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

AUG 1 1995

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Subject: Re-review of 28 day Rat Inhalation Study on Sumilarv. Barcode DP 216840 Submission No S489325 MRID 421783-08

To: Joseph Tavano/Rick Keigwin, PM #10
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(HED Doc #010682)

Toxicology Branch I has previously reviewed a 28 day inhalation study of Sumilarv in Sprague-Dawley rats at concentrations of 269, 482, and 1000 mg/m^3 for four hours/day and classified it Supplementary not Upgradeable based on the following deficiencies: (1) no information was provided on the stability of the test material; (2) inadequate characterization of the exposure atmospheres; (3) inadequate dynamic air flow in the exposure chamber; (4) inappropriate statistical analyses, and (5) insufficient duration of exposure.

Based on the recommendation of the RfD Peer Review Group, Toxicology Branch I has recently re- evaluated the information contained in the study report, and now concludes that the study is Upgradeable if the above deficiencies are removed. It is recognized that the duration of exposure can not be upgraded. Toxicology Branch I's conclusion is based on the relative low toxicity observed in this and other studies in the data base for Sumilarv. The NOEL in this study is 483 mg/m^3, while the LEL is 1000 mg/m^3 based on salivation in 30-40% of the high dose animals during the first few days of exposure. Cumulative body weight gain was reduced in high dose male rats, but the decrement was only significant at two reporting periods (approximately 15%). Although there was a statistically significant increase in lactic acid dehydrogenase (LDH) in high dose male rats when compared to the vehicle controls, this by itself is not necessarily indicative of toxicity, since the LDH concentration of 104 U/L was within the normal range of 121-930 IU/L in Sprague-Dawley rats. (Reference Range. Hematology and

Clinical Chemistry. Hazleton Laboratories, America, Inc., 1985). This enzyme is ubiquitous, occurring in multiple tissues. Its diagnostic value rests primarily in its isoenzymes, which are specific for each tissue. These were not measured in this study. Moreover, the increase in enzyme concentration was not accompanied by any gross or histopathological lesions in lung, liver, myocardial or skeletal muscle. Therefore Toxicology Branch I does not consider the increase in LDH concentration to be of biological significance.

The data base contains four acceptable acute inhalation studies which demonstrate LC_{50} values of >5 mg/L. The 28 day inhalation study doses were based on an acute inhalation study using a 50% a.i. which demonstrated an acute LC_{50} of >5 mg/L in male and female Sprague-Dawley rats.

40 CFR 158.340 requires that a 90 day inhalation study be performed on the technical grade of the active ingredient if the product to be used will result in repeated exposure at concentrations which are likely to be toxic. Based on the data submitted in this study and the concentrations of a.i. on representative labels, Toxicology Branch I does not believe that a 90 day inhalation study is warranted. Therefore, the registrant is encouraged to supply the Agency with information on the concentration, homogeneity, and stability of the chemical in the vehicle, with other pertinent information which were cited in the DER.