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

SEP 28 1989

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MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: 241-317. Event™ Herbicide. Comments on Company Response to Toxicology Branch Review of Registration Application for a Terrestrial Noncrop Use Pattern.

Tox. Chem. Nos. 3F, 3I, [redacted]
Project No. 9-1665

TO: Robert Taylor, PM #25
Fungicide, Herbicide Branch
Registration Division (H7505C)

FROM: Pamela M. Hurley Ph.D., Toxicologist Pamela M. Hurley 9/7/89
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Insecticide, Rodenticide Support
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THRU: Edwin R. Budd, Section Head
Section I, Toxicology Branch I
Insecticide, Rodenticide Support
Health Effects Division (H7509c)

Budd 9/14/89

Record No(s). 247,037

Background and Request:

American Cyanamid Company submitted an application for registration of Event™, a grass growth regulator for use on tall fescues, perennial ryegrasses, bluegrasses, and bahiagrasses. The formulation contained two active ingredients, imazethapyr and imazapyr, at the following concentrations: 17.26% and 0.64%, respectively. Imazapyr is already registered as an active ingredient and imazethapyr has passed the Toxicology Branch review process for registration for another product and either is already registered for use or will be registered shortly.

In the original review of this application, the Toxicology Branch (TB) stated that it could not support registration of this product until deficiencies in the toxicity testing requirements were fulfilled (see memorandum from P. Hurley to R. Taylor, dated 4/11/89). The deficiencies consisted of 2 mutagenicity studies on imazapyr and a 21-day dermal study on the Event™ formulation. American Cyanamid has responded to the Toxicology Branch review and TB has been asked to comment on the Registrant's response.

Toxicology Branch Response:

The Toxicology Branch (TB) accepts the arguments submitted by the Registrant concerning the deficiencies in the toxicity testing requirements and has no objection to registration of the Event™ formulation. The following paragraphs summarize the reasoning provided by the Registrant and TB's response.

The required mutagenicity studies had already been submitted to the Agency. TB verifies that the studies had been submitted, but had not been sent to TB for review. The studies are now in the Branch and are being reviewed by our geneticist. The results of the review will be forwarded under separate cover. Since the Registrant has indicated that the results of these studies are negative, since imazapyr is present in the formulation in such a low concentration, and since this is a use in which there is such a low exposure of the formulation to the general population, TB will not delay registration of this product due to a delayed review of the mutagenicity studies.

The Registrant stated that a 21-day dermal study is not necessary for the formulation for the following reasons:

1) Four 21-day dermal studies have already been conducted on products which contain either one or the other of the two active ingredients: one study on each of the two technical products, one study on a formulation containing 23% of the imazapyr salt and one study on a formulation containing 22% imazethapyr. The NOEL's for these studies were all at the highest dose level tested, the lowest NOEL was 400 mg/kg/day for imazapyr technical. The Registrant stated that since the percentages of each of the active ingredients in the present formulation are less than the percentages in any of the previously conducted 21-day dermal studies and since the NOEL's were so high, it appears unlikely that the toxicological response for Event™ would be any greater.

2) [redacted]

3) Imazapyr and imazethapyr differ in structure only by an ethyl group attached to one of the rings. Therefore, one would not expect potential synergy of toxicological effects from their combination in the Event™ formulation.

TB accepts these arguments as feasible and therefore, waives the requirement for a 21-day dermal toxicity study on the Event™ formulation.