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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON D.C., 20460

ENVIRONMENTAL FATE AND EFFECTS DIVISION  
OFFICE OF PESTICIDE PROGRAMS

Chemical: Penoxsulam  
PC Code: 119031  
DP Barcode: D328346  
MRID 467583-01

MEMORANDUM

2008 September 24

Subject: Effect of penoxsulam degradates on plants and "Exhibit A."

From: James J. Goodyear, Ph.D.,  
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Environmental Risk Branch 3  
Environmental Fate and Effects Division (7507P)

Through: Mark Corbin, Ph.D., Chief  
Environmental Risk Branch 3  
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To: Joanne Miller, Product Manager 23  
Philip Errico, PM Team Reviewer  
Herbicide Branch  
Registration Division (7505P)

EFED has reviewed D328346, MRID 467583-01, "Herbicidal Activity of XDE-638 Soil, Aquatic and Photolytic Metabolites on Weeds and Crops in Discovery Weed Management Screens." The submission does not claim that it addresses a specific guideline. The study is not scientifically sound and is **Invalid** for fulfillment of guideline requirements. It is a study done for the company's information and was never intended to be a guideline study. The targets of the studies were not the plants mentioned in §122a&b or §123a&b. Not all of the required degradates were used, especially for lesser pigweed (*Lemna minor*). The population of the study plots could not be determined and there were too few replicates. The study solutions were referenced in terms of their concentration (ppm) rather than their volume. There is no relevant statistical analysis of the results.

The submission includes a separate portion that is entitled "Exhibit A." The purpose of "Exhibit A" is to argue that certain studies on degradates need not be done because they do not occur in significant quantities in field use. Lucy Shanaman, the chemist who reviewed penoxsulam technical made comments on "Exhibit A."



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*"The submitted aquatic field dissipation studies (MRID's 45820804 and 45830805) for penoxsulam do indicate that penoxsulam degradates do form in quantifiable amounts under actual use conditions, and are detected at later time points. Additionally, it should be remembered that field dissipation studies conducted in support of pesticide registrations are never as rigorous as laboratory studies. Material balances are almost never calculated for field dissipation studies, and these are not exceptions.*

*In general, the lack of detections of degradates at any sampling interval in a field dissipation study does not necessarily indicate accumulation does not occur. Without a material balance, it only indicates that a particular residue was not detected at a give sampling interval. In this case, the submitted studies indicates that degradation products were present up to one year after application, and that they were detected moving through the soil profile. While some of these degradation products are intermediates, they do persist long enough to be detected in both laboratory and field studies.*

*Finally, the standard laboratory tests requested by EFED for biotic metabolism are not limited to terrestrial conditions. A typical suite of fate studies to support registration for rice pesticides includes aerobic aquatic and anaerobic aquatic metabolism studies. While photolysis is expected to be the predominate route of dissipation for penoxsulam used on rice crops, other dissipation pathways do exist, and, as indicated by submitted aquatic field dissipation studies, can not be ruled out for penoxsulam."*

"Exhibit A" calculates RQs based on faulty data. The population of the study plots could not be determined and the number of replicates is not stated. The study solutions were referenced in terms of their concentration (ppm or mg/L) rather than their volume. There is no relevant statistical analysis of the results.

## Herbicidal Activity of Penoxsulam Metabolites

**Data Requirement:** PMRA Data  
**Code:**

**EPA DP Barcode:** D328346

**MRID:** 467583-01

**OECD Data Point:**

**EPA Guideline:** None

**Test Material:** Penoxsulam parent and metabolites (soil, aquatic and photolytic)

**Purity:** Not reported

**Common name:** Penoxsulam

**Chemical name:** IUPAC: Not reported CAS name: Not reported

CAS No.: Not reported Synonyms: X638177, XDE-638

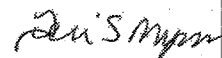
**Primary Reviewer:** John Marton  
**Staff Scientist,**  
**Cambridge Environmental, inc. Date:** 8/14/06

