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

MEMORANDUM

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

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

Budd
2/27/83

SUBJECT: Captan Rabbit Teratology Study, Acc. No. 246624,
Reg. No. 239-1246.

TOX Chem. No. 159

Registrant: Chevron Chemical Company
Richmond, California 94004

Contract Laboratory: Huntingdon Research Centre
Huntingdon, Cambridgeshire,
England

Project Number: CHR/15/8114, May 12, 1981

Chemical: Technical Captan - 89% purity

Recommendations:

No teratogenic effects were seen at Captan levels up to 60 mg/kg/day when administered by oral intubation in the New Zealand White rabbit.

Study Classification: Core Minimum.

Materials and Methods:

Animals used: 12 to 20 week old New Zealand White rabbits from Cheshire Rabbit Farms, Ranch Rabbits, and Buxted Rabbit Company, Ltd. Five groups of 15 female rabbits were mated with proven fertile males, caged individually, and treated by intragastric intubation on day 6 through day 28 of pregnancy. The dose levels were 0 (control), 6, 12, 25, and 60 mg/kg/day of Captan in 0.5% sodium carboxymethylcellulose. The dosage was calculated for individual animals initially, and on days 10, 14 and 18 of pregnancy.

The rabbits were killed on day 29 and examined for macroscopic changes in maternal organs. Live fetuses were examined and killed by pentobarbitone injection. They were then dissected, skinned, and fixed in 740P industrial methylate spirit. The brain was then examined before clearing and staining.

Results:Maternal Effects:

There were one or two deaths in each group but no dose relationship were seen. There was a reduction in the number of pregnancies at the highest dose but, since there was no increase in abortions or "resorptions", this was not related to the Captan treatment.

Animals	Dose (mg/kg/day Captan)				
	0	6	12	25	60
Mated	15	15	15	15	15
Dead	2	1	2	2*	1*
Non-pregnant	1	0	0	1	6
Abortion or Resorption	0	1	2	3	0

* One animal each group killed by intubation error.

There was a small dose related reduction in weight gain at 12, 25 and 60 mg/kg although the rate of weight gain was similar. The highest dose group lost weight during the first 4 days of dosing but there after responded similarly to the control group. The high dose group during the first part of the dosing period also showed increased anorexia, reduced water intake and decreased feces output.

There were no dose related changes seen at autopsy.

Litter Counts: The 6 mg/kg dose group showed a lower litter size, corpora lutea count, and total implantations in conjunction with higher embryonic deaths and post implantation losses. No effects were seen at the other dose levels for numbers of live young, embryonic deaths, implants, corpora lutea, preimplantation losses or post implantation losses.

Weights and Measurements: The 6 mg/kg group had lower litter weights and higher mean fetal weights while the 60 mg/kg group showed lower litter and mean fetal weights. No other effects were seen for uterine weights, litter weights, mean fetal weights and mean crown/rump lengths.

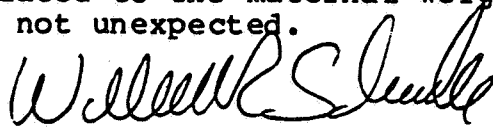
Malformations and Anomalies: Full descriptions of each fetus with abnormalities and variations were presented. No dose related or statistically significant effects were seen.

	Dose (Captan mg/kg/day)				
	0	6	12	25	60
Total Fetuses:	101	91	96	79	68
Major malformation:					
Total:	1	4	2	1	3
Percent	0.99	4.40	2.08	1.27	4.41
Mean % by Litter	1.4	6.1	2.4	2.2	3.8
Major anomalies by gross autopsy:					
Total	1	0	1	1	1
Percent	0.99	0	1.04	1.27	1.47
Mean % by Litter	0.8	0	1.0	1.1	1.0
Minor anomalies by skeletal examination:					
Total	13	13	11	6	11
Percent	12.87	14.29	11.46	7.60	16.18
Mean % by Litter	13.6	15.6	12.0	8.4	16.5

Conclusions:

This study was performed in an acceptable manner and can be classified as Core Minimum data. The maximum dose level was sufficiently high to induce maternal weight loss. No positive control was performed, however, it is not absolutely necessary in this case.

The study shows that Captan is not a teratogen in New Zealand White rabbits under these conditions. The higher levels of embryonic deaths and post implantation losses at 6 mg/kg are not seen in the higher dose groups and are therefore not of concern. The lower litter and mean fetal weights in the high dose group are probably related to the maternal weight loss in early pregnancy and are not unexpected.


 William R. Schneider, Ph.D. *WRS*
 Toxicology Branch
 Hazard Evaluation Division (TS-769) *11/18/83*