Summary Tables on the Health Effects Data for Hazardous Air Pollutants (HAPs) - Group I

Prepared By:

Michael W. Neal, Nancy Goddard, and Heather Printup
Environmental Science Center
Syracuse Research Corporation
Merrill Lane
Syracuse, NY 13210

August 1995

Table of Contents by Chemical Name

Table of Contents by CAS Registry Number

TECHNICAL APPROACH FOR DEVELOPING HEALTH EFFECTS PROFILES FOR HAPS

Scope of this document: The information contained in this document is not intended to be an exhaustive review of the scientific health effects literature on these chemicals, but to provide a summary of the relevant literature needed to make a decision as to whether additional testing is needed to understand the toxicity of these compounds following inhalation exposure. To fulfill this goal, the following criteria were used for the inclusion of studies, and the final summaries were reviewed by EPA

- **Acute, Subchronic, and Chronic Systemic Noncancer Toxicity** - Since the main concern of this review is inhalation risk, only inhalation studies were reviewed. Although oral studies can provide important information on target organ toxicity and should be considered in the design of any testing protocol, these studies usually provide no information on the effects of a compound on the respiratory tract. In addition, the systemic dose of many compounds are affected by "first pass" effects at the portal of entry into the body making extrapolation between oral and inhalation exposure problematic unless extensive pharmacokinetic data are available. An exception to this is dibutyl phthalate, which, because of its low vapor pressure, is being considered for oral testing. For this chemical, oral acute, subchronic, and chronic toxicity studies were reviewed and summarized.

- **Reproductive Toxicity, Developmental Toxicity, Neurotoxicity and Carcinogenicity** - These endpoints were considered to be very important in evaluating the potential health effects of the chemicals and for these endpoints, studies were reviewed regardless of the route of administration. In the evaluation of these endpoints, studies that were considered to provide no useful information because of inadequate study design or poor reporting of experimental procedures were not included in the tables.

- **Pharmacokinetics** - For pharmacokinetics, only a summary statement was provided on the availability of pharmacokinetics data. The source of information on pharmacokinetics data was obtained from secondary sources initially consulted for evaluation of the HAPs. The purpose of this pharmacokinetics summary statement was to indicate whether there was potentially sufficient information on the pharmacokinetics from the oral and inhalation routes to allow route-to-route extrapolation of toxicological studies.

- **Genotoxicity** - This toxicological endpoint was not included in this document, but summarized separately in Waters, 1990 which is available in the docket for the Test Rule.

- **Adequacy of Data** - In the tables, adequacy is used to indicate if the conduct and design of the study are sufficient to meet the requirements of OPPT's Test Guidelines. It should be noted that a study does not have to specifically meet the TSCA testing guideline, but it must have such qualities as sufficient numbers of test animals so that adequate statistics can be performed and sufficient doses tested to define a dose-response relationship. When a study is indicated as inadequate, it is not implied that the study was necessarily poorly conducted or does not provide useful and accurate test data, but only that the study does not meet OPPT's test guidelines and that it would not provide the best basis for a risk assessment using current EPA methodology.

Identification of relevant scientific literature: Under EPA's direction, SRC performed searches of the literature in a step-wise manner to save both time and expense. The first step was to identify and review secondary source health effect documents. EPA realizes that using secondary sources of information is not ideal, since the secondary source can miss important information or incorrectly interpret a study. If information appeared to be missing or the interpretation was unclear, SRC obtained the original article for clarification. The second step was to conduct up-date searches of the scientific literature, identify studies, obtain the original articles, and review these studies for inclusion in this document. The following details the strategy that was utilized:

- For this group of HAPs, EPA, IARC, or ATSDR health effects documents were identified and relevant data were extracted from these secondary sources and placed in the tables. If essential information was missing from the review documents, then the original article was consulted

