILV]</td>
<td>An independent laboratory method validation [ILV] was not submitted with this method.</td>
</tr>
<tr>
<td>Linearity</td>
<td>The detector response was linear over the range of 0.025 to 1 µg/mL; r = 0.999 for both compounds.</td>
</tr>
<tr>
<td>Specificity</td>
<td>The analytical method employs a highly specific and selective detector; therefore, a confirmatory method is not necessary.</td>
</tr>
</tbody>
</table>

C.2. Independent Laboratory Validation (ILV)

The ILV was not submitted with this method.

| Recovery Results Obtained by an Independent Laboratory Validation of the Method for the Determination of Florasulam (XDE-570) and Its Metabolite 5-Hydroxy XDE-570 in | Spiking Level (µg/L) | Average Recoveries Obtained (%) | Relative Standard Deviation (%) |
| surface water. | | | |
| Compound | Not provided. | | |

D. CONCLUSION

From a review of this method, Butcher, S., Gibson, R., August 29, 1996, "Determination of the Residues of XDE-570 and Its 5-Hydroxy Metabolite in Surface Water", ECL concludes that this method is unacceptable as submitted.
MEMORANDUM

SUBJECT: Florasulam - ECM0234S1-S2  DP # 340787

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

TO: Cara Dzibow ECM Gatekeeper
EISB 7507P

The EFED/Environmental Fate and Effects Division has requested an Environmental Chemistry Method Review of a method (MRID No. 468082-05) for the determination of Florasulam and its metabolites in soil/sediment using the method submitted by Bayer CropScience in accordance with the registration of the above mentioned analyte.

ECB did not receive an independent laboratory validation (ILV) for this method. Due to the lack of an ILV for this soil method, ECB finds the method unacceptable and will not perform a review of the method at this time.

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