



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

MAR 24 1981

MAR 24 1981

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Comments on the Proposed Study: "Evaluation of Health Effects of Captan on Chemical Industry Workers"

FROM: Chemist
Environmental Fate Branch, HED (TS-769)

TO: Joe Boyd
Project Manager, CRB I
Special Pesticide Review Division (TS-791)

THRU: Harold Day *HMP*
Acting Chief, Review Section 4
EFB, HED (TS-769)

As requested in your 3/10/81 memorandum (attached), I have reviewed the proposed study entitled "Evaluation of Health Effects of Captan on Industrial Workers" (also attached) and have the following comments:

1. Reproductive Effects

Captan has been shown to produce gene mutations as well as metabolic activation in bacteria (Ficsor et al., 1970 a,b, 1972; Legator et al., 1968; Clarke, 1971; Seiler, 1973; Marshal et al., 1976; Simon et al., 1977; and McCann et al., 1975). Captan has also been shown to cause DNA damage to bacteria (Simon et al., 1977) and hamster cells (Swenberg, 1976). Although there are conflicting studies in the area of teratogenicity, the majority of studies do indicate that captan is teratogenic (Earl et al., 1973; Alnot et al., 1974; Golden-thal, 1978; Verrett et al., 1969; FAO/WHO, 1970; and Fabro et al., 1965).

Because of the mutagenicity and possible teratogenicity of captan, I believe it would be important to clarify whether or not captan causes reproductive problems in an exposed human population. This study as proposed would not necessarily identify such problems.

To identify if such problems occur, a two-phased scheme could be done. First, the medical histories which will be taken should contain questions regarding genetic and reproductive factors (libido, erectile ability, perceived infertility, birth defects of children, results of previous semen analyses, genitourinary tract malformation, family history of spontaneous abortions, current and past birth control measures), prior and current exposure to chemicals, drugs, radiation, infectious diseases, particularly those of viral origin, as well as the obvious questions such as plant job function and length of time at that job. For statistical analysis the employees should be subdivided into several different groups according to location in the plant, exposure to chemicals, and educational levels.

Second, if the medical histories indicate that there could be a problem, cytogenetic surveillance should be initiated, possibly using the method of Kilian and Picciano, 1976. The pros and cons of cytogenetic surveillance are clearly delineated by Evans and O'Riordan (1979) and Kilian and Picciano (1976). Because of the ease of obtaining human blood, the method using human blood lymphocytes for analysis of chromosomal observations could be used (Badell, 1980).

2. Carcinogenicity

Because the study will be conducted in Israel, information should be included with the completed study as to the incidence of intestinal, liver, and duodenal tumors in the population of that country.

3. Quality Control

No quality control measures were mentioned in this proposal. For example, if there is a problem reaching any of the participants, will a standard number of call-backs per questionnaire be made?

4. References Cited

Alnot, M.O., et al.; Preliminary Observations on Toxicity and Teratogenicity of Captan in Wistar Rats; C.R. Society Biol. (Paris); 168(10, 11, 12), 1173-77, (1974).

Badell, D. Private communication between D. Badell at Idaho Health Department and J. Jensen 3/26/80. (1980).

Clarke, C.H., "The Mutagenic Specificities of Pentachloronitrobenzene and Captan, Two Environmental Mutagens," Mutat. Res., 11(2):247-248 (1971).

Earl, F.L., E. Miller, and E.J. Van Loon, "Reproductive Teratogenic and Neonatal Effects of Some Pesticides and Related Compounds in Beagle Dogs and Miniature Swine/" E.D. William and B. Deichmann, Pesticides and the Environment, a Continuing Controversy, Intercontinental Medical Book Corporation, New York, New York (1974).

Evans, E.J. and J.L. O'Riordan. "Human Peripheral Blood Lymphocytes for the Analysis of Chromosome Aberrations in Mutagen Tests. Handbook of Mutagenicity Test Procedures, Kilbey (ed), Elsevier Scientific Publishing Company, New York. (1979).

Fabro, S., R.L. Smith, and R.T. Williams, "Embryotoxic Activity of Some Pesticides and Drugs Related to Phthalimide," Food Cosmet. Toxicol., 3:587-590. (1965).

