CASWELL FILE

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

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OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Mancozeb - Company Response to Previous Agency Review of a Rabbit Developmental Toxicity Study
EPA Registration No. 707-78

TOX Chem No.: 913A
TB Project No.: 9-0933
RD Record No.: 240318

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Health Effects Division (H7509C)

Registrant: Rohm & Haas Company
Philadelphia, PA

Request

Appraise company response to maternal effect levels established in the Agency's review of the following study:

Oral (Gavage) Developmental Toxicity Study in Rabbits, performed at the Toxicology Department, Rohm & Haas, Spring House, PA, Report No. 86R-021, dated March 31, 1987 (EPA Accession No. 40433001).

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Background

In our review and evaluation of this rabbit study (DER attached to memorandum: Mauer to Rossi, April 26, 1988, TB Document No. 006679), we judged it CORE-MINIMUM DATA, and set the following effect parameters:

Maternal NOEL = 10 mg/kg (although the authors of the study proposed 30 mg/kg).

Maternal LEL = 30 mg/kg (death)

Developmental NOEL > 80 mg/kg (HDT)

A/D Ratio = 0.125

(Doses Tested: 0, 10, 30, and 80 mg/kg)

We considered 30 mg/kg to be an effect level based upon an insufficiently explained death of one mid-dose doe, characterized by the investigator as due to "mis-dosage," with only the inadequate pathology notation: "yellow material within the thoracic cavity." None of the other mid-dose does showed treatment-related maternal toxicity (including death), definitively found at the HDT, 80 mg/kg. We suggested that if the registrant can document more completely the circumstances of the death of the single doe in the mid-dose group (in addition to the "mis-dosage" cause alluded to, and the pathologist's statement about "yellow material within the thoracic cavity"), the maternal NOEL could be raised to 30 mg/kg.

Company Response

Under a cover letter of January 30, 1989, Rohm & Haas provided additional information with respect to the circumstances of death of Doe 85-27945, gavaged at 30 mg/kg, as follows: 1) Until the day of death, this animal had not shown any signs of toxicity, although it had been dosed for days; 2) Within 20 minutes of the day's dosing, the doe was found dead; 3) The animal was necropsied immediately, and the aforementioned yellow material was discovered in the thoracic cavity; and 4) Since the mancozeb dosing solution is yellow, and none of the high-dose does that died presented similar gross observations, it was concluded this death was due to an intubation error, the oesophagus having been penetrated and the test material deposited into the thorax.

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TB Conclusion

We accept this additional information as being the logical explanation for the accidental death of a single mid-dose doe, part of a test group showing no other clinically adverse signs. Therefore, the maternal NOEL can be raised to 30 mg/gk/day, and thus the LOEL becomes the HDT, 80 mg/kg/day.

A/D RATIO = 0.375