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

MAR 04 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Endosulfan - Registrant's Response to May 15, 1992 RfD/Peer Review Report.

TO: Robert Richards
PM Team Reviewer (72)
Reregistration Branch, SRRD (H7508W)

FROM: Linda L. Taylor, Ph.D Linda Lee Taylor 2/23/93
Toxicology Branch II, Section II
Health Effects Division (H7509C)

Thru: K. Clark Swentzel. K. Clark Swentzel 3/4/93
Toxicology Branch II, Head Section II
Health Effects Division (H7509C)

and

Marcia van Gemert, Ph.D. Marcia van Gemert 3/4/93
Chief, Health Effects Division (H7509C)

Registrant:	Hoechst Celanese Corporation
Chemical:	6,7,8,9,10,10-hexachloro-1,5,5a,6,9,9a-hexahydro-6,9-methano-2,4,3-benzodioxathiepin-3-oxide
Synonyms:	Endosulfan; Thiodan; Benzoepin; Endocide
Shaughnessy No.:	079401
CASWELL No.:	420
MRID No.:	none
DP Barcode:	D184981
Submission:	S429938
Action Requested:	None specified.

Comment: The Registrant has requested that the HED RfD/Peer Review Committee consider the one-year dog and the two-year rat studies as the appropriate studies on which to base the RfD for Endosulfan.

Arguments are presented to substantiate the determination that 15 ppm, rather than the 3 ppm chosen as a tentative NOEL by the RfD Committee, is the NOEL for the 2-generation reproduction study. Additionally, it is stated that the NOEL in the 2-generation reproduction study was calculated to be ≈ 1.20 mg/kg/day, which is higher than the NOEL obtained in either of the chronic studies.

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In a meeting on October 1, 1992, the HED RfD/Peer Review Committee concluded that the reproduction study was adequate but recommended that the chronic rat and dog studies be used as co-critical studies for setting the RfD. As noted in the RfD/Peer Review Report of Endosulfan, the Committee dismissed effects (increased liver weight) observed at the mid-dose (15 ppm) level in the reproduction study and determined that the NOEL for systemic toxicity was 15 ppm (0.75 mg/kg/day, using the standard conversion factor). It was recommended that an RfD be established for Endosulfan on the basis of a "no-observable effect level" of 0.6 mg/kg/day for reduced body weight gain in male and female rats, and increased incidence of marked progressive glomerulonephrosis and blood vessel aneurysms in male rats.

NOTE: The ATSDR representative to the RfD/RfC Workgroup disagreed with the above assessment and submitted an assessment of the effects observed and their appropriateness for use in setting the RfD. The ATSDR Minimal Risk Level (MRL) Workgroup recently derived a chronic oral MRL for Endosulfan based on increased alkaline phosphatase and lactate dehydrogenase levels observed in the chronic dog study. The low-dose level in that study was chosen as the NOEL (3 ppm; 0.2 mg/kg). The ATSDR representative also disagreed with the use of the chronic rat study in setting the RfD. TB II does not agree with the ATSDR representative's conclusions regarding either study and will present our assessment of the issues raised to the HED RfD Committee in the near future for their consideration.

CONCLUSION

The HED RfD/Peer Review Committee recommended that the chronic rat and dog studies be used as co-critical studies for setting the RfD for Endosulfan and that an RfD be established on the basis of a "no-observable effect level" of 0.6 mg/kg/day for reduced body weight gain in male and female rats, and increased incidence of marked progressive glomerulonephrosis and blood vessel aneurysms in male rats. This is in agreement with the Registrant's request and is the result of a re-review of the 2-generation reproduction study, which was requested by the Committee at the May 15, 1992 meeting.

cc: Karen Samek/PM 50, SRRD (H7508W)

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