



**DuPont Dow elastomers**

cc: Dr. G. Lucier, NTP  
Dr. J. Bucher, NTP

October 24, 1997

Dr. C.W. Jameson  
Report on Carcinogens  
MD: EC-14  
PO Box 12233  
Research Triangle Park, NC 27709

Dear Dr. Jameson:

We would like to take this opportunity to express some of our thoughts on the events and issues leading up to the classification of beta-chloroprene as a chemical "reasonably anticipated to be a human carcinogen". First, we want to correct some of the errors and omissions in the Draft Background Document, especially as it relates to nomenclature, production, use, and exposure potential for beta-chloroprene. Our comments are described in more detail below.

Second, we share your concern for the health of employees and customers who may be exposed to beta-chloroprene. To this end, an interindustry group of chloroprene manufacturers has been formed; we have agreed to pool resources and conduct studies that can directly address health and safety issues. We have begun collaborative mechanistic studies to define a physiologically-based pharmacokinetic model that will be critical in assessing the relationship between the animal and human responses to beta-chloroprene.

Third, this interindustry group is considering a multinational epidemiological study on the association of chloroprene exposure with cancer; it is the goal of this study to employ exposure data to materially improve the quality of the study.

As this multidisciplinary program unfolds, we look forward to sharing this information with you.

Very sincerely yours,

Michael A. Lynch  
Project Manager

Enclosure

## Comments on the Draft Background Document for Chloroprene

### Proposed RC Listing for Chloroprene

Page RC-1, Carcinogenicity, second paragraph

It should be understood that the one case of liver angiosarcoma was reported for a worker involved with handling polychloroprene not beta-chloroprene monomer. If this individual were handling dry polychloroprene, there would be no exposure as this product contains essentially no beta-chloroprene monomer (detection limit of 0.5 ppm).

### Chemical Identification

Page 1-1, Section 1.1

alpha-chloroprene is not a synonym for beta-chloroprene.  
Alpha-Chloroprene is 1-chloro-1,3-butadiene not  
2-chloro-1,3-butadiene.

### Physical Chemical Properties

Page 1-2, last sentence

The text mentions the formation of chlorine ion (Cl<sup>-</sup>); this material is not normally generated during combustion of either beta-chloroprene or polychloroprene except at extremely low concentrations.

### Production Processes and Volume

Section 2.2, Page 2-1, first paragraph

The draft document states that vapor phase chlorination at 300 deg C produces a mixture of 1,4- and 3,4-dichlorobutenes. We suggest you take out the reference to the temperature and the specific process as both liquid and vapor phase chlorination processes exist and do not necessarily occur at 300 deg C.

Section 2.2, Page 2-1, second paragraph

Westlake Monomers does not produce beta-chloroprene for on site use. Rather, it is a by-product of their vinyl chloride manufacturing process; typically, the chlorine value from beta-chloroprene is recovered as HCl by catalytic oxidation. Additionally, the Bayer Houston facility does not produce beta-chloroprene.

Page 2-2, second paragraph

The production values cited do not accurately reflect the actual volumes of polychloroprene manufactured. The total estimated production of polychloroprene in 1986-1988 is approximately 250-300 million lb. The volume in 1995-1996 is approximately 200-250 million lb.

### Environmental Exposure

Section 2.3, page 2-2, first paragraph

As noted earlier, only one site actually produces beta-chloroprene; the other two sites convert beta-chloroprene to polychloroprene.

Page 2-3, second paragraph

Some of the values reported for the ambient air concentrations for beta-chloroprene are incorrect. The survey for the 6 cities in NJ represent a maximum detected concentration of 4 ppb (vs 40 as cited in the Draft document) at one specific site. beta-Chloroprene was found in only 64 of 263 quantifiable air samples with an average of 0.097 ppb; had the time weighted average for all samples been cited, the actual air concentration of beta-chloroprene would be markedly lower. This alternative expression of the ambient air concentration data was not considered in either the original report or the NTP Draft document. Additionally, the original data for Houston area shows that the average concentration of beta-chloroprene for all samples taken in 1976 was actually 0.069 ppb vs 0.59 ppb as cited in the Draft document (only 2 of 17 air samples actually contained detectable quantities of beta-chloroprene; 0.073 and 1.11 ppb).

#### Occupational Exposure

Page 2-4, first paragraph

The Infante (1977) citation does not say that 2500 to 3000 workers were exposed to levels up to 6760 ppm during manufacture. The citation does state that 2500 to 3000 workers were exposed to chloroprene during its manufacture and polymerization but does not provide a reference for this value. Infante (1977) goes on to explain that air concentrations up to 6760 ppm have been measured in some beta-chloroprene manufacturing processes, but does not infer that all of these workers were exposed up to these levels. In fact, the specific data cited was from a 1973 DuPont workplace survey intended to identify potential high level, point sources of beta-chloroprene based on instantaneous grab samples. At no point do the values cited represent time weighted average exposures to employees. Based on these air samples, control procedures were implemented to limit exposures.

Our own records show that a more realistic estimate of the number of people potentially exposed to beta-chloroprene during manufacture is well under 500; even so based on monitoring data from the 1970's onward, exposures have been controlled to 25 ppm or less as required by OSHA. We currently meet the internal control limit of 10 ppm, with the majority (greater than 95% of the time weighed exposures) below 2 ppm.

