MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

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TO: File

FROM: Catherine Simon, Toxicologist, Air Quality Division

SUBJECT: Risk Assessment for Dimethylvinyl Chloride (CAS No. 513—37—1)

A review of the available literature revealed only one chronic animal study which evaluated the carcinogenic potential of dimethylvinyl chloride. In this study, sponsored by the National Toxicology Program (NTP, 1986), dimethylvinyl chloride was administered by gavage to male and female P344/N rats and B6C3FI mice at dose levels of 0, 100, and 200 mg/kg/day, for five days per week, for 103 and 102 weeks, respectively. The results of this study showed there was clear evidence of carcinogenicity of dimethylvinyl chloride for both sexes of rats and mice. In rats, this was based on increased incidences of neoplasms of the nasal cavity, oral cavity, esophagus, and forestomach. In mice, both sexes showed increased incidences of squamous cell neoplasms of the forestomach, and additionally in male mice, there was an increased incidence of squamous cell carcinomas of the preputial gland.

No human epidemiology studies were available to evaluate the carcinogenic potential of dimethylvinyl chloride; however, this compound was tested for mutagenicity in several short term tests sponsored by the NTP (NTP, 1986). The results of these studies showed that dimethylvinyl chloride was not mutagenic in four strains of Salmonella typhimurium with or without metabolic activation, and did not increase the frequency of chromosomal aberrations in Chinese hamster ovary (CHO) cells. However, dimethylvinyl chloride was mutagenic in the mouse lymphoma L5178Y/TK+/— forward mutation assay in the absence of metabolic activation, and also induced sister chromatid exchanges in CHO cells in both the presence and absence of metabolic activation. In addition, this compound produced significant increases in the frequency of both sex—linked recessive lethal mutations and reciprocal translocations in Drosophila. Overall, there is sufficient evidence showing the mutagenic activity of dimethylvinyl chloride. A quantitative risk assessment was done to determine the incremental unit risk estimate for dimethylvinyl chloride. The incremental unit risk estimate is defined as the additional lifetime cancer risk that would result in a population in which all individuals were exposed for a lifetime to 1 μg/m^3 of the chemical. The data used for the quantitative risk estimate were taken from the NTP bioassay. The linearized multistage model (GLOBAL 82), was fit to the dose—response data from this study. Unit risk values were determined from the dose—response data for various tumor types in rats and mice. Table 1 summarizes the dose—response data used in the risk assessment, and Table 2 summarize the unit risk estimate for each data set. The unit risk value of 1.18×10^{-5}, estimated from the incidence of forestomach neoplasms in male mice, is used to estimate the risk to human populations exposed to dimethylvinyl chloride. Using this unit risk value, the concentration of dimethylvinyl chloride in air resulting in an increased cancer risk of one in one million (1×10^{-6}) is 0.008 μg/m^3.

REFERENCES

National Toxicology Program (NTP). 1986. Toxicology and Carcinogenesis Studies of Dimethylvinyl Chloride (1—Chloro—2—Methylpropene) (CAS No. 513-37-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies)

U.S. Department of Health and Human Services. NTP TR 316. August 1986.

TABLE 1
Dose Response Data for Dimethylvinyl Chloride

I. Dose levels of dimethylvinyl chloride administered to rats and mice (NTP, 1986).

Dose Group	Administered Dose (mg/kg/day)	T.W.A. Dose* (mg/kg/day)
Control	0	0
Low	l00	71.4
High	200	142.8

II. Tumor incidence for each data set (number of animals with tumor/number animals in group).

	Dose Group		
Data Base	Control	Low	High
Male rats—Nasal cavity tumors	0/47	23/46	28/32
Female rats—Nasal cavity tumors	0/50	16/49	35/41
Male rats—Forestomach neoplasms**	0/49	14/50	0/50
Female rats—Forestomach neoplasms**	1/50	9/50	2/49
Male mice—Forestomach neoplasms**	1/48	43/47	41/44
Female mice—Forestomach neoplasms**	0/50	40/47	38/43

* T.W.A. Dose Time weighted average dose = Administered Dose x 5 days/7 days
** Includes squamous cell papillomas or carcinomas

TABLE 2
Cancer Potency and Unit Risk Estimates for Dimethylvinyl Chloride

I. Potency (q1*) or slope estimates for each data set.

Data Base	q1* (mg/kg/day)
Male rats—Nasal cavity tumors	7.52×10^{-2}
Female rats—Nasal cavity tumors	2.98×10^{-2}
Male rats—Forestomach neoplasms	3.89×10^{-2}
Female rats—Forestomach neoplasms	2.83×10^{-2}
Male mice—Forestomach neoplasms	$4.13 \times l0^{-1}$
Female mice—Forestomach neoplasms	3.34×10^{-1}

Calculation of assumes that mg/surface area/day is an equivalent dose between species, and that surface area is proportional to the two—thirds power of body weight. The following average body weights were used to estimate q1*: humans = 70 kg; male rats = 400 g; female rats 250 g; male mice 35 g; female mice = 30 g.

II. Unit Risk Estimates (risk from continuous exposure to 1 µg/m³ in air)

Data Base	Unit Risk Value
Male rats—Nasal cavity tumors	2.15×10^{-5}
Female rats—Nasal cavity tumors	8.51×10^{-6}
Male rats—Forestomach neoplasms	1.11×10^{-5}
Female rats—Forestomach neoplasms	8.09×10^{-6}
Male mice—Forestomach neoplasms	1.18×10^{-4}
Female mice—Forestomach neoplasms	$9.55 \times l0^{-5}$

In estimating risk from inhalation exposure based upon oral data, it is assumed that a 70 kg person inhales 20 m^3 of air per day, and that absorption efficiencies by the oral and inhalation routes are equivalent.