CASWELL FILE

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

November 19,1984

SUBJECT: Addendum to Toxicology Chapter, PD 2/3, Concerning Deletion of Reproduction Study Requirements

TO: Carol Langley, Review Manager
Special Review Branch

FROM: William R. Schneider, Ph.D.
Toxicology Branch
HED (TS-769)

THROUGH: William Burnam, Chief
Toxicology Branch
HED (TS-769)

WRS 11.19.84

Compound Captan Tox. Chem. No. 159

On reexamination of our original review of the three generation reproduction study submitted by the registrants, we find that an additional one generation reproduction study was performed in order to resolve the problem found in the three generation study. We had reviewed these studies in 1983 and, although neither would satisfy the data requirement alone, the data as a whole has been classified as core minimum.

Please add the following paragraph to the reproduction section following the description of the IRDC Three Generation Rat Study, IRDC # 153-096, EPA Accession # 249334:

A one generation rat study, submitted by Chevron Chemical Company, was performed by IRDC, October 11, 1982, IRDC # 153-190, EPA Accession # 249332. Captan was administered in the diet at 0, 6, 12.5, and 25 mg/kg/day to 15 male and 30 female COBS rats per dose level. No treatment related effects due to captan were seen. This study is not adequate by itself but is sufficient

when used to supplement the 3 generation rat study (IRDC #153-096, Jan. 7, 1982) to satisfy the reproduction testing requirements. When used in conjunction with the 3 generation rat study, the NOEL is 12.5 mg/kg/day and the LEL is 25 mg/kg/day.

In addition, please delete the requirement for futher reproductive testing as stated in the summary and the draft of the 3c2b letter.

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PESTICIDES AND TOXIC SUBSTANCES

AUG 12 1983

MEMORANDUM

TO: Henry Jacoby
Product Manager (21)
Registration Division (TS-767)

THRU: Edwin R. Budd, Section Head
Section II, Toxicology Branch
Hazard Evaluation Division (TS-769)

SUBJECT: EPA Registration No. 239-1246. Captan. Review of One Generation Reproduction Study in Rats. IRDC #153-190, October 11, 1982. Submitted by Chevron Chemical Company. EPA Accession No. 249332.

TOX. Chem. No. 159

SUMMARY

This is a well conducted one generation rat reproduction study. Captan was administered in the diet at 0, 6, 12.5, and 25 mg/kg/day to 15 male and 30 female COBS CD rats per dosage level.

No treatment related effects due to captan were seen.

This study is not adequate by itself but is sufficient when used to supplement the 3 generation rat study (IRDC #153-096, ~~June 13, 1980~~ Oct. 7, 1982) to satisfy the reproduction testing requirement.

Core classification: Core supplementary (by itself)
Core minimum (when used in conjunction with the 3 generation rat study.)

NOEL (in conjunction with the 3 generation rat study) = 12.5 mg/kg/day.

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LEL=25 mg/kg/day.

DETAILED REVIEW OF STUDY

Study Title and Description: One Generation Reproduction Study in Rats with Captan, IRDC, October 11, 1982, submitted by Chevron Chemical Company.

Identification: EPA accession number: 249332. IRDC Laboratory study number: 153-190.

Laboratory: Internation Research and Development Corp. (IRDC) Mattawan, Michigan 49071.

Test Material: Captan Technical SX-1086. 10 containers, 2/6/81.

Study Methods

Animals: Male and Female COBS CD weanling rats from the Charles River Breeding Laboratories, Inc., Portage, Michigan.

Dosing: Captan was given in the diet at dosage levels of 0, 6, 12.5 and 25 mg/kg/day, adjusted weekly for body weight and food consumption and was prepared weekly. All rats received the diet (after weaning).

Study Conduct:

After 102 days of treatment, 15 males were mated with 2 females each for each of the treatment groups. Parents were necropsied after weaning of F_1 pups; observations were made for signs of toxicity, changes in general behavior, appearance and survival (in parents and pups); body weights and food consumption (in parents); male and female fertility, length of gestation, litter sizes. Pup survival was recorded at birth (lactation day 0) and at lactation days 1, 4, 7, 14, and 21. Litters were randomly reduced to 10 pups on lactation day 4. Group litter weights were recorded on lactation days 1, 4, 7, and 14. Individual pup weights by sex were recorded on day 21. Female parents which did not deliver were examined for implantation sites.

Results

Survival:

Parental survival: All parents survived.

Pup survival: The only statistically significant difference in survival from the controls seen was a 98.4% survival at day one for pups in the 6 mg/kg/day treatment group.

Body weights:

Parental body weights: No differences in body weights could be attributed to treatment.

Litter body weights: No statistically significant difference or dose related effect was seen for litter body weights. A slight but not statistically significant reduction was reported at 25 mg/kg/day for lactation days 4, 7, and 14.

Mean Litter Body weights (gms) at lactation days 1 to 21

Captan mg/kg/day	1	4		7	14	21	
		B.R.	A.R.			Male	Female
	Mean	Mean	Mean	Mean	Mean	Mean	Mean
0	7.4	11.3	11.3	17.3	30.6	43.0	41.8
6	7.5	11.4	11.4	17.6	30.9	43.8	42.9
12.5	7.3	10.9	10.9	16.9	30.3	43.2	42.6
25	7.3	10.7	10.7	16.2	28.9	42.5	44.6

B.R. = Before reduction
A.R. = After reduction

Food and compound consumption:

No compound related differences were reported:

Average Daily Food and Compound Consumption

	0 (Control)		Captan (mg/kg/day) 6			12.5			25		
	g/ rat/ day	g/ kg/ day	g/ rat/ day	g/ kg/ day	mg/* kg/ day	g/ rat/ day	g/ kg/ day	mg/* kg/ day	g/ rat/ day	g/ kg/ day	mg/* kg/ day
MALE:	25.8	64.3	26.3	65.0	5.89	26.9	66.2	12.1	26.7	65.9	24.5
FEMALE:	22.2	88.0	22.1	87.5	6.30	22.8	91.3	13.3	22.5	89.3	26.4

* Calculated intake of Captan.

Visual Observations:

No compound related effects were seen. Visual appearances were unremarkable and no treatment related lesions were found at necropsy of the parents. On lactation day 21 an ocular syndrome (eyes closed or covered with a clear film) was seen in both treated and control pups with similar frequency. Hydronephrosis was found in two pups in the 12.5 mg/kg/day group.

Reproductive Parameters:

These were no differences between controls and treated groups in the mean number of implantation sites, percent gravid females, or percent of fertile males.

Discussion

This study suffers from being only a one generation reproduction study. No compound related effects were seen. This study would have to be classified as core supplementary by itself. However, when used to supplement the 3 generation rat study (IRDC #153-096, ~~June 12, 1980~~), it supplies enough information to be able to satisfy the requirement for a reproduction study and a NOEL of 12.5 mg/kg/day for reduced litter weights can be established. These effects were similar in each generation so this one generation test is adequate to examine this parameter.

William R. Schneider, Ph.D.
Toxicology Branch
Hazard Evaluation Division (TS-769)

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