- To obtain unpublished studies submitted to EPA under TSCA, the TSCATS data base was searched by CAS Registry number, the documents were retrieved, and the study information was entered into the table.
- A current (1993) printout of the NTP Results Report (generated from NTP's CHEMTRACK data base) was reviewed to determine if there were completed studies conducted by NTP and obtain the status of studies in progress or planned.
- The *National Toxicology Program Review of Current DHHS, DOE, and EPA Research Related to Toxicology* Fiscal year 1993 was reviewed to determine the status of on-going toxicity studies on these HAPs
- If few studies were identified, then searches were conducted on CAS ONLINE
- The EPA IRIS data sheets were reviewed to ascertain if additional data had been identified by the working group, and if studies were found, they were retrieved and added to the table.
- An up-date search of the open literature was conducted on TOXLINE from 3 years prior to the date of the review document used to initially obtain toxicity information. These searches were reviewed, hard copies of relevant articles were retrieved, and the data from these articles were entered into the tables.
- The literature searches were conducted in the latter part of 1992 and early in 1993, however, additional studies have been added through the middle of 1994 as these studies were identified during the review process by EPA and SRC.
- In general, translations of foreign articles were not available and few such articles are included in this document. Exceptions occurred when the translation was readily available in SRC's achives or through EPA.
- The tables were reviewed by a committee in EPA
- Representatives from NIOSH, OSHA, FDA, and NIEHS were consulted to determine if these organizations had any information on completed or on-going studies that might not be included on any readily available database.
- Representative trade organizations of the chemical industry were contacted to determine if they were aware of any on-going testing.

Other related documents: Two additional documents were prepared for the evaluation of the testing needs for these HAPs. One was a support document on physical chemical properties, environmental transport and persistence, and exposure (occupational, consumer, environmental, and general population) entitled *Exposure Profile for HAPs – Group 1* prepared by SRC (May 25, 1994) The second was an evaluation of the genotoxic potential of these HAPs entitled *Genetic Activity Profiles of 110 Hazardous Air Pollutants Listed Under Title III of the Clean Air Act* prepared by Waters at EPA. Both of these documents are included in the docket for this Test Rule.

Table of Toxicity Data for HAPs

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Vinylidene chloride	75-35-4	Epidemiology (Cohort study)	Humans	Occupational	Inhalation	Less than 12 to over 120 months	Less than 500, 500-999, 1,000-1,999, to over 2,000 ppm months	28 to 32 in the three higher exposure groups and 50 in the lowest exposure group	There was no increase in lung cancers in exposed workers	Inadequate because study cohort was small and there was no allowance for a latency period	There was exposure to other chemicals including vinyl chloride.	Ott et al 1976
Vinylidene chloride	75-35-4	**Epidemiology - Summary**								No adequate epidemiological studies were located; however, some information regarding occupational exposure is available (ATSDR, 1992).		
Vinylidene chloride	75-35-4	Acute toxicity	Rats and mice	Inhalation	Vapor	6 hours	0, 10, and 50 ppm	Males	Tissue damage and increased DNA replication were noted in kidneys of exposed mice	Inadequate because of too few concentration levels tested and the use of only one sex.	The authors suggested that tumors in mice arose primarily through effects of the chemical on non-genetic components of the cells	Reitz et al , 1980
Vinylidene chloride	75-35-4	Acute toxicity	Rats	Inhalation	Vapor	4 hours	Not reported	6/exposure group	LC_{50} = 32,000 ppm	Adequacy could not be determined.	This is a brief description of study results.	Carpenter et al., 1949
Vinylidene chloride	75-35-4	**Acute toxicity - Summary**								No adequate acute inhalation toxicity studies are available		
Vinylidene chloride	75-35-4	Subchronic toxicity	Rats	Inhalation	Not reported	90 days; continuous exposure	0, 20, 61, 101, and 189 mg/m³ (0, 5.04, 15.39, 25.47, and 47.67 ppm)	15/treatment group, 304 control rats; sex not reported	Reduced weight gain and elevated liver alkaline phosphatase and serum glutanic-pyruvic transaminase activities were observed in high-exposure animals. Microscopic liver and kidney lesions were also observed only in high-dose animals	This is a marginally adequate subchronic toxicity study because of the number of animals in the treated groups	LOAEL = 189 mg/m³ (NOAEL = 101 mg/m³) for subchronic inhalation toxicity.	Prendergast et al , 1967

