CASWELL FILE

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

004440

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MAY 9 1985

MEMORANUDM

SUBJECT: Review of Some Studies Requested by Guidance Package.

FROM: Thomas Edwards, Pharmacologist TEdwards 4-30-85
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TO: Registration Division (TS-767)

THRU: Clint Skinner, Section Chief C. Skinner 4-31-85
Review Section III

and

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Chemical: Diallate

Caswell No.: 299
Registration: Nos.:524-306; 524-119
Accession No.: 254488

Results of reviews are shown in attached one-liner page.

Reviews are attached.

The teratology studies and the inhalation study support the need for a subchronic neurotoxicity study in rats as requested in Standard and not received.

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TOXICOLOGY BRANCH
DATA REVIEW

Study Type: Teratology study, rat

Accession Number: 254488 (IA)

MRID Number:

Sponsor: Monsanto, EHL 810056

Contracting Lab:

Date: May 15, 1984

Test Material: Diallate, technical

Protocol:

See Materials and Methods excerpt attached.

Results:

All dams survived until sacrifice.

It was stated that no treatment related effects were evident from clinical observations or gross postmortem findings.

Weight changes of dams were significantly reduced ($P<0.01$) compared to controls only in the highest dosage group, 30 mg/kg (Table 4).

Reduction in food consumption by the highest dosage group appeared related to reduced weight (Table 5).

Mean live litter weight was only slightly (although significantly) reduced in the highest dosage group (Table 6). This reduction may have been dosage related. No other reproduction data appeared to be dosage related.

Retarded ossification was noted in the highest dosage group, especially of the skull (Table 7).

Conclusions:

Diallate was not determined to be a teratogen.

Fetoxicity NOEL: 10 mg/kg/day.
LEL: 30 mg/kg/day (retarded ossification).

Maternal toxicity NOEL: 10 mg/kg/day.
LEL: 30 mg/kg/day (reduced weight gain).

Core Classification:

Minimum.

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TOXICOLOGY BRANCH
DATA REVIEW

Study Type: Teratology range finding, rats

Accession Number: 254488 (IB)

MRID Number:

Sponsor: Monsanto, EHL 810054

Contracting Lab:

Date: February 3, 1983

Test Material: Diallate, technical

Protocol:

See excerpted and attached Materials and Methods section from the study report and also Table 2.

Results:

No dams died except in the two highest dosage groups, 120 and 180 ppm (Table 3).

Dams' body weight gains diminished compared to controls in the 20 and 40 ppm groups. There was weight loss in the 80 ppm group (Table 4).

Increased resorptions and dead fetuses were seen in the 80 ppm group (Table 6).

There were no clinical signs reported for control and lowest (20 ppm) dosage groups (Appendix V). Signs reported for the 40 ppm dosage group included urinary staining, piloerection, poor grooming, and alopecia. Signs reported for the 80 ppm and higher group included neurological effects in addition to those found for the 40 ppm group.

The neurological effects included head movements (raising and extension), tremors (head and/or body), circling movements, hyperesthesia, loss of muscular control and/or weakness, irregular respiration, and prostration.

Conclusions:

Dose-related, maternal toxic effects were observed at doses of 20 mg/kg/day and above. Based on these results, dosage levels of 0, 3, 10 and 30 mg/kg/day were selected for the definitive teratology study with diallate.

Indications of neurotoxicity support need for subchronic neurotoxicity study in rat.

Core Classification:

Satisfactory for range finding.

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TOXICOLOGY BRANCH
DATA REVIEW

Study Type: Acute Inhalation Toxicity (4 hr), rat

Accession Number: 254488 (IIA)

MRID Number:

Sponsor: Monsanto, MSL-3130

Contracting Lab:

Date: September 7, 1983

Test Material: Diallate (S-(2,3-dichloroally) diisopropylthiocarbamate) 98.14% lot number LBDD-07-28

Protocol:

The Materials and Methods section of the study report has been excerpted and is attached.

Exposure groups, nominal concentrations, and analytical concentrations are shown in Table 1. Particle size analysis is shown in Table 2.

Results:

Only one death occurred.

Principal immediately post-exposure observations in treated animals were reddish-brown discharge around nose and mouth, hypoactivity, hypopnea, conjunctival edema or congestion, and reddish coloration around eyes (Table 3).

Animals were observed for gross signs of toxicity for 14 days after exposure. The signs seen included reddish discharge or residue around nose and mouth, urine stained fur, head jerking or bobbing motion, and ataxia. In males none of these effects lasted 14 days. In females those signs suggesting neurological effects (head jerking or bobbing motion, ataxia, circling backward walk, and somersault) were still seen on the 14th (sacrifice) day, except in the lowest dosage group (1.1 mg/l) (Tables 4 and 5).

No significant gross organ pathology was reported from necropsy.

Weight gains, although apparently reduced in treated groups as compared to controls, did not appear to be dosage related (Table 6).

Conclusions:

Acute (4 hr) inhalation LC_{50} (rat) more than 4.4 mg/l.

Acute inhalation toxicity category: III

Neurological effects are of concern. A subchronic neurotoxicity study in rats is needed.

Core Classification:

Minimum

TOXICOLOGY BRANCH
DATA REVIEW

004440

Study Type: Dermal sensitization, guinea pig

Accession Number: 254488 (IIB)

MRID Number:

Sponsor: Monsanto

Contracting Lab: Bio/dynamics, Inc. No. 4542-83

Date: January 17, 1984

Test Material: Avadex 4EC (47.9% diallate) lot no. XLD-139

Protocol:

See excerpted and attached Materials and Methods section from the study report.

Results:

See Table III attached.

Positive control was sensitizing.

Note that rechallenge increased duration of effect to more than that of the first challenge.

Conclusions:

Results indicate that Avadex 4EC is mildly sensitizing in guinea pig.

Core Classification:

Minimum