Page 2-4, first paragraph

The 1983 NIOSH sponsored NOES survey of workplace exposure to beta-chloroprene was intended to determine how many people were involved in occupations where there was exposure potential to beta-chloroprene. Beta-Chloroprene is not generally commercially available. It is only sold to three companies in the United States. Except for the sale of under 20 lbs/yr for research applications, all of the domestically produced beta-chloroprene is used to make polymer.

Additionally, the NOES survey was not based on air sampling data but only on whether beta-chloroprene (or products thought to contain beta-chloroprene) were observed to be present in the workplace. By the method of data entry, this survey did not distinguish between beta-chloroprene monomer and polychloroprene, an important distinction since dry polychloroprene does not contain residual beta-chloroprene monomer using analytical methods with a 0.5 ppm detection limit. We believe that the survey, while well intentioned, considerably overestimates the actual number of people exposed to beta-chloroprene monomer.

It should also be noted that the most exposed group in the survey is from the auto repair services, primarily garages. Their inclusion is believed to be attributable to their use of belts, hoses, gaskets and adhesives used in this industry; most of the exposure will be to polychloroprene for which only the polychloroprene latex may contain appreciable amounts (up to 0.5%) of beta-chloroprene.

#### Regulations and Criteria

Page 2-5, second paragraph

While the NIOSH Pocket Guide to Hazardous Chemicals has listed a 15-min ceiling of 1 ppm for beta-chloroprene, according to the Federal Register (vol 54(12), 1/19/89) NIOSH concurred with the 10 ppm 8-hr TWA rendering the 1 ppm ceiling value ineffective.

#### Human Studies

Page 3-1, second paragraph

The Draft document describes several previously reviewed epidemiology studies and the conclusions of those papers from the 1979 IARC monograph on beta-chloroprene. There are several omissions and clarifications that should be duly noted. First, Khachatryan (1972 a and b) reported skin and lung tumors in Armenian workers. DuPont queried the Soviet government about the source of this epidemiologic information and the conclusions drawn from the data. The Soviet Ministry of Health subsequently retracted the conclusions on Khachatryan's work based on the methodological errors contained in these studies; this unusual retraction of a scientific study was described in Infante's (1977) paper. Secondly, the IARC review of the 1978 Pell study of chloroprene mortality in two DuPont sites did not conclude that there was an increase in digestive and lymphatic/hematopoietic tumors; Pell did report that the incidence of these tumor types were slightly elevated in one cohort but that

the increases were not statistically significant. Thirdly, the reference to the Centers for Disease Control 1976 memorandum regarding development of angiosarcoma in a worker vulcanizing polychloroprene is sensationalistic. The 1979 IARC monograph cites that beta-chloroprene concentrations in processes where polychloroprene was applied to cylinders prior to vulcanization were about 0.2 ppm (well below even the current ACGIH TLV value of 10 ppm); the paper does not state what contribution beta-chloroprene degradation products formed during the vulcanization process had in the development of angiosarcoma. Finally, we are aware of another epidemiological study not described in the Draft document; a copy of this will be forwarded. For these reasons, additional conservatism should be placed on the interpretation of the epidemiologic data cited.

Page 3-1, third paragraph

The Li Shouqi (1989) paper contains a number of methodological errors and/or omissions which are not described in the Draft. Notably, like all other epidemiologic studies to date, there is no data relating the level and duration of exposure to beta-chloroprene with disease development. No discussion was given to the fact that the starting chemicals involved in this study were very different from those used in the Western World to make beta-chloroprene. Shouqi described tumors associated with beta-chloroprene manufactured from the acetylene process while the synthetic route used in the Western World is from 1,3-butadiene; the confounding effects of exposure to the intermediates involved in the acetylene process were not described. The small size of the study, and the unusually low number of cancer deaths (16 of 1213 workers vs. 44 deaths in 1559 workers from the Pell study) suggests there might be a fundamental problem with the selection process used to identify workers for the Shouqi study. The finding of such low numbers of specific cancer types and the absence of confidence limits with these data does not allow a conclusion of cause and effect. This is particularly germane since most tumors occurred in the monomer area where, as noted above, most of the world's production of beta-chloroprene does not use acetylene as a starting material.

#### Experimental Carcinogenesis

Page 4-1, first paragraph

Additional animal carcinogenesis data has been developed. A 1980 industry sponsored inhalation study in rats and hamsters was conducted at concentrations up to 50 ppm. This data did not show

beta-chloroprene to be an animal carcinogen at levels up to 50 ppm. These studies have been submitted for publication and will be made available to the NTP upon completion of the peer review.

#### Genotoxicity

Page 5-1, third paragraph

The data described showing that beta-chloroprene caused dominant lethal mutations in mice and rats is not referenced and should be evaluated in the same regard to data source and integrity as the other data cited in this draft. We believe the data referred to as that reported by Sanotskii in 1976. This report was based on data reported previously by other Soviet investigators (Fomenko and Katosova) at concentrations as low as 0.036 ppm, a level which would have been extremely difficult to measure today let alone in 1976.

#### Structure Activity Relationships

Page 7-2

Did isoprene really cause k-ras mutations in the lung and harderian gland?

#### Appendix D

This report contains a number of issues which we have previously raised including the levels of beta-chloroprene in polychloroprene, descriptions of the numbers and levels of workers potentially exposed to beta-chloroprene, NOES survey data, the inappropriateness of the NIOSH 15-min ceiling value, the retraction of the Khachatryan epidemiology data, and the incomplete citations of epidemiology data.

Page 25.

The explosive limits cited are incorrect. The actual values are 1.9-10% in air.