**Signature:**



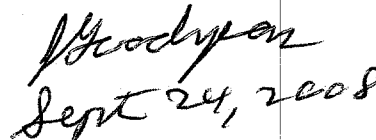
**Secondary Reviewer:** Teri S. Myers  
**Senior Scientist,**  
**Cambridge Environmental, inc. Date:** 8/21/06

**Signature:**



**Primary Reviewer:** James J. Goodyear, Ph.D.  
**Ecological Effects Biologist**  
**U.S. EPA/OPP/ EFED/ ERB3**

**Signature:**



**Date:**

**Reference/Submission No.:** {.....}

**Company Code** {.....} [For PMRA]

**Active Code** {.....} [For PMRA]

**Use Site Category:** {.....} [For PMRA]

**EPA PC Code** 119031

**Date Evaluation Completed:** {24-09-2008}

**Citation:** Mann, R.K., *et al.* 2001. Herbicidal Activity of XDE-638 Soil, Aquatic and Photolytic Metabolites on Weeds and Crops in Discovery Weed Management Screens. Unpublished study submitted by Dow AgroSciences LLC, Indianapolis, Indiana 46268. Study ID 051601RKM.

### Executive Summary:

This study is not scientifically sound and is **Invalid** for fulfillment of guideline requirements. This study was done for the company's information and was never intended to be

a guideline study. The targets of the studies were not the plants mentioned in §122 a & b or §123 a & b. Not all of the required degradates were used, especially for lesser pigweed (*Lemna minor*). The population of the study plots could not be determined and there were too few replicates. The study solutions were referenced in terms of their concentration (ppm) rather than their volume. There is no relevant statistical analysis of the results.

Penoxsulam is a rice sulfonamide herbicide that can be used in rice-growing conditions around the world. The metabolites will often degrade further into more simple metabolites. To complete the registration processes, the herbicidal action of these known metabolites should be determined.

In its review of penoxsulam for a §3 registration in 2004 (119031 D288160 + S3NC), EFED wrote,

*"Penoxsulam degrades by two different transformation mechanisms, producing thirteen different identified transformation products, eleven of which meet the criteria to be classified as major degradates<sup>1</sup>. . . It is possible that some of them pose additional phytotoxicity concerns. In the absence of such information, estimates of required holding times to avoid non-target effects are severely constrained. To eliminate this uncertainty, vegetative vigor and seedling emergence data would be needed on all major degradates."*

<sup>1</sup>*BSA, 2-amino-TP, TPSA, BSTCA methyl, BSTCA, 2-amino-TCA, 5-OH-penoxsulam, SFA, sulfonamide, 5, 8-di-OH and 5-OH 2 amino TP."*

The registrant new submission lists eleven metabolites for penoxsulam (also known as XDE-638 and X638177) are as follows: X012548 (3-amino TCA), X514901 (2-amino-TP), X689643 (5-OH penoxsulam), X697134 (BST), X732143 (5-OH, 2-amino TP), X741277 (BSA), X768359 (BSTCA), X768360 (Sulfonamide), X776128 (BSTCA-methyl), X776129 (SFA or sulfonyl-formamidine), and X776130 (TPSA).

It was noted that the registrant did not do a study on two of the metabolites (2-amino-TCA and 5,8-di-OH amino TP) that are mentioned in EFED's review. They studied two metabolites that were not requested (BST and 3-amino TCA). These chemicals may be the same as the requested chemicals, but EFED has not made that determination.

The list of metabolites in the study report does not completely agree with the list in the "preface" under the heading "EXHIBIT A." That list includes 2-Amino-TP instead of 3-Amino TP.

Dow did not claim that these studies were done in response to EFED's request. Indeed, the studies were done in 2001, whereas, EFED did the §3 review in 2004. This study is better viewed as a §6a2 submission, the submission of data that is possibly adverse information. The submission refers to the study as a "management screening."

The effects of penoxsulam and its metabolites were studied on sensitive indicators for broadleaf weed control *Arabidopsis thaliana* (thale cress, or mouse-ear cress, a small flowering plant related to cabbage and mustard) and *Lemna minor* (lesser pigweed).

