MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

September 25, 1986

TO: File

FROM: Catherine Simon, Toxicologist

SUBJECT: Risk Assessment for 3—Chloro—2-methylpropene (CAS No. 563—47—3)

A review of the available literature revealed only one chronic animal study which evaluated the carcinogenic potential of 3—chloro-2-methylpropene. In this study, sponsored by the National Toxicology Program (NTP, 1986), 3—chloro—2-methylpropene was administered by gavage to male and female F344/N rats and B6C3F1 mice for five days per week for 103 weeks. Dose levels for rats were 0, 75, or 150 mg/kg/day, and for mice were 0, 100, or 200 mg/kg/day. The results of this study showed there was clear evidence of carcinogenicity for 3—chloro—2-methylpropene, as shown by an increased incidence of squamous cell neoplasms in the forestomach of both male and female rats and mice.

No human epidemiology studies were available to evaluate the carcinogenic potential of 3—chloro—2-methylpropene, however, this compound has been tested for mutagenicity in several short term tests. Positive results have been obtained in several systems (NTP, 1986; EPA, 1985) including the mouse lymphoma L5178Y/TK+/—forward mutation assay, induction of sister chromatid exchanges (SCE) and chromosomal aberrations in cultured Chinese hamster ovary cells, and the induction of unscheduled DNA synthesis (UDS) in human HeLa cells. Conflicting results have been obtained in assays using various strains of Salmonella typhimurium.

A quantitative risk assessment was done to determine the incremental unit risk estimate for 3—chloro—2-methylpropene. 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 $\mu g/m^3$ 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 both sexes of rats and mice for forestomach neoplasms. Table I summarizes the dose—response data used in the risk assessment, and Table 2 summarizes unit risk estimates for each data set. The unit risk value of 3.83×10^{-5}, estimated from the incidence of forestomach carcinomas/papillomas in male mice, is used to estimate the risk to human populations exposed to 3—chloro—2—methylpropene. Using this unit risk value, the concentration of 3—chloro—2—methylpropene in air resulting in an increased cancer risk of one in one million (1×10^{-6}) is 0.03 $\mu g/m^3$.

REFERENCES

National Toxicology Program (NTP). 1986. Toxicology and Carcinogenesis Studies of 3—Chloro—2—Methylpropene (Technical grade containing 5% dimethylvinyl chloride) (CAS NO. 563—47—3) in F344/N Rats and B6C3F1 Mice (Gavage Studies). NTP TR 300. June 1986.

U.S. Environmental Protection Agency (EPA). 1985. Chemical Hazard Information Profile. Draft Report. 3—Chloro—2—methylpropene. CAS NO. 563—47—3. September 19, 1985.

TABLE 1
Dose Response Data for 3—Chloro--2—methylpropene
(CAS No. 563—47—3)

I. Dose—response data for incidence of forestomach neoplasms (carcinomas/papillomas) in rats (NTP, 1986)

Administered Dose (mg/kg/day)	T.W.A. Dose* (mg/kg/day)	Tumor Incidence Males	Tumor Incidence Females
0	0	1/50	1150
75	53.6	5/50	1/50
150	107.1	30/48	10/50

II. Dose—response data for incidence of forestomach neoplasms(carcinomas/papillomas) in mice (NTP, 1986)

Administered Dose (mg/kg/day)	T.W.A. Dose* (mg/kg/day)	Tumor Incidence Males	Tumor Incidence Females
0	0	3/49	0/50
100	71.4	24/49	16/48
200	142.8	36/49	31/44

* T.W.A. Dose = Time weighted average dose Administered dose x 5 days/7 days

TABLE 2
Cancer Potency and Unit Risk Estimates for 3—Chloro—2—methylpropene
(CAS No. 563—47—3)

I. Potency (q1*) or slope estimates based on the incidence of forestomach neoplasms in mice and rats.

Data Base	q1* $(mg/kg/day)^{-1}$
Male Rats	1.14×10^{-2}
Female Rats	9.14×10^{-3}
Male Mice	1.34×10^{-1}
Female Mice	1.11×10^{-1}

Calculation of q1* 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 = 350 g; female rats 250 g; male mice 40 g; female mice = 30g.

II. Unit Risk Estimates (risk from continuous exposure to 1 $\mu g/m^3$ in air)

Data Base	Unit Risk Value
Male Rats	3.26×10^{-6}
Female Rats	2.61×10^{-5}
Male Mice	3.83×10^{-5}
Female Mice	3.17×10^{-5}

In estimating risk from inhalation exposure, 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.

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