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

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

JUN 10 1991

MEMORANDUM

SUBJECT: Oxyfluorfen - Goal 1.6E - 6(a)(2) Data in Rat
Teratology Study - Preliminary Findings of
Two-Generation Rat Reproduction Study

Chemical No.: 111601-000707
Caswell No.: 188AAA
Project No.: 1-0633, 1-0702
Reregistration Case No.: 2490
Submission No.: S390582,
S391155

FROM: William Dykstra *William Dykstra 3/5/91*
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THRU: Roger Gardner, Section Head *JG Review 06/09/91*
Review Section I *(on RG) KB 6/7/91*
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Requested Action

Evaluate preliminary findings of rat teratology study
submitted as 6(a)(2) data and recommend appropriate action.
Also, evaluate preliminary findings of two-generation rat
reproduction study.

Conclusions and Recommendations

1. The final report is scheduled to be submitted after March 1, 1991. Based on the preliminary rat teratology report, fetal skeletal malformations, present as bending of the scapula and bending of one or more forelimb or hindlimb bones (humerus, radius, ulna, femur, or fibula), and fetal skeletal variations, present as delayed ossification of pubis, ischium, thoracic vertebrae, and wavy ribs, were demonstrated at the mid dose of 150 mg/kg. The no-observable-effect level (NOEL) for these developmental findings appears to be the low dose of 15 mg/kg.

Toxicology Branch (TB) recommends that the final report of the study be submitted for review as soon as available.

Based on surrogate exposure estimates by OREB and using a developmental toxicity NOEL of 10 mg/kg/day (rabbit teratology study), TB has calculated margins of exposure (MOE) for oxyfluorfen ranging from 300 to 200,000 for registered uses.

Currently, risk estimates for exposed workers are being calculated using a carcinogenic Q^*_1 of $0.128 \times (\text{mg/kg/day})^{-1}$.

Nevertheless, the developmental malformations and variations seen in the preliminary results may warrant oxyfluorfen to be submitted to the Developmental Toxicity Peer Review Committee when a completed review is available.

2. The two-generation rat reproduction preliminary findings indicate a NOEL of 100 or 400 ppm may be established. The final report should be submitted for review as soon as possible.

Review

1. Rat Teratology Study

Laboratory: Not stated (presumably a Rohm & Haas Lab.).

Test Material: Oxyfluorfen technical, 71.4% active ingredient (ai), Lot No. 2-0965, TD No. 90-001

Rohm & Haas Material Code: 879665-3

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Oxyfluorfen was administered by gavage to pregnant rats (strain not specified) on days 6 to 15 of gestation at dose levels of 0 (control), 15, 150, or 750 mg/kg.

The NOEL for maternal and developmental effects was 15 mg/kg. Maternal effects were not reported in detail, although moderate maternal toxicity was stated to have occurred at 150 mg/kg.

Developmental toxicity at 150 mg/kg was reported as bending of the scapula and bending of one or more forelimb or hindlimb bones (humerus, radius, ulna, femur, or fibula) and skeletal variations in the form of delayed ossification of the pubis, ischium, thoracic vertebrae, and wavy ribs.

2. Two-Generation Rat Reproduction Study

Laboratory: Not stated (presumably a Rohm & Haas Lab.).

Test Material: Oxyfluorfen technical, 71.4% ai, Lot No. 2-0956, TD No. 90-001

Results Reported: Decreased body weight was observed at 1600 ppm in P₁ and P₂ adult females and offspring of the P₁/F_{1a} and P₂/F_{2a} generations. Additionally, a decrease in the number of offspring per litter among P₂/F_{2a} females was observed at 1600 ppm. The NOEL is stated to be 400 ppm. The doses were 0, 100, 400, and 1600 ppm.

cc: Joanne Miller, PM 23
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