8-21-86

# REFERENCE DOSES (RFDs) FOR ORAL EXPOSURE

Chemical: Malathion

CAS #: 121-75-5
Caswell #: 535

Carcinogenicity: No evidence of carcinogenicity in rats.

Systemic Toxicity: See below.

Preparation Date: 8/21/86

| Endpoint | Experimental Doses | UF | MF | RfD |
|---|---|---|---|---|
| Moeller and Rider (1962) | 0.23 mg/kg/day NOEL | 10 | 10 | 0.002 mg/kg/day |
| Subchronic Human Feeding Study | | | | |
| RBC ChE depression | 0.34 mg/kg/day LEL | | | |

16 mg/day for 70 kg (male) = 0.23 mg/kg/day

Endpoint and Experimental Doses:

Moeller, H.C. and S.A. Rider (1962)
Subchronic Human Feeding Study
Toxicol. Appl. Pharmacol. 4: 123-130

Malathion was administered by gelatin capsules to groups of five healthy male volunteers ranging in age from 23-63 years at doses of either 8 mg/day for 32 days, 16 mg/day for 47 days or 24 mg/day for 56 days. Cholinesterase activity was determined twice weekly before, during and after administration of the chemical. The intermediate doae was a NOEL. The high-dose was associated with a depression in plasma and RCB cholinesterase activity with no clinically manifested side effects.

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Uncertainty Factors (UFs):

An uncertainty factor of 10 was used to account for the intraspecies differences.

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Modifying Factors (MFs):

An additional MF of 10 was used to account for the fact that the data base on chronic toxicity is incomplete and therefore, the most sensitive toxicological endpoint can not be established.

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Additional Comments:

A 47-day human study with a ChE NOEL of 0.23 mg/kg and a ChE LEL of 0.34 mg/kg (RBC depression) is published in Tox. Appl. Pharmacol. 4:123-130; 1962

Data Considered for Establishing the RfD

1) 2-Year Feeding/Oncogenic - Rat (NOEL = 100 ppm (5 mg/kg/day); LEL = 1000 ppm (50 mg/kg/day); decreased brain cholinesterase and body weight; guideline)

2) Reproduction - Rat (Reproductive NOEL < 240 mg/kg (only dose tested); reduced number of live pups and reduced pup body weight)

3) Teratology - Rat (i.p. injection) (Reproductive NOEL and Terata NOEL > 900 mg/kg)

4) 4-Week Inhalation - Dog (NOEL < 5 ppm [one dose and one dog tested])

Data Gap(s)

1) Chronic Dog Feeding Study
2) Rat Reproduction Study
3) Rat Teratology Study
4) Rabbit Teratology

Other Data Considered

1) 80-Week Oncogenic - Rat (Oncogenic NOEL > 8150 ppm (HDT); minimum)

2) 80-Week Oncogenic - Mice (Oncogenic NOEL < 16000 ppm (HDT) (questionable liver findings); minimum)

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Confidence in the RfD:

Study: Medium-Low  Data Base: Medium  RfD: Medium-Low

The critical study is of fair quality and is given a medium-low confidence rating. Since the data base on chronic toxicity is incomplete, the RfD is given a medium-low confidence rating.

Documentation of RfD and Review:

Registration Files

Agency RfD Review:

First Review: 8/22/85
Second Review: 9/29/86
Verification Date: 9/29/86

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