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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

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

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

Budd 5/12/83

SUBJECT: Interim Final Reports for Oral Carcinogenicity Study with Merpan (Captan) in Rats. #11678-12.

Tox. Chem. No. 159

Registrant: Makhteshim-Agan
Beer-Sheva, Israel

Contract Laboratory: TNO for applied scientific research
3700 AJ Zeist
Netherlands

Project No. B80-0153

Report No. V 83.019/200153 January 1983

EPA Acc. No. 249781

Chemical: Merpan (technical captan)
(further information not given in this interim report).

Recommendations: Hold this report for reference when the final report is submitted. A statement in the final report should relate the exact composition of "Merpan" to captan as available in the U.S.A. The final report is expected near the end of 1983.

Materials and Methods:

Fifty "albino rats" per sex per group were administered 0, 125, 500, and 2000 ppm of Merpan in the diet for 130 weeks. No other details of the protocol were presented here.

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Interim Results:

Dietary analysis: Analysis of diet samples in August 1981, November 1981, February 1982, and June 1982 showed that the dietary merpan concentration was close to the intended concentrations of 0, 125, 500, and 2000 ppm. Evidently, no attempt was made to administer merpan in mg/kg using actual body weights.

Mortality: There was slightly higher mortality in the high dose group but it was not statistically significant.

Mortality at Day 910

Dose (ppm)	0	125	500	2000
Mortality, males (%)	54	48	60	62
Mortality, females (%)	52	52	42	60

Body weights:

The body weights were depressed in the high dose groups but were not statistically significant after week 118 for males and week 124 for females due to a more rapid weight reduction in the controls as they became older.

Mean food intake

The mean food intake reported for week 107, 108, 119, 120, 129, and 130, did not deviate statistically significantly from the controls for the males or females.

Organ weights:

The pituitaries, thyroids, adrenals, gonads, kidneys, brains, spleens, hearts and livers in both the males and females were weighed. Of these only the increase in the male liver weights relative to their body weights was statistically significant ($p. < 0.05$).

Macroscopic observations:

The following were examined for tumors or other gross pathology: Skin, Axillary lymph nodes, Preputial/clitoral glands, Mammary glands, Abdominal cavity, Spleen, Adrenals, Kidneys, Stomach, Small intestines, Coecum, Colon, Mesentry, Pancreas, Mesenteric lymph nodes, Urinary bladder, Seminal vesicles, Coagulation glands, Prostate, Testes, Epididymides, Ovaries, Uterus, Liver, Thoracic cavity, Thymus, Heart,

Mediastinal lymph nodes, Lungs, Esophagus, Trachea, Aorta, Spinal cord, Cervical lymph nodes, Submaxillary salivary glands, Sublingual salivary glands, Parotid salivary glands, Exorbital lachrymal glands, Thyroid, Eyes, Brain, Pituitary, Nose, and Oral cavity. All animals have been subjected to gross necropsy. Twenty seven animals, evenly distributed throughout the study groups were partially lost to autolysis or cannibalism.

The only dose related differences between controls and the test groups was a granular surface appearance noted in the high dose kidneys in males.

	Dose (ppm)			
	0	125	500	2000
Kidneys: granular surface, males (%)	10(20%)	12(24%)	18(36%)	24(48%)
Kidneys: granular surface, females (%)	3(6%)	2 (4%)	4 (8%)	3 (6%)

Discussion

Assuming a conversion factor of 0.050 (using an average rat weight) the dose levels would be equivalent to 0, 6.25, 25, and 100 mg/kg/day. It is possible that the upper level is not a maximum tolerated dose since IRDC (1982) used an upper dose of 250 mg/kg/day. In any event this study will be very valuable to complement the IRDC rat study.

The granular surface findings in the kidneys are especially interesting. This area deserves close examination when the final report is received.

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