#### METHODOLOGY:

***Arabidopsis thaliana*:** Sterilized seeds were exposed to nominal concentrations of 0.000128, 0.00064, 0.0032, 0.016, 0.08, 0.4, 2, 10 and 50 ppm of penoxsulam (and all eleven metabolites)



for nine days. The nutrient medium was autoclaved and supplemented with micronutrients. Two replicates of each treatment level were incubated at 24°C under continuous lighting and inhibition of growth was visually assessed using a numerical rating scale of 0-100.

**Lemna minor:** Organisms were exposed to nominal concentrations of 10 or 25 ppm of penoxsulam and three major metabolites (X689643, X697134, and X741277) for 9 days. The nutrient media consisted of 3.1 g/L of Gamborg's B-5 and 4.4 g/L of Murashige and Skoog in distilled water with a pH of 5.5. Test vessels were placed in a growth chamber under continuous lighting with a temperature of 26°C. Inhibition of growth was visually assessed at test termination using a numerical rating scale of 0-100.

**Pre-Emergence Treatment:** Penoxsulam and all eleven metabolites were applied to pre-emerged seeds of the following plants: cotton, soybean, sugar beet, oilseed rape, cocklebur, lambsquarter, ivyleaf morningglory, redroot pigweed, velvetleaf, wild poinsettia, corn, rice, wheat, blackgrass, wild oat, barnyard grass, large crabgrass, giant foxtail and Rox orange sorghum. Penoxsulam was applied to test plants at nominal application rates of 9, 18, 35, 70 and 140 g ai/ha; all metabolites were applied at nominal application rates of 17.5, 35, 70, 140 and 280 g ai/ha. The test material was dissolved in a General Purpose Solvent (GPS; Acetone/DMSO 97:3 v/v) for application; final spray solution contained deionized water, GPS, and Tween 20 (88:12:0.1 v/v).

Seeds were planted in mineral soil medium consisting of 80% mineral soil and 20% crushed, washed stone. Cocklebur, lambsquarter, and blackgrass seeds were treated to enhance germination prior to testing. No other species receives any treatment prior to test initiation. During the test, all pots received applications of EXCEL fertilizer and water as needed. Water was applied directly to the soil surface.

After 21 days of exposure, visual observations were made using a numerical rating system with 0% representing no plant damage and 100% representing plant death.

**Post-Emergence Treatment:** Penoxsulam and all eleven metabolites were applied to seedlings of the following plants: soybean, oilseed rape, chickweed, cocklebur, lambsquarter, ivyleaf morningglory, redroot pigweed, velvetleaf, field pansy, wild buckwheat, wild poinsettia, Canada thistle, corn, rice, wheat, blackgrass, wild oat, barnyard grass, large crabgrass, giant foxtail, Rox orange sorghum and yellow nut sedge. Penoxsulam and all eleven metabolites were sprayed onto the foliage of all test species at nominal application rates of 31.3, 62.5, 125, 250, and 500 ppm. The test material was dissolved in a General Purpose Solvent (GPS; Acetone/DMSO 97:3 v/v) for application; final spray solution contained, acetone, deionized water, DMSO, Atplus 411F (crop oil concentration), Triton X155 (48.5:39:10:1.5:1.0:0.02 v/v), plus the active ingredient.

The desired growth stage at the time of application was 2 to 2.5 leaves, with a range of 1-4 leaf stages. Seedling age averaged 10 days and ranged from 6 to 28 days at test initiation. Seeds were grown in Grace-Sierra Metromix 306 [Vermiculite, sphagnum, pearbark, ash: (37-47%, 31-15%, 12-25%) pH 6.0-6.8].

Treated pots were placed in a greenhouse and were given a 1/2X solution of EXCEL fertilizer daily via sub-irrigation. Supplemental lighting was provided, giving average illumination of 500  $\mu\text{Em}^{-2}\text{s}^{-1}$  PAR with a 14 hour daily photoperiod.

