

4/13/1989

Pebulate

Supplement to DER, MRID 00143576 - Subchronic Inhalation Study in Rats
This supplement provides an executive summary to upgrade the original DER

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AMENDED DATA EVALUATION RECORD

STUDY TYPE: Subchronic Inhalation Study in Rats

DP BARCODE: N/A

PC CODE: 041403

CASWELL No.: 710

TEST MATERIAL (PURITY): Pebulate (97.7%)

SYNONYMS: Tillam

SPONSOR: Stauffer Chemical Company

CITATION: Knapp, H.F. and Frank, D.W. (1982?) Subchronic Inhalation Study with Tillam Technical in Rats. Stauffer Chemical Company, Study No. T-10840. Report date not cited. Study was conducted in the 1981. MRID 00143576. Unpublished.

EXECUTIVE SUMMARY: In a subchronic inhalation study (MRID 00143576), Sprague-Dawley rats (24/sex/group) were exposed (whole body exposure) to Pebulate technical (97.7%) aerosol at an analytical concentration of 0, 0.0034, 0.016, or 0.079 mg/L (MMAD 3-7.7 µm) for 6 hours per day, 5 days per week for 14 weeks.

No treatment-related mortality was observed. An earlier onset and an increased incidence of salivation were observed in a dose-related fashion. Body weight gain was depressed (↓12% and ↓9% in males and females, respectively) at 0.079 mg/L at the end of the study whereas food consumption remained unaffected by treatment. No treatment-related changes were noted in hematology and clinical chemistry at 3, 9, or 14 weeks. Brain, plasma, and RBC cholinesterase (ChE) activities were measured at weeks 3, 9, and 14 of the study. Significant inhibitions of RBC ChE (↓42% in males and ↓39% in females) and brain ChE (↓26% in males only) were observed only in weeks 14 of the study. In vitro blood coagulation time (evaluating clotting factors) was prolonged in males and females at 0.016 and 0.079 mg/L; in vivo bleeding times (test for platelet function) were not significantly increased by treatments. Relative liver weights in both sexes, relative adrenal weights in females and relative testes weight in males were significantly increased at the highest dose tested. However, none of these changes were correlated with histopathologic lesions in these organs. In contrast, the relative kidney weights, which were significantly increased in both sexes of the high-dose at 14 weeks, are associated with histopathological changes in the kidney. In males, regenerative tubular hyperplasia was observed to increase with doses at incidences of: 4/12, 6/12, 8/11, and 9/11 in control, 0.0034, 0.016, and 0.079 mg/L, respectively. Degeneration and vacuole formation in kidney epithelium of female rats increased from 0/12 in

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control to 4/12 and 6/12 at the two highest dose levels. Furthermore, an increase in the incidence of mucigenic epithelial hyperplasia of the nasal turbinate was observed in both sexes (becoming dose-related in females), suggesting possible irritative effects of Pebulate to the nasal passage at all doses over the 14-week course of exposure.

Under conditions of this study, **the NOAEL was 0.0034 mg/L and the LOAEL was 0.016 mg/L** based on prolonged coagulation time, degenerative effects in kidney of both sexes which in males were associated with degenerative tubular hyperplasia, and increased incidences of mucigenic epithelial hyperplasia of the nasal turbinate increase at all dose levels. The study was classified **Acceptable (Guideline)**.

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