FAO/WHO, "Captan," 1969 Evaluations of Some Pesticide Residues in Food, pp. 33-44, Geneva (1970).

Ficsor, G., and G.M. Nii Lo Piccolo, "Captan-Induced Reversions of Bacteria," Newslett. Environ. Mutagen. Soc., 3:38 (1970a).

- Ficsor, G., and G.M. Nii Lo Piccolo, "The Effect of Temperature on the Mutagenicity of Captan," Environ. Mutagen. Soc., 3:38 (1970b).
- Ficsor, G., and G.M. Nii Lo Piccolo, "Survey of Pesticides for Mutagenicity by the Bacterial-Plate Assay Method," Environ. Mutagen. Soc., 6:6-8 (1972).
- Goldenthal, E.I., Pilot Teratology Study in Hamsters; International Research and Development Corporation for Chevron Chemical Company; Unpublished. (1978)
- Kilian, D.J. and D. Picciano. Vol 4 Cytogenetic Surveillance of Industrial Populations. Chemical Mutagens. A Hollaendor (ed), Plenum Press p. 321-339. (1976)
- Legator, M.S., F.J. Kelly, S. Green, and E.J. Oswald, "Mutagenic Effects of Captan," Ann. N.Y. Acad. Sci., 160:344-351 (1969).
- Marshall, T.C., et al.; Screening of Pesticides for Mutagenic Potential using Salmonella typhimurim mutants; J. Ag. Food Chem.: 24(3), 560-563, 1976.
- McCann, J., et al., Detection of Carcinogens as Mutagens: Bacterial Tester Strains with R. Factor Plasmids; Proc. Nat'l. Acad. Sci. USA; 72(3), 979-83, 1975.
- Seiler, J.P., "A Survey on the Mutagenicity of Various Pesticides," Experientia, 29:622-623 (1973).
- Simmon, V.F., et al., In vivo and In vitro Studies of Selected Pesticides to Evaluate Their Potential as Chemical Mutagens, SRI Report Prepared for U.S. EPA, Contract 68-01-2458, 2/77 (1977).
- Swenberg, J.A., Petzoid, G.L. and P.R. Harbach, 1976. In vitro DNA damage/alkaline elution assays for predicting carcinogenic potential. Biochem. Biophys. Res. Commun. 72:732-738.
- Verrett, M.J., M.K. Mutchler, W.F. Scott, E.F. Reynaldo, and J. McLaughlin, "Teratogenic Effects of Captan and Related Compounds in the Developing Chicken Embryo," Ann. N.Y. Acad. Sci., 160:334-343 (1969).

Janice Jensen



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

MAR 10 1981

OFFICE OF TOXIC SUBSTANCES

SUBJECT: OPP Review of Proposed "Evaluation of Health Effects of Captan on Chemical Industry Workers"

FROM: J. B. Boyd ~~_____~~
Project Manager, CRB I
Special Pesticide Review Division (TS-791)

TO: Addressees

Makhteshim Chemical Works, Ltd., a registrant of captan developed the attached protocol for conducting an epidemiological study of captan production workers and bystanders. They requested the Agency to comment on the proposed study so that it can be planned and executed to provide the most useful results. Please review the protocol and provide written comments within the next three weeks.

Attachment

cc: Judy Heckman

ADDRESSEES: William Schneider, TB/HED
Hale Vandermere, HEB/HED
Ann Barton, HED
Janice Jensen, EFB/HED ✓

4

Captan Science Reviews

Page _____ is not included in this copy.

Pages 5 through 11 are not included in this copy.

The material not included contains the following type of information:

- _____ Identity of product inert ingredients.
- _____ Identity of product inert impurities.
- _____ Description of the product manufacturing process.
- _____ Description of product quality control procedures.
- _____ Identity of the source of product ingredients.
- _____ Sales or other commercial/financial information.
- _____ A draft product label.
- _____ The product confidential statement of formula.
- _____ Information about a pending registration action
- X FIFRA registration data.
- _____ The document is a duplicate of page(s) _____
- _____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.
