MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

November 4, 1987

TO: File

FROM: Catherine A. Simon

SUBJECT: Chlorinated Paraffins (63449-39-8)

In a study sponsored by the National Toxicology Program (NTP, 1986), male and female F344/N rats and B6C3F1 mice were administered chlorinated paraffins by gavage five times per week for 103-104 weeks. Rats received dose levels of 0,312 or 625 mg/kg body weight per day, while mice were administered dose levels of 0,125, or 250 mg/kg. The material used in the study was a mixture of chlorinated paraffins (C10-C12) with an average molecular weight of 415 and 60% chlorine content.

The results of this study showed there was clear evidence of carcinogenicity for rats based on increased incidences of hepatocellular neoplasms in male and female rats, of adenomas or adenocarcinomas (combined) of the kidney tubular cells in male rats, and of follicular cell adenomas or carcinomas (combined) of the thyroid gland in female rats. There was also clear evidence of carcinogenicity for mice as shown by increased incidences of hepatocellular adenomas or carcinomas (combined) in male and female mice, and increased incidences of thyroid gland follicular cell adenomas or carcinomas (combined).

The NTP (NTP, 1986) also sponsored mutagenicity testing of chlorinated paraffins (C10-C12, 60% chlorine) in Salmonella typhimurium. This compound was not mutagenic for strains TA97, TA89, TA100, or TA1535 in the presence or absence of a liver S9 fraction from Aroclor 1254 induced male rats or male Syrian hamsters.

No epidemiology studies were available which evaluated the carcinogenic effects of chlorinated paraffins in humans. Based upon the finding of sufficient evidence of carcinogenicity in laboratory animals, however, chlorinated paraffins (C10-C12, 60% chlorine) should be considered a potential human carcinogen.

A quantitative risk assessment was done to determine the incremental unit risk estimate for chlorinated paraffins. 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 ug/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. Table 1 and Table 2

provide the specific data used in the quantitative risk assessment. Only animals surviving at least 52 weeks were used in the quantitative risk assessment, since those dying earlier were not considered to have been exposed long enough to be at risk. Table 3 provides a listing of the carcinogenic potency factor, or 95% upper limit maximum likelihood estimate of the linear component (q_1^*), of the multistage model for each tumor type that was significantly increased due to exposure to chlorinated paraffins. In calculating q_1^* for the kidney tubular cell adenomas or adenocarcinomas for male rats, only the control and low dose groups were used, since the multistage model did not fit the data adequately when the high dose group was included. (Chi-square (X^2) was larger than the cumulative 99% point of the chi square distribution.)

The carcinogenic potency factor of 1.01×10^{-1} $(mg/kg/day)^{-1}$, estimated from the incidence of hepatocellular adenomas or carcinomas in male mice is used to estimate the risk to human populations. Based upon this value, and assuming 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, the unit risk value is 2.9×10^{-5}. Utilizing this unit risk value, the concentration of chlorinated paraffins (C10-C12, 60% chlorine) in air resulting in an increased cancer risk of one in one million (1×10^{-6}) is 0.03 ug/m^3.

References

National Toxicology Program (NTP). 1986. Toxicology and Carcinogensis Studies of Chlorinated Paraffins (C12, 60% Chlorine) (CAS No. 63449-39-8) in F344/N Rats and B6C3F1 Mice (Gavage Studies). U.S. Dept. of Health and Human Services. NTP TR 308.

Table 1

Does Levels of Chlorinated Paraffins
Administered to Rats and Mice (NTP, 1986)

I. Dose levels administered to rats

Dose Group	Administered Dose (mg/kg/day)	Continuous Lifetime Dose* (mg/kg/day)
Control	0	0
Low	312	223
High	625	446

II. Dose levels administered to Mice

Dose Group	Administered Dose (mg/kg/day)	Continuous Lifetime Dose* (mg/kg/day)
Control	0	0
Low	125	89
High	250	179

* Continuous Lifetime Dose = Administered Dose x 5 days/7 days

Table 2

Tumor Incidence in Rats and
Mice Surviving to Week 52 (NTP, 1986)

Species	Sex	Tumor Type	Tumor Incidence		
			Control	Low Dose	High Dose
Rats	M	Hepatocellular neoplasms	0/50	13/50	16/47
Rats	F	Hepatocellular neoplasms	0/50	5/50	7/49
Rats	M	Kidney tubular cell adenoma/adenocarcinoma	0/50	9/50	3/47
Rats	F	Thyroid follicular cell adenoma/carcinoma	0/50	6/50	6/49
Mice	M	Hepatocellular adenoma or carcinoma	20/50	34/50	38/49
Mice	F	Hepatocellular adenoma or carcinoma	3/48	22/47	28/48
Mice	F	Thyroid follicular cell adenoma/carcinoma	8/48	12/46	15/47

Table 3

Cancer Potency (q_1^*) Estimates for Chlorinated Paraffins

Data Base	q_1^* $(mg/kg/day)^{-1}$
Male Rats - Hepatocelluar Neoplasms	7.99×10^{-3}
Female Rats - Hepatocellular Neoplasms	3.93×10^{-3}
Male Rats - Kidney Tubular Cell Adenoma/Adenocarcinoma	8.10×10^{-3}
Female Rats - Thyroid Follicular Cell Adenoma/Carcinoma	3.92×10^{-3}
Male Mice - Hepatocellular Adenoma or Carcinoma	1.01×10^{-1}
Female Mice - Hepatocellular Adeonma or Carcinoma	8.41×10^{-2}
Female Mice - Thyroid Follicular Cell Adenoma/Carcinoma	2.86×10^{-2}

Calculation of q_1^* 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 q_1^*: humans = 70 kg; male rats = 0.425 kg; female rats = 0.250 kg; male mice = 0.042 kg; female mice = 0.035 kg.