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

JUN 22 1987

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

TO: Jeff Kempter, PM # 32
Disinfectants Branch
Registration Division TS-767C

THRU: R. Bruce Jaeger, Section Head
Rev. Sec.#1/Toxicology Branch
Hazard Evaluation Division TS-769C 5/11/87

FROM: D. Ritter, Toxicologist DR 5-11-87
Rev. Sec. #1/Toxicology Branch
Hazard Evaluation Division TS-769C

RBJ 6/2/87

Subject

53501-1; Methyl Bromide (MeBr): Request to waive 158.135 Toxicology data requirements.

Sponsor: Great Lakes Chemical Corporation/Methyl Bromide Industry Panel, West Lafayette, IN.

Caswell #: 555.

The Sponsor is seeking waiver of toxicity data requirements for MeBr for the following studies:

82-4 90 day inhalation, rat & rabbit; 83-1 Chronic toxicity, 2 species, rat & dog; 83-2 Oncogenicity, 2 species, rat & mouse; 83-3 Teratogenicity, rabbit; 83-4 Reproduction, 2 generation rat; 84-2 Structural chromosomal abberation; 84-2 Other Genotoxic effects .

The Sponsor suggests justification for waiver of each category as follows:

82-4: 90 day inhalation, rat & rabbit
83-3: Teratogenicity, Rabbit

Justification:

A 90 day mouse inhalation study in mice has been performed at Brookhaven National Laboratory (BNL 34506). In addition, a two

generation rat inhalation study was sponsored by the Methyl Bromide Industry Panel (MBIP). No citation is given for this study. Rabbits and rats were exposed by inhalation for up to 36 weeks (Anger, et al, Scand. J. Work environ. Health 7, 1981:4, 40-47.). The Sponsor also cites Irish (Irish et al, J. Ind. Hyg. Toxicol., 22:218, 30. 1940), which was used by the Rfd Comittee to set a provisional Rfd. for residues of MeBr in feed and water.

Our Response:

The two-generation study is currently under review in the Branch. The Sponsor must provide hard copies of the studies cited, except for the Irish study, which we have. If these prove to be adequate for regulatory purposes, we will consider whether they satisfy the data requirements. However, it should be noted that these subchronic inhalation studies were requested, in part, based on the toxicity seen in the Irish, et al, study.

84-2,4: Mutagenicity studies

Justification:

The 90 day mouse study cited above, as well as published data are currently available to fulfill these requirements.

Our Response:

The Sponsor must provide hard copies of the published studies. If these prove to be adequate for regulatory purposes, we will consider whether they satisfy the data requirements.

83-1,2: Chronic/Oncogenicity testing by gavage

Justification:

The Sponsor requests waiver of these chronic studies because gavage is not an appropriate mode of administration. Moreover, human oral exposure is at a very low level, and further dilution of MB-treated food will occur due to simultaneously ingested non-treated food. MeBr will be consumed at or below the detection limit. Inhalation is the more suitable route of exposure for MeBr toxicity testing.

Our Response:

At the present time we do believe that people may be exposed to MeBr in the food. Data have been requested by RCB to resolve this. We disagree that oral gavage studies using MeBr are not appropriate. In the Danse study (Danse, et al, 1984), MeBr was dissolved in peanut oil at up to 50 ppm and achieved excellent toxicity in rats by gavage. It should be possible to do this in other studies. Although food residues may well be at very low levels, these

levels are not known. RCB in their discussion of the nature of the residue in the Registration Standard Chapter (C. Trichilo, 3/28/86) have stated that the levels anticipated from soil fumigation may require Sensitivity-of-the-Method (SOM) tolerances of > 0.01 to > 0.001 ppm. For post-harvest fumigation additional residue data will be required in order to establish finite tolerances of MeBr per se in racs and processed foods.

In summary, based on the need for tolerances of MeBr per se, we are requesting that all chronic, oncogenic, a second teratology and reproduction studies be carried out by the gavage route. However, since a multi-generation reproduction study (by the inhalation route) is under review, our request for this same study by the gavage route should be reserved pending its final evaluation and complete review of residue information.

The registrant may also consider alternatives to carrying out all studies by the gavage route. Pharmacokinetic data comparing blood levels between the inhalation and oral gavage routes may be needed if such alternatives are to be considered.

No RR (STB)