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
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; Simmon 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; Goldenthal, 1976; 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


Goldenthal, E.I., Pilot Teratology Study in Hamsters; International Research and Development Corporation for Chevron Chemical Company; Unpublished. (1978)


Janice Jensen

cc: Judy Heckman, Hed
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 H Eckman

ADDRESSEES:  William Schneider,  TB/HED
             Hale Vandermeer,  HEB/HED
             Ann Barton,    HED
             Janice Jensen,  EFB/HED
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- 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.
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