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Vinylidene chloride	75-35-4	Subchronic *toxicity*	Guinea *pigs*	Inhalation	Not reported	90 days; continuous exposure	0, 20, 61, 101, and 189 mg/m^3	15/treatment group, 314 control guinea pigs; sex not reported	Reduced weight gain and elevated liver alkaline phosphatase and serum glutamic-pyruvic transaminase activities were observed in high-exposure animals No gross or histopathological changes were observed	This is a marginally adequate subchronic toxicity study because of the number of animals in the treated groups	These data suggest a LOEL of 189 mg/m^3 (NOEL = 101 mg/m^3) for subchronic inhalation toxicity.	Prendergast et al., 1967
Vinylidene chloride	75-35-4	**Subchronic toxicity - Summary**								Available data suggest a potential for subchronic inhalation toxicity, with liver and kidney as possible target organs (HEEP, 1986).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Vinylidene chloride	75-35-4	Chronic toxicity	Rats	Inhalation	Vapor	6 hours/day, 5 days/week, for 18 months	Nominal vapor concentrations of 0, 10, and 40 ppm (during first month), 0, 25, and 75 ppm (during remaining 17 months) Interim sacrifices occurred after 1, 6, and 12 months of exposure A 6-month observation period followed the exposure period	85-86/sex/group	No treatment-related changes were observed with respect to appearance and demeanor, hematology, clinical chemistry, or urinalysis. Statistically significant increases in absolute liver (males) and kidney (females) weights were observed in the treated groups at 12 months Organ weights returned to control level by 24 months Increased cumulative incidences (all sacrifices) were observed in midzonal hepatic fatty changes (females, 75 ppm), chronic or acute tracheitis (males and females; 25 and 75 ppm), and chronic murine pneumonia (males and females, 25 and 75 ppm) Both hepatic and pulmonary effects were diminished after cessation of exposure.	This is an inadequate chronic toxicity study; a NOAEL was not identified	A free-standing LOAEL of 25 ppm for respiratory effects in males and females during exposure is supported by these data.	Rampy et al., 1977, 1978, McKenna et al., 1982, Quast et al., 1986
Vinylidene chloride	75-35-4	Chronic toxicity	Mice	Inhalation	Whole-body	4 hours/day, 4-5 days/week for 12 months	0 10 or 25 ppm (maximum tolerated exposure)	30 to 120/sex/ group	Decreased body weight and kidney lesions occurred in high-dose animals, no effects were noted on survival	An inadequate duration of treatment was utilized, but was sufficient to identify effects.	NOAEC = 10 ppm; LOAEC = 25 ppm	Maltoni et al , 1985

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Vinylidene chloride	75-35-4	Chronic toxicity	Mice	Inhalation	Not reported	6 hours/day, 5 days/week for 12 months	0 or 55 ppm	16/sex/exposure	Two males died and had acute toxic hepatitis and tubular necrosis of the renal cortex Decreased body weight and hepatocellular changes were noted in treated mice of both sexes, along with hepatic lesions including focal degeneration and necrosis, microfoci of mononuclear cells, and other	Inadequate because of the use of only one exposure level and a low number of test animals for a short exposure period	Additional groups of 4 mice/sex were sacrificed after 1, 2, 3, 6, and 9 months of treatment with similar results	Lee et al , 1977, 1978
Vinylidene chloride	75-35-4	Chronic toxicity	Mice	Inhalation	Not reported	6 hours/day, 5 days/week for 6 months	0 or 55 ppm	12/sex/exposure	Eleven died or were killed when moribund during the 18-month observation period	Inadequate, because only one exposure level was used in a low number of test animals for a short exposure period	Cause of death was not reported, but tumor incidence did not differ significantly between treated and untreated animals	Hong et al., 1981
Vinylidene chloride	75-35-4	Chronic toxicity	Rats	Inhalation	Not reported	6 hours/day, 5 days/week for 10 months	0 or 55 ppm	15 or 16/sex/group	20/30 died or were killed when moribund during the observation period, as compared to 13/32 deaths among controls	Inadequate because of the short exposure duration and use of too few test animals and treatment levels	Cause of death was not reported, but tumor incidence did not differ significantly between treated and untreated animals.	Hong et al , 1981
Vinylidene chloride	75-35-4	**Chronic toxicity - Summary**								Available data indicate hepatic and pulmonary toxicity (Quast et al , 1986, HEEP, 1986).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Vinylidene chloride	75-35-4	Carcinogenicity	Rats	Oral	Drinking water	2 years	Nominal drinking water concentrations of 0, 50, 100, and 200 ppm (calculated TWA doses of: 0, 7, 10, and 20 mg/kg/day for males; 0, 9, 14, and 30 mg/kg/day for females)	48 rats/sex/group for treated groups; 80 rats/sex for control group	No significant treatment-related carcinogenic effect was observed	This is an adequate assay	Systemic toxicity was indicated by hepatocellular changes at 9 mg/kg/day in females and at 20 mg/kg/day in males	Quast et al., 1983; Rampy et al., 1977; 1978, Humiston et al , 1978
Vinylidene chloride	75-35-4	Carcinogenicity	Rats	Inhalation	Vapor	6 hours/day, 5 days/week, for 18 months	Nominal vapor concentrations of 0, 10, and 40 ppm (during first month), and 0, 25, and 75 ppm (during remaining 17 months) Interim sacrifices occurred after 1, 6, and 12 months of exposure A 6-month observation period followed the exposure period	85-86/sex/group	No treatment-related significant increases in tumors were observed in males or females.	This is an adequate carcinogenicity assay Exposure duration was as in testing guidelines, however, animals were observed for lifetime	A free-standing LOAEL of 25 ppm for respiratory effects in males and females during exposure is supported by these data	Quast et al., 1986.

