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

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SEP 26 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: I.D. Number 239-1246; Captan: Misc. data, hamster teratology study.
Tox. Chem. No.: 159

TO: H. Jacoby (PM 21)
Registration Division (TS-767C)

FROM: Marion P. Copley, D.V.M. 9/11/85 M. Copley
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THRU: Jane Harris, Ph.D., Section Head JH 9/11/85
Section VI, Toxicology Branch
Hazard Evaluation Division (TS-769C) for CWTB 9/26/85

BACKGROUND:

Toxicology Branch stated in a meeting with Chevron (June 20, 1985, 1:00 P.M.) and in a memorandum by Bill Schneider (7/12/85) that the requirement for further data regarding the teratogenesis of captan in the Golden Syrian Hamster could be met by submitting additional historical data on teratogenesis in the Golden Syrian Hamster. This data would be in addition to that received by the U.S.E.P.A. acc. #249681 (Chevron Letter of 6/18/85) "Amended final report, IRDC, Jan. 17, 1983" and the attached historical control data from IRDC. The additional historical control data need not be from IRDC, but should be on Golden Syrian Hamsters, presented by fetus and litter for each study if possible, along with the date and testing facility. This information is needed in order to determine whether the increase in rib anomalies in captan-treated groups are treatment related.

The hamster study (IRDC #415-005) was previously reviewed (see memorandum by W. Schneider, 7/12/85) and the maternal toxicity no observable effect level (NOEL) and lowest effect level (LEL) were set at 50 and 200 mg/kg/day, respectively. In order to determine if the rib anomalies, observed in all treatment groups, were captan related, Chevron submitted the following additional data:

1

004692

1. Historical data from IRDC.

The historical data from IRDC has been evaluated previously. It consisted of a summary table of 71 litters with a total of 853 fetuses, 561 of these examined skeletally. Rib anomalies were not defined but occurred in 4 fetuses, one in each of 4 litters (0 - .8 % of the fetuses, 0 - 10 % of the litters).

2. Control hamster data submitted by C. C. Willhite obtained from 14 control groups in published articles and 2 tables from an article to be published.

Dr. Willhite summarized some data obtained from his teratology studies with golden Syrian hamsters purchased form the Charles River Breeding Labs, Inc., Wil., Mass, Lak:LVG (SYR) strain. There were 15 separate studies control groups listed with treatments of none, Tween 20, saline, dehumidified air or distilled water. The first 14 groups give numbers of examined and affected litters, malformation types and number of affected fetuses. The spontaneous occurrence of fused ribs occurs (with low frequency) only in 6 of the 14 studies (in up to 14 % of the litters). The percent of fetuses affected could not be determined. The most recent study, presented separately, had 18 litters with 214 fetuses examined. Two fetuses were effected with fused ribs (< 1% of the fetuses).

3. An article by Khera, K.S. "Maternal toxicity: A possible etiological factor in embryo-fetal deaths and fetal malformations of rodent-rabbit species." Teratology, 31:129-153 (1985).

The article by Khera is a survey of numerous rodent and nonrodent (rabbit) teratology studies, "to determine whether embryo-fetal mortality and fetal malformations result from a primary action of the agent on the conceptus or if they are secondary to maternal toxicity - a consequence of administration with high dose levels of test chemicals. The authors concluded that, in hamsters, embryo-fetal mortality, exencephaly, encephalocele, microphthalmia or anophthalmia and fused ribs were often maternal toxicityassociated fetal malformations.

4. Letter from J. Schardein, the teratologist who reevaluated the IRDC hamster teratology study.

This letter reiterated tha view presented in the IRDC hamster study that there is no apparent dose relationship for fused ribs.

004692

Toxicology Branch Conclusions

Fused ribs occurred in the IRDC hamster teratology study in up to 15 % of the litters (low and mid dose groups). Although this lesion may be due to maternal-toxic effects, it is probably within normal background incidence for this species based on the historical data from IRDC and other laboratories.

Toxicology Branch therefore considers this study Core-minimum and sufficient to satisfy the requirement for a teratogenic study with captan in one species.

There is no indication of teratagenic potential.
Teratogenic NOEL > 400 mg/kg/day
Maternal toxic NOEL = 50 mg/kg/day
Maternal toxic LEL = 200 mg/kg/day due to body weight loss and mortality
Fetal toxic NOEL = 200 mg/kg/day
Fetal toxic LEL = 400 mg/kg/day due to reduced ossification decreased weights, increased resorption