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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

AUG 26 1985

MEMORANDUM

SUBJECT: Blazer; acifluorfen
EPA Registration Nos. 707-149 and 707-150;
Laboratory Audit Report

Caswell #7550

FROM: William Dykstra, Ph.D.
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THRU: Robert P. Zendzian, Ph.D.
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Hazard Evaluation Division (TS-769)

Requested Action:

Review lab audit reports to determine the impact of lab audit findings on Toxicology Branch reviews of these studies.

Conclusion:

EPA lab audit noted discrepancies in the reporting of test results. Additional analysis and statistical evaluation of the mouse study needs to be performed, and reported to Toxicology Branch.

The fact that Blazer (RH-6201) technical in the mouse study was a liquid, whereas Blazer technical used in acute studies was a solid needs to be further explained by the registrant.

Toxicology Branch also requires that additional statistical analysis of the data in the 3-generation reproduction study in rats be performed.

Background:

On days March 26, 1984, to March 30, 1984, EPA audited studies conducted by IRDC for Rohm and Haas. The first study that Rohm and Haas sponsored was the lifetime feeding study in mice (IRDC #285-013a) using Blazer herbicide (RH-6201). Additionally, the histopathology report for this same study was also audited at this time.

The second study audited by EPA was the 3-generation reproduction study in rats (IRDC #285-014a) using Blazer herbicide (RH-6201).

Review:

The following deficiencies were reported in the EPA audit of the lifetime feeding study in mice (IRDC #285-013a):

1. Statistical analysis of BUN in females showed a significant dose-related decrease in BUN, which was not reported in the final IRDC report.

2. Table of individual organ weights for high dose (270 ppm) group was missing from final report. Pages 139 and 140 were duplicates, both containing data for the 7.5 ppm group. This discrepancy also existed in the copy of the report submitted to the EPA.

3. Statistical analysis of liver weights of terminally sacrificed male animals showed a significant dose-related increase in weight of livers which was not indicated in the final IRDC report.

4. Diet analysis data were missing for weeks 78, 96, and 103. (Data generated by sponsor.)

5. Two (2) different lots of test compound were used during the course of study, each having somewhat different characteristics (assay and color).

6. Records did not indicate what type of basal diet was used.

Toxicology Branch Response to EPA Audit

With respect to deficiencies (1), no effect on BUN was noted in the November 23, 1983, Toxicology Branch review.

The findings in the audit demonstrate that a NOEL for BUN was not established in the study due to the negative dose-response effect.

Deficiency (3) of the EPA audit demonstrates that a NOEL for increased liver weight was not established in the study. This finding was reported in the November 23, 1983, Toxicology Branch review.

The Toxicology Branch review also reported a dose-related significant increase in kidney weight. This finding was not observed in the EPA audit report.

Deficiency (4) of the audit report states that diet analyses data were missing for weeks 78, 96, and 103. Review of the sponsor's analytical reports indicated that analyses were done at weeks 1, 4, 8, 26 and 104.

The same observations of the audit were also reported in the Toxicology Branch review. The Toxicology Branch review also states that "the compound concentration in the feed varied acceptably."

Deficiency (5) of the audit report states that two different lots of test compound were used in the study. The two lots had somewhat different characteristics.

The Toxicology Branch review did not report the fact that two different lots of Blazer were used. The Toxicology Branch review, however, does state that the purity of the test material was 39.4 to 40.5 percent.

The "technical" used in the mouse study and other studies was a liquid, whereas the technical used for the acute studies was a 70 percent (a.i.) solid.

This discrepancy was reported in the EPA audit but not in the Toxicology Branch review.

This discrepancy needs to be further explained by the Registrant.

Deficiency (6) states that the records did not indicate what type of basal diet was used. This deficiency was not reported in the Toxicology Branch review.

The audit report further states that IRDC studies were using Purina 5001 at the time of the mouse study. This discrepancy should be incorporated into the Toxicology Branch review of the study.

The histopathology report by Dr. Curt Barthel was audited by EPA. Ante-mortem and post-mortem gross findings in group VI males and females were compared to histological findings. The audit report states that "No significant inconsistencies between the two" were found.

In the EPA audit of study number 285-014a (3-generation reproduction study in rats), the only reported deficiency was that a statistical trend analysis was not performed which would highlight dose-related findings.

Also, a two-tailed test was used, which is not as appropriate as a one-tailed test when response is in one direction only.

Toxicology Branch requires that additional and appropriate statistical analysis of the data be performed.