CASWELL FILE

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

AUG 13 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Oxyfluorfen; Goal; Waiver Request for Repeat of Rabbit Teratology Study (83-3(b)); ID # 111601-000707

Tox.Chem No.: 188AAA
MRID No.: None
HED Project No.: 2-0614
Submission No.: S407729

TO: Bruce Sidwell, PM # 53
Reregistration Branch
Special Review and Reregistration Division (H7508W)

FROM: William Dykstra, Ph.D., Toxicologist
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William Dykstra 8/7/92

THRU: Roger Gardner, Section Head, Toxicologist
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ACTION REQUESTED: Rohm and Haas Company submitted a 90-day response to the FIFRA '88 Phase 4 review of oxyfluorfen. In the response, the Registrant requested a waiver for the repeat of the rabbit teratology study which had been conducted with GOAL 25WP rather than technical oxyfluorfen. Although this study was previously accepted by Toxicology Branch (TB-I), the FIFRA '88 Committee rejected the study, since it was conducted with the formulation (GOAL 25WP) rather than with the technical.

The rabbit teratology study was a gavage study in which randomized groups of 19 inseminated NZW rabbits received 0 (water), 0 (GOAL 25WP blank), 10, 30, or 90 mg/kg/day (calculated as the active ingredient) of GOAL 25WP once daily on days 6-18 of gestation. The study was graded core-minimum.

The Registrant states "The use of a formulated product of GOAL Herbicide in the rabbit teratology study was scientifically justified because the pure technical could not be used for a developmental toxicity study in this species. GOAL technical is not soluble in water nor in commonly used gavage solutions (e.g., aqueous 0.5% methylcellulose). GOAL is soluble in organic solvents such as acetone, DMSO, and ethyl alcohol, but these are inappropiate for a developmental toxicity study for obvious reasons. GOAL is soluble in corn oil to a limited extent, but rabbits dosed repeatedly with corn oil develop diarrhea. This condition adversely affects the consistency of their night stools (which they normally consume and from which they obtain B vitamins and other nutrients necessary to maintain a balanced diet and a normal pregnancy). If a rabbit develops diarrhea not only will its night stools be excreted and lost through the wire-grid cage floor, but the potential loss of weight from diarrhea is indistinguishable from weight loss induced by the test article. To overcome the technical limitations presented by this species, Rohm and Haas chose to admister GOAL technical to the rabbits in this developmental toxicity study as a formulated product of the technical material with inert ingredients that were compatible with an aqueous dosing media. This study should not be rejected because it was technically not feasible to conduct the study with technical grade material dissolved or suspended in more commonly used vechicles".

The Toxicology Branch was requested to review and comment on the waiver request.

CONCLUSIONS: Toxicology Branch agrees with the comments made by the Registrant. The waiver request can be toxicologically supported.

TB-I concludes that the rabbit teratology study does not have to be repeated with technical oxyfluorfen. The present study, using GOAL 25WP, is acceptable for the reasons stated in the 90-day response by the registrant.
In summary, oxyfluorfen is not water soluble. It is only soluble in solvents which are inappropiate for a developmental study. In addition, the use of corn oil as a vehicle is also inappropriate since rabbits repeatedly dosed with corn oil develop diarrhea, which would adversely affect the outcome of the study.

TB-I concludes that the use of the formulated product, rather than the technical, is appropiate in this circumstance. There is no need to repeat the study.