**RESULTS:**

***Arabidopsis thaliana*:** The percent injury ratings at the nominal 0.000128, 0.00064, 0.0032, 0.016, 0.08, 0.4, 2, 10 and 50 ppm treatment levels were 0, 7, 35, 65, 88, 93, 95, 97 and 99%, respectively, indicating a clear dose-response relationship. Five of the eleven metabolites (X514901, X697134, X732143, X768359, and X776129) did not result in any deleterious effects. The six remaining metabolites (X012548, X689643, X741277, X768360, X776128, and X776130) caused some visible damage; however, the damage was restricted to only the two or three highest treatment levels. At the highest treatment level (50 ppm), the percent damage was 50, 70, 30, 15, 20, and 25% for X012548, X689643, X741277, X768360, X776128, and X776130, respectively. At the second highest treatment level (40 ppm), the percent damage did not exceed 40%.

***Lemna minor*:** Penoxsulam resulted in a 95% injury score at 10 ppm. X689643 and X697134 were tested at 10 ppm as well; however, they caused no noticeable effect on the *Lemna*. X741277 was tested at 25 ppm and caused no noticeable damage to the test species.

***Pre-Emergence and Post-Emergence*:** Penoxsulam caused significant injury to all exposed species when applied to pre-emergent seeds. The injury percentages were  $\geq 30\%$  at all treatment levels for all species. Redroot pigweed appeared to be the most sensitive with complete mortality observed at all treatment levels. None of the eleven metabolites caused any observable injury to the pre-emergent seeds.

During the post-emergence treatment, penoxsulam caused significant injury to all species at all treatment levels with the exception of rice, wheat, and blackgrass. The injury scores for rice were 0, 0, 10, 30, and 40% at the 31.3, 62.5, 125, 250 and 500 ppm treatment levels, respectively. The injury scores were the same for wheat and blackgrass, 0, 0, 0, 10 and 20% at the 31.3, 62.5, 125, 250, and 500 ppm treatment levels, respectively. Only two of the eleven metabolites tested, X689643 and X776129, caused noticeable injury to species during the post-emergence test. When exposed to X689643, oilseed rape and chickweed exhibited injuries of less  $\leq 30\%$  and redroot pigweed exhibited injuries of  $\leq 40\%$ , with 20% injury observed at the lowest treatment level. When exposed to X776129 oilseed rape, lambsquarter, redroot pigweed, velvetleaf and wild buckwheat exhibited minor injury ( $\leq 20\%$ ). All of these species exhibited these effects in the highest treatment level only (500 ppm), with the exception of lambsquarter, which also exhibited minor injury at the next highest treatment level (250 ppm).

In both the pre-emergence and post-emergence tests, all species exhibited an apparent dose-dependent relationship based on the visual injury scores.

**REGISTRANT'S DISCUSSION:**

The registrant's report says that, at low concentrations, penoxsulam can cause significant injury to several crops and weed species, particularly exhibiting high selectivity to grass crops.

Of the eleven metabolites, none had any noticeable effect during the pre-emergent tests and none had any noticeable effect during the post-emergence treatment. Of the two metabolites that did cause injury during the post-emergence treatment, X689643 and X776129, effects were restricted to the higher treatment levels.

The metabolites of penoxsulam seem to have little herbicidal activity on a wide array of grass and broadleaf whole plants and on sensitive indicator species (*Arabidopsis thaliana* and *Lemna minor*), and pose a very low probability of causing injury to non-target plants.

**REVIEWER'S DISCUSSION:**

This study is not scientifically sound and is **Invalid** for fulfillment of guideline requirements. The study cannot be repaired. This submission is better called a "\$6a2" study, because it is a study done for the company's information and was never intended to be a guideline study.

The targets of the experiments were not the plants mentioned in the guideline. Not all of the required degradates were used, especially for lesser pigweed (*Lemna minor*). The population of the study plots could not be determined and there were too few replicates. The study solution was referenced in terms of its concentration (ppm) rather than its volume. There is no relevant statistical analysis of the results.

**REFERENCES:**

Alexander, A. and K. Devore. 1997. Weed Management Level 3 Post and Pre-emergence Test Methodology, DEI #0426.

Somerville, C.R. and W.L. Ogren. 1982. Isolation of photorespiration mutants in *Arabidopsis thaliana*. In GM Edelman, RD Balli, N-H Chua, eds, Methods in Chloroplast Biology. Elsevier Biomedical Press, Amsterdam, pp 129-138.

XDE-638 Technical Profile, Feb 2001.



