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DATA EVALUATION REPORT

STUDY TYPE: Teratogenicity Study In The Rat

TOX. CHEM. No.:753

MRID No.:

ACCESSION No.: 40464-01 in 2 volumes.

TEST MATERIAL: Sodium Chlorate

SYNONYMS: $NaClO_3$

SPONSOR: The Sodium Chlorate Task Force

TESTING FACILITY: Biodynamics Inc., East Millstone, NJ 08875-2360

STUDY NO.: 86-3117

REPORT TITLE: A Teratogenicity Study In Rats With Sodium Chlorate

AUTHOR(S): Raymond E Schroeder and Ira W Daly

REPORT ISSUED: 9/24/87

CORE GRADE: ~~Guideline.~~ minimum

CONCLUSIONS: No dose or treatment related effects in dams or embryos/fetuses occurred at any dose level.

Doses Administered by gavage: 0, 10, 100, and 1000 mg/kg/day.

A. MATERIALS:

1. Test compound: Sodium chlorate, Description granular white solid. Source:Kerr-McGee Chemical Corp., Hamilton, MS 39746, Purity, considered 100%, contaminants: list in CBI appendix.

2. Test animals: Species: Rat, Strain: CD Sprague Dawley derived, Age: 9 weeks, Weight: 174-247 g, Source:Charles River Breeding laboratories, Inc., Portage, MI 49081. Photoperiod: 12:12 = dark:light. Temperature: 64-76° F. Relative humidity: 33-67%. Acclimatization period was 2 weeks.

B. STUDY DESIGN:

1. Animal Assignment - Animals were assigned randomly such that body weights were approximately equal in all groups. Mating was conducted by natural insemination. Day 0 of gestation was considered the day sperm was detected.

2. Test Substance Administration: Test substance was administered by gavage with distilled water as the vehicle. Total volume of the dose was 5.0 ml/kg/day. Dates of administration were on gestational day(gd) 6, 2/17-20/87, 2/23-27/87, and 3/2-5/87, through gestational day(gd) 15, 2/26-28/87, 3/1, 4-6, 11-14/87.

Test group	Dose mg/kg/day	Volume of Doses ml/kg/day	Number of Females
1. Cont.	Distilled water vehicle	5.0	24
2. Low (LDT)	10	5.0	24
3. Mid (MDT)	100	5.0	24
4. High(HDT)	1000	5.0	24

3. Analysis of Dosing Solutions: Stock dosing solutions were prepared weekly and stored at room temperature in dark bottles. Stability studies were conducted 1, 4, and 8 after preparation. The studies indicated that the solutions were stable to within 0.5 - 3.0% of nominal after 8 days at room temperature. Homogeneity was within experimental error and satisfactory. The concentration of the dosing solutions from group 2 were found to be within ±15% of nominal,but generally within ±3% of nominal. Group 3 was ±1% of nominal, and group 4 was ±1% of nominal. All dosing solutions were within a satisfactory range of the nominal concentration range.

4. Food and Water: - The food was Purina Certified Rodent Chow # 5002, the water was from the Elizabethtown Water Company, both were supplied ab libitum.

5. Statistics - The following procedures were utilized in analyzing the numerical data: Bartlett's test, ANOVA, Dunnett's test, Kruskal-Wallis test, and Jonckheere's test.

Statistical analysis of incidence data was performed using contingency tables. First, a standard Chi-square analysis was performed to determine if the proportion of incidence differed between the groups tested. Next, each treatment group was

compared to the control group using a 2*2 Fisher Exact test; the significance level was corrected via the Bonferroni inequality to assure an overall test of the stated significance level. Thirdly, Armitage's test for linear trend in the dosage groups was performed. In keeping with standard statistical practice, if any one cell had an expected value less the 5, the Fisher exact test (corrected via Bonferroni inequality) was performed and reported.

All tests were reported at the 5% and 1% level of significance.

5. Quality assurance was signed by Florence S Gilson, Supervisor of Quality Assurance at Biodynamics, Inc., on August 11, 1987, Elizabeth Hay of the Sodium Chlorate Task Force, and Raymond P Schroeder, the Study Director.

C. METHODS AND RESULTS:

1. Observations - Animals were inspected twice daily for signs of toxicity and mortality.

Results - Toxicity - No adverse effects were reported.

Mortality (Survival) - Only one control died prior to terminal sacrifice.

2. Body Weight - They were weighed on gd 0, 6, 10, 12, 15, and 20.
Results - No biologically significant or statistically significant weight changes occurred during the study. The two highest dose groups demonstrated a nominally increased body weight gain of 3 g at the MDT, and 4 g at the HDT between gd 6-15, and a decreased body weight gain of 1 g at the HDT between gd 15-20.

3. Food consumption and compound intake - Consumption was determined and mean daily diet consumption was calculated. Efficiency was not calculated and could not be easily calculated from formate of the data reported. It was reported as g food consumed per kg body weight per day. However, if any large changes in the efficiency of food utilization occurred it could have been seen from the reported g/kg/day data, and body weight changes.

Food consumption was determined gd 6, 6-10, 10-15, and 15-20.

Results - No dose related effects were seen. A nominal decrease was seen in food consumption between gd 10-15, and gd 15-20 at the HDT, of 2 g/kg/day and 3 g/kg/day, respectively. The standard deviations for these periods were 9 and 7, respectively.

4. Necropsy of Mothers and Fetal Examinations: Dams were

sacrificed on gd 20. Pregnant uteruses were weighed and subtracted form the weight of the dam. Corpora lutea and the number of viable fetuses, dead fetuses, resorptions, and implantation sites were counted. Reproduction data and fetal weights were reported in Table G.

All the fetuses were examined externally(Table K), and about 1/2 of each litter were examined viscerally(Table L) by the method of Staples, and about 1/2 of each litter were examined skeletally (Table M) after being stained with Alizarin.

Tables were copied from study report submitted.

a. Gross pathology - Dams in dosed groups appeared to demonstrate dose related discoloration in the lungs. One in control and the LDT, and 2 and 4 at the MDT and the HDT, respectively. One rat demonstrated a nodule/mass in the lung each at the LDT and the MDT.

b. Fetal Examination - The results of the examination are reported in Tables K, L, and M. No dose or treatment related effects were demonstrated when considered individually or when summed. The only effects demonstrated were low level random background effects in all groups.

D. DISCUSSION:

No dose or treatment related effects were detected by this study in dams or embryos/fetuses.

Body weights and food consumption by the dams were comparable with control values. At necropsy, 4 of 24 dams demonstrated discolored lungs, but the pathologist indicated that the number were insufficient to establish a treatment related response. There were no dose relationships in pregnancy rate, corpora lutea, implantation sites, viable fetuses, dead fetuses, resorptions, or fetal weights.

In fetuses, external, and visceral malformations and variations, skeletal malformations and variations were all comparable with control values when considered individually or when summed by category. Only low level random background anomalies occurred in all groups.

NOEL: > 1000 MG/KG/DAY.
LEL: > 1000 MG/KG/DAY.

RIN 2906-01

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