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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D C 20460

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: June 4, 1981

SUBJECT: 279-1721: Review of Published Rat Teratology Study on Naled (Dibrom)
CASWELL #586

FROM: Gary J. Burin, Toxicologist
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THRU: Chris Chaisson, Acting Chief
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Submitted By: Chevron Chemical Co.
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Recommendations/Summary:

Due to lack of identification of the precise composition of the test material, the submitted study is classified as invalid. In addition, maternal toxicity was not demonstrated.

Review:

"Teratologic Assessment of Maleic Hydrazide and Daminozide, and Formulations of Ethoxyquin, Thiabendazole, Naled" by K.S. Khera, C. Whalen, G. Trivett, and G. Angers, J. Environ. Sci. Health B14(6), 563-577, 1979.

Female Wistar rats of 175-225 grams body weight were paired overnight with proven males. Twenty mated females with positive vaginal smears were randomly assigned to groups treated with either 0, 25, 50 or 100 mg/kg of a naled (dibrom) formulation containing 36% naled and 64% unknown ingredients. Test substance was administered by gavage in a corn oil vehicle for a total volume of 10 ml/kg of body weight.

The day that a positive vaginal smear was first observed was counted as day one of gestation. Compound was administered on days 6-15 of gestation and animals were sacrificed on day 22 (method of sacrifice not reported). Dams were necropsied, uteri were removed, corpora lutea counted, fetuses weighed and examined for external malformations, and early resorptions and implantation sites were counted. Two thirds of the live fetuses from each litter were stained with alizarin red for skeletal examination and the remaining third were fixed in Bouin's fluid and examined viscerally.

Results:

The report stated that "No sign of toxicity or any adverse effect on maternal body weight was noticed during pregnancy, in any treatment or control group". However, no data was included to support this statement.

The proportion of those females that were inseminated and became pregnant was not effected by treatment with Naled. The mean number of corpora lutea, implants per pregnancy, total resorptions, percent resorptions, total number of dead fetuses, total number of "runted" fetuses and mean fetal weight also did not appear to be effected by treatment.

Anomalies found in treated animals included wavy ribs, extra ribs, missing or rudimentary 13th rib, fused sternebrae, delayed ossification of the sternebrae or calvarium, runted fetuses, hydroureter and hydronephrosis. Most of these anomalies were also found in control litters. The only anomalies that appeared to be increased in treated animals were delayed ossification of the sternebrae (1, 5, 5 and 6 effected animals out of 190, 203, 172 and 186 animals examined in the 0, 25, 50 and 100 mg/kg groups, respectively) and delayed ossification of the calvarium (0, 3, 1 and 3 effected). However, an examination of values for these parameters in controls paired with ethoxyquin, thiabendazole, maleic hydrazide and daminozide treated animals (whose data was also presented in this article) found a great deal of variability. Numbers of control fetuses with delayed ossification of sternebrae were 0, 2, 7 and 3 out of 215, 198, 183 and 181 examined. Numbers of control fetuses with delayed ossification of the calvarium were 0, 0, 2, and 0. Thus the effect of Naled on ossification of the calvarium and sternebrae is equivocal; although an effect is suggested in this portion of the study it is not demonstrated. Single instances of hydroureter and hydronephrosis were found in treated groups but not in controls.

Conclusions

The precise composition of the test material was ~~not identified~~, apparently it was a formulation rather than the technical ingredient. No maternal toxicity was reported at the highest level tested (100 mg/kg) but values for maternal body weight and maternal food consumption were not reported.

An effect on the rate of ossification of the sternebrae and calvarium was suggested in Naled treated animals. The effect was not dose related and the effect is obscured by a rather large degree of background variability in other concurrent control groups.

In summary, this study can not be considered adequate to define the teratogenic potential of Naled.

Core-Classification

Invalid due to lack of identification of test material. If that data is submitted, the study can be upgraded to Supplementary status. However, due to the lack of evidence of maternal toxicity at any dose level, this study can not be graded higher than Supplementary status.

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