



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

APR 22 1988

OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

Subject: Change of the Reference Dose (RFD) for Dimethoate

To: William Miller PM# 15 Tox Chem 358  
Insecticide/Rodenticide Branch  
Registration Division

From: Joycelyn E. Stewart, Ph.D. *JS 4/20/88*  
Section VII, Toxicology Branch  
Hazard Evaluation Division

Thru: Albin B. Kocialski, Ph.D. *ABK 4/21/88*  
Supervisory Pharmacologist  
Section VII, Toxicology Branch  
Hazard Evaluation Division (TS-769) *ab for WTS 4/22/88*

The Agency RFD Committee met on 3/31/1988 to consider the RFD for oral exposure for Dimethoate.

The Committee determined that the two year rat chronic/oncogenicity study was a more appropriate indicator of cholinesterase inhibition than the 57 day human volunteer study on which the previous PADI was based because brain cholinesterase was measured and found to be depressed in the rat study. Therefore, the previous RFD of 0.02 mg/kg/day which was based on a NOEL of 0.2 mg/kg/day for blood cholinesterase inhibition in human volunteers and an uncertainty factor of 10 was deleted.

Based on rat brain cholinesterase inhibition at 5, 25, and 100 ppm, the Committee selected a NOEL of 1 ppm, equivalent to 0.05 mg/kg/day, and an RFD of 0.0002 mg/kg/day using an uncertainty factor of 100 to account for inter and intraspecies differences. An additional uncertainty factor of 3 was used to account for the lack of a chronic study in a second species.

Based on the change in the RFD for dimethoate, a new Tolerance Reassessment will be conducted and an addendum written to the Dimethoate FRSTR.