CMA

CHEMICAL MANUFACTURERS ASSOCIATION

COURTNEY M. PRICE
VICE PRESIDENT
CHEMSTAR

April 8, 1998

VIA CERTIFIED MAIL

Document Processing Center
Mail Code 7407
Room E-G99 East Tower
Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

Attention: TSCA § 8(e) Coordinator

Dear Sir:

Described conditions not considered a reportable finding but decided 8(e) notification would manage potential for interpretive conflict w/agency

The Vinyl Chloride Health Committee of the Chemical Manufacturers Association submits the enclosed preliminary results from an ongoing inhalation two-generation reproductive toxicity study in Charles River CD rats sponsored by the Health Committee. These results are submitted pursuant to § 8(e) of the Toxic Substances Control Act.

As indicated in the enclosed preliminary macroscopic and microscopic pathology report, microscopic changes were seen in the livers of high-dose (1,100 parts per million (ppm)) parental rats of both generations. Hepatocellular hypertrophy was seen in the livers of all high-dose rats, and foci of cellular alteration in hepatocytes were significantly increased in the livers of P2 generation parental rats. An increased incidence of hepatocellular foci was seen in 18 of 30 high-dose males and 19 of 30 high-dose females. One focus of cellular alteration was seen in male controls; none was observed in females.

These effects are largely corroborative of results previously reported. Til, H.P. *et al.* observed a variety of treatment-related liver lesions in the high-dose (1.3 mg/kg body weight/day) group of Wistar rats tested in a lifetime oral carcinogenicity study of vinyl chloride. *Food Chem. Toxicol.* 29: 713-18 (1991). The lesions included increased incidences of liver cell polymorphism, hepatic cysts, foci of cellular alteration, neoplastic nodules, hepatocellular carcinomas, and angiosarcomas.

An earlier study of the age-dependence of the induction of pre-neoplastic enzyme-altered hepatic foci demonstrated that there is a period of increased sensitivity to the production of liver foci in response to vinyl chloride exposure in newborn rats. Lai R.L. *et al.*, *Carcinogenesis* 6: 65-68 (1985). This is consistent with the observation of hepatic foci induction in the P2, but not the P1, rats in the reproductive toxicity study. The P2 rats would presumably have been exposed to vinyl chloride during the lactation period (days 4-25 after birth), whereas the P1 animals would not. The period of sensitivity appears to correspond with the period of rapid increase in the number of cells of the liver (proliferation) in newborn rats.

Any significant supplemental data obtained as a result of further pathology evaluation will be reported in a follow-up communication.

The member companies of the CMA Vinyl Chloride Health Committee on whose behalf this submission is being made include:

Borden Chemicals and Plastics
180 E. Broad Street, 15th Fl.
Columbus, OH 43215
Panel Contact: Mr. Mark Gruenwald
Telephone: (614) 225-3459

CONDEA Vista Company
900 Threadneedle
P.O. Box 19029
Houston, TX 77079
Panel Contact: Dr. David A. Penney
Telephone: (281) 588-3059

The Dow Chemical Company
1803 Dow Center
Midland, MI 48674
Panel Contact: Dr. Colin Park
Telephone: (517) 636-1159

Formosa Plastics
9 Peachtree Hill Rd.
Livingston, NJ 07039
Panel Contact: Mr. David Pun
Telephone: (973) 716-7279

GEON Company
One Geon Center
Avon Lake, OH 44012
Panel Contact: Mr. Ed Beeler
Telephone: (440) 930-3030

Georgia Gulf Corporation
26100 Highway 405
P.O. Box 629
Plaquemine, LA 10165
Panel Contact: Mr. Jay Strange
Telephone: (504) 685-2642

Occidental Chemical Corp.
P.O. Box 809050
5005 LBJ Freeway, Room 904
Dallas, TX 75380
Panel Contact: Dr. Steve Phillips
Telephone: (972) 404-2413

PPG Industries, Inc.
One PPG Place - 36W
Pittsburgh, PA 15272
Panel Contact: Dr. James Barter
Telephone: (412) 434-2801

Westlake Chemical Corp.
2801 Post Oak Blvd.
Suite 600
Houston, TX 77056
Panel Contact: Mr. John Gamble
Telephone: (713) 960-9111

If you have any questions regarding this letter, please contact Wendy Sherman or my staff at (703) 741-5639.

Sincerely yours,

Courtney M. Price
Vice President, CHEMSTAR

Enclosure

cc: Vinyl Chloride Health Committee