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

MAR 1 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

John A. Gray
Attorney
2030 Willard H. Dow Center
The Dow Chemical Company
The Dow Center
Midland, MI 48640

Dear Mr. Gray:

This acknowledges your letter of October 5, 1984, providing information on vinyl chloride to the U.S. Environmental Protection Agency. Your submission has been screened as part of our current awareness program on existing chemicals and assigned the following FYI (For Your Information) Document Control Number: FYI-OTS-1084-0353. In any further communication with the Agency regarding this submission, please refer to the above Document Control Number and address your reply to:

Document Control Officer (TS-793)
ATTN: Mr. Terry O'Bryan
Office of Toxic Substances
U.S. Environmental Protection Agency
Washington, D.C. 20460

The Agency looks forward to continued cooperation with the Dow Chemical Company in its efforts to evaluate potential risks posed by chemicals to health and the environment.

Sincerely,

Frank D. Kover

Frank D. Kover, Chief
Chemical Screening Branch/ECAD

THE DOW CHEMICAL COMPANY

THE DOW CENTER
MIDLAND, MICHIGAN 48640

October 5, 1984

AIRBORNE

Document Control Officer
Management Support Division
Office of Toxic Substances (WH-557)
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

R&S 002460

Dear Sir/Madam:

Attached for your information please find a copy of a summary of a report on a Lifespan Oral Carcinogenicity Study of Vinyl Chloride in Rats which we recently received and which I discussed with David Williams on Tuesday, October 2, 1984. This study was conducted in Europe by Civo Institutes TNO and was sponsored by Verband Kunstofferzeugende Industrie E.V. (VKI).

It is our understanding from VKI that the EPA will soon be receiving a copy of the final report. We do not have a copy.

Upon review of this summary, we have been unable to determine whether this study presents any substantial risk information under the EPA's Statement of Interpretation and Enforcement Policy. 43 Fed. Reg. 11110 (March 16, 1978). It appears from the minimal data presented in this summary that the study is corroborative of effects already documented in the scientific literature.

Sincerely,

John A. Gray

John A. Gray
Attorney
2030 Willard H. Dow Center
517/636-0933

Attachment

bcc: F. D. Hoerger, 2020 WHDC
H. Schumacher, Horgen

SUMMARY

1. The oral carcinogenicity of vinyl chloride monomer (VCM) was examined in a lifespan study (149 weeks) with five groups of Wistar rats, each consisting of 100 males and 100 females, except for the top-dose group which comprised 50 males and 50 females. VCM was administered by incorporating polyvinyl chloride (PVC) powder with a high VCM content into the diet. The diet was provided daily for a period of 4 consecutive hours, whereas food was withdrawn during the other 20 hours. The use of this way of oral VCM administration resulted in the following exposure levels: 0 (control), 0.014, 0.13 and 1.3 mg VCM/kg body weight/day. An extra control group of 100 rats/sex was housed in a separate room.
   Additional satellite groups of 18 male and 10 female rats, each receiving the same treatment as the main groups were used for determinations of glutathione levels in the liver after 9 and 18 months.
   Observations were made of general appearance mortality, growth, food intake, thrombocyte count, prothrombin time, glutathione levels in the liver, gross pathology and microscopic pathology of the liver and of all grossly visible tumours or presumable tumours in the abdominal cavity, the glands of Zymbal and the mammary glands.

2. General health, behaviour, body weight and food intake were not adversely affected by the test substance.

3. In the second half of the experimental period, mortality in the extra control group was higher than in all other groups. This was most probably due to a high incidence of chronic respiratory disease in the extra control group. In the final stage of the study, the mortality in the top-dose group was slightly higher than in the lower dose groups and the controls.

4. Thrombocyte count, prothrombin time and liver glutathione levels did not show treatment-related differences among the groups.

5. A clearly higher incidence of grossly visible, tumourous, liver nodules was found in both males and females of the top-dose group than in any of the other groups. Moreover, in females of the top-dose group the incidence of hepatic cysts was considerably higher than in controls.

6. Microscopic examination of the liver revealed increased incidences of liver-cell polymorphism, hepatic cysts, foci of cellular alteration, neoplastic nodules and hepatocellular carcinomas in the top-dose group as compared to the control group. Moreover, a hepatic angiosarcoma was found in one male and two females of the top-dose group, whereas no such tumours were encountered in any of the other groups.
The number of animals bearing foci of cellular alteration in the liver was also statistically significantly increased in females of the mid-dose group as compared to controls. In addition, in females but not in males, the incidence of basophilic foci of cellular alteration in the liver was statistically significantly higher in both the low- and the mid-dose group than in the control group.

7. There was no evidence of VCM-feeding affecting the incidence of abdominal mesotheliomas or the type and incidence of mammary gland tumours. No Zymbal gland tumour was found.

8. It was concluded that under the conditions of the present experiment:

- VCM at a level of 1.3 mg/kg body weight/day induces neoplastic and non-neoplastic changes in the liver of rats,

- VCM at a level of 0.13 mg/kg body weight/day may lead to more female rats bearing foci of cellular alteration in the liver,

- VCM at levels of 0.014 or 0.13 mg/kg body weight/day may result in an increased incidence of basophilic foci of cellular alteration in the liver of female rats,

- 0.13 mg VCM/kg body weight/day is a "no-observed-adverse-effect-level" with respect to the induction of tumours in rats.

9. Risk estimation based on the results of the present rat study and taking into account the prudence of the linear model applied and a lesser sensitivity of humans to the carcinogenic action of VCM in comparison with rats, indicates that the cancer risk of a likely maximum oral daily intake of 0.1 µg VCM per person per day can be practically neglected.

Meeting - October 5, 1984

Present: C. Goodman, J. LeBeau, F. Hoerger, T. Torkelson, J. Gray, K. Beutel

J. Gray advised those present that David Williams of EPA had called him at 5:00 P.M. on October 4, 1984 and told him that Cotruvo had been told nothing other than he would receive a study on vinyl chloride soon.

Those present decided to submit the abstract (titled a summary) to the 8(e) office as a FYI. It was also decided to check with SPI to make sure the complete report would soon be submitted to EPA. We had information that VKI had sent the report to SPI.

JPG
10/11/84