

Endothall

11-25-86
RfD-1REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name: Endothall
CASRN: 145-73-3

The Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis, but may not exist for other toxic effects such as carcinogenicity. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Oral RfD Background Document for an elaboration of these concepts.

RfDs can also be derived for the noncarcinogenic health effects of compounds which are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in the Carcinogenicity Assessment Section of this file when a review of that evaluation is completed.

RfD ASSESSMENT SUMMARY TABLE

Crit. Dose: 2 mg/kg-day [Study 1 NOAEL(adj)]
UF: 100 MF: 1 RfD: 2E-2 mg/kg-day Confidence: Medium

Crit Effect: (1) Increased absolute and relative weights of stomach and small intestine

	NOAEL (Study 1)	LOAEL (Study 1)
Reported	100 ppm (diet)	300 ppm (diet)
ADJ	2 mg/kg-day	6 mg/kg-day
Study Type	Two-Year Feeding Study in Dogs	Two-Year Feeding Study in Dogs
Reference	Pennwalt Agchem., 1965	Pennwalt Agchem., 1965

- 1) Pennwalt Agchem., 1965
Two-Year Feeding Study in Dogs

Critical Effect: Increased absolute and relative weights of stomach and small intestine

Defined Dose Levels:

NOAEL= 100 ppm (diet)
NOAEL(ADJ)= 2 mg/kg-day
LOAEL= 300 ppm (diet)
LOAEL(ADJ)= 6 mg/kg-day

Conversion Factors: Dose adjusted for assumed dog food consumption (2.5% bw/day) and expressed as endothall ion.

DISCUSSION OF PRINCIPAL AND SUPPORTING STUDIES

Pennwalt Agchem. 1965. MRID No. 00101735. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

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Three male and 3 female dogs were administered diets that initially contained 0, 100, 300 or 800 ppm of disodium endothall. The concentration in the high-dose group was gradually increased over months 19-22 to a final concentration of 2000 ppm. The doses were calculated on the basis of the amount of endothall ion in the diet, and the standard equivalence factor for dogs (0.025 kg of diet/kg of bw/day). No effect on weight gain, hematology, BSP clearance, SGOT or urinalysis was noted. At necropsy, increased absolute and relative weights of stomach and small intestine were noted in intermediate and high-dose dogs. Increased "mucosal gland activity" was noted in the stomachs of high-dose dogs, along with slight edema of the pyloric region.

UNCERTAINTY AND MODIFYING FACTORS

UNCERTAINTY FACTORS:

An uncertainty factor of 100 was used to account for inter- and intraspecies differences.

ADDITIONAL COMMENTS / STUDIES

Data Considered for Establishing the RfD:

- 1) Two-Year Feeding - dog: Principal study - see previous description; no core grade
- 2) 3-Generation Reproduction - rat: NOEL=100 ppm (5 mg/kg/day); LEL=2500 ppm (125 mg/kg/day) [weight loss, kidney and adrenal discoloration, F2B pup mortality (dose discontinued)]; core grade minimum (Pennwalt Corp., 1965)
- 3) 2-Year Feeding (oncogenic) - rat: Systemic NOEL=2500 ppm (125 mg/kg/day) (HDT); no core grade (only 10 animals/sex were used) (Pennwalt Corp., 1977)
- 4) Teratology with postnatal phase - rat: Maternal NOEL=10 mg/kg/day; Maternal LEL=20 mg/kg/day (death); Fetotoxic NOEL=10 mg/kg/day; Fetotoxic LEL=40 mg/kg/day (increased number of skeletal variations); core grade minimum (Pennwalt Corp., 1982)
- 5) Teratology - mouse: Teratogenic NOEL=20 mg/kg/day; Teratogenic LEL= 40 mg/kg/day (HDT) (skeletal malformations noted at HDT with maternal toxicity); Maternal NOEL=5 mg/kg/day; Maternal LEL=20 mg/kg/day (death); Fetotoxic NOEL=20 mg/kg/day; Fetotoxic LEL=40 mg/kg/day (skeletal anomalies); core grade minimum (Pennwalt Corp., 1981)
- 6) 6-Week Feeding - dog: NOEL=10 mg/kg/day; LEL=20 mg/kg/day (100% mortality at this dose level and higher; congested and edematous stomachs with occasional erosion and hemorrhage); no core grade (Pennwalt Corp., 1953)

Data Gap(s): Chronic Rat Feeding Study (repeat study in progress)

CONFIDENCE IN THE RfD

Study: Medium

Data Base: Medium

RfD: Medium

The critical study appears to be of fair quality and is given a medium

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confidence rating. The data base is generally supportive but since there is a data gap existing for endothall, the data base is also given a medium confidence rating. Medium confidence in the RfD follows.

EPA DOCUMENTATION AND REVIEW

Source Document: This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation: Pesticide Registration Files

Agency Work Group Review: 04/22/86, 11/25/86

Verification Date: 11/25/86

EPA CONTACTS

William Burnam / OPP -- (703)305-7491

George Ghali / OPP -- (703)305-7490

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REVISION HISTORY

03/91 RfD Add Com: Citations added