4/13/1999

Supplement to DER, MRID 41920705 - Carcinogenicity study in mice
This supplement provides an executive summary to upgrade the original DER

EPA Reviewer: Yung G. Yang, Ph.D.
Toxicology Branch 1, HED (7509C)
EPA Secondary Reviewer: Brian Dementi, Ph.D.
Toxicology Branch 1, HED (7509C)

AMENDED DATA EVALUATION RECORD

STUDY TYPE: Carcinogenicity
DP BARCODE: D166879
PC CODE: 041403
CASWELL No.: 710
SUBMISSION No: S400055
CASE No: 2500
TEST MATERIAL (PURITY): Pebulate (97.1%)
SPONSOR: ICI Agrochemicals
CITATION: Tinston, DJ (1991) Pebulate: 18 month carcinogenicity study in mice. ICI Central Toxicology Laboratory, England. Report No. CTL/P/3119. March 14, 1991. MRID 41920705.

EXECUTIVE SUMMARY: In a carcinogenicity study (MRID 41920705), pebulate technical (97.1% a.i.) was administered via diet to C57BL/10JfCD-1/Alpk mice (50/sex/group) at dose levels of 0, 300, 1000, or 3000 ppm (achieved doses of 0, 34, 116, or 371 mg/kg/day for males and 0, 47, 161, or 445 mg/kg/day for females, respectively) for 18 months.

The mortality and clinical observations were not affected by the pebulate administration. Significant decreases in body weight gains were observed at doses of 1000 ppm (↓1-9% for both sexes) and 3000 ppm (↓8-24% for males and ↓8-33% for females) throughout the study. Food consumption was significantly lower in males at 1000 ppm (↓5-10%) and 3000 ppm (↓8-18%) and females at 1000 ppm (↓3-10%) and 3000 ppm (↓10-27%). Hematological findings showed increased platelet counts at 1000 and 3000 ppm (both sexes). Increased absolute and relative liver weight of treated mice (both sexes) were observed at doses of 1000 and 3000 ppm. Necropsy findings revealed an accentuated lobular pattern of the liver and hepatic pallor in the high-dose males only. Microscopic findings showed an increased incidence of hepatocyte fat vacuolation in the high-dose (both sexes) and mid-dose (males only) when compared to the controls. There were no increased incidence of tumors which could be attributed to treatment with pebulate. Dosing was considered adequate based on decreased body weight gain at the high dose.

The systemic NOAEL was 300 ppm (achieved dose of 34 mg/kg/day for males and 47 mg/kg/day for females) and the LOAEL was 1000 ppm (achieved dose of 116 mg/kg/day for males and 161 mg/kg/day for females) based on decreased body weight gain and food consumption; increased platelet counts; and increased absolute and relative liver weights for both sexes and decreased food utilization and increased hepatocyte fat vacuolation in males only. **There was no evidence of carcinogenic potential for pebulate.**

This study is classified as **Acceptable (Guideline)** and satisfies guideline requirement for a carcinogenicity study in mice (83-2b).

1

SignOff Date:	4/13/99
DP Barcode:	D254687
HED DOC Number:	013311
Toxicology Branch:	TOX1