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Vinylidene chloride	75-35-4	Carcinogenicity	Mice	Inhalation	Vapor	4 hours/day, 4-5 days/week, for 52 weeks	0, 10, and 25 ppm (acute toxic effects in 50, 100, and 200 ppm groups necessitated discontinuing treatment at these exposure concentrations)	30-120 males and females/group	Significant increases in the incidence of renal adenocarcinomas (dose-related) and mammary carcinomas (not dose-related) were observed in males (25 ppm) and females (10 and 25 ppm), respectively. Pulmonary adenomas (not dose-related) were increased in males and females of both treated groups	This is an inadequate carcinogenicity study on the basis of exposure duration, however, it is adequate to qualitatively determine carcinogenicity since the results were positive	This study indicates a potential for carcinogenicity after prolonged inhalation exposure	Maltoni et al., 1985
Vinylidene chloride	75-35-4	Carcinogenicity	Mice	Inhalation	Vapor	6 hours/day, 5 days/week for 12 months	0 or 55 ppm	16/sex/exposure	Increased incidence of hepatic hemangiosarcomas and lung, skin, and liver cell tumors was noted, but the increases were not significantly different from that of controls.	Inadequate because of the use of only one exposure level, and a low number of test animals for a short exposure period	Additional groups of 4 mice/sex were sacrificed after 1, 2, 3, 6, and 9 months of treatment with similar results.	Lee et al., 1977; 1978
Vinylidene chloride	75-35-4	Carcinogenicity	Mice	Inhalation	Vapor	6 hours/day, 5 days/week for 1, 3, or 6 months	0 or 55 ppm	8 or 12/sex/ exposure	No significant increase in incidence of tumors was noted	Inadequate, because only one exposure level was used in a low number of test animals for a short period of time	Negative results were obtained.	Hong et al., 1981

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Vinylidene chloride	75-35-4	Carcinogenicity	Rats	Inhalation	Vapor	4 hours/day, 4-5 days/week for 52 weeks	0, 10, 25, 50, or 100 ppm	30/sex/exposure	Increased total number of rats with mammary tumors in 10 and 100 ppm groups and in total number of rats with fibromas and fibroadenomas in all groups, but a clear dose-response was not seen. Mammary carcinoma incidence in treated groups was not significantly different from that of controls.	Inadequate due to the low number of test animals and short exposure duration.	A clear dose-response was not observed	Maltoni et al , 1985
Vinylidene chloride	75-35-4	Carcinogenicity	Rats	Inhalation	Not reported	4 hours/day, 4-5 days/week for 52 weeks	0, 10, 25, 50, or 100 ppm	30/sex/exposure	Life-time observations indicated incidences of brain tumors (gliomas, meningiomas, or ependymomas) were not significantly increased over control values	Inadequate due to the low number of test animals and short exposure duration.	No evidence of carcinogenicity was seen.	Maltoni et al , 1982
Vinylidene chloride	75-35-4	Carcinogenicity	Rats	Inhalation	Vapor	6 hours/day, 5 days/week for 18 months	0, 10, and 40 ppm for first 42 days, then 25 and 75 ppm for remainder	85-86/sex/exposure	Increased incidence of mammary adenocarcinomas was noted at 25 ppm, but not at 75 ppm.	Inadequate due to the short duration of exposure	An exposure-related response was not seen, so the mammary tumor incidence was not considered treatment-related	Rampy et al., 1977, 1978; McKenna et al , 1982, Quast et al , 1986
Vinylidene chloride	75-35-4	Carcinogenicity	Rats	Inhalation	Not reported	4 hours/day, 5 days/week for a total of 12 months	0 and 200 ppm for 5 months, followed by 100 ppm for 7 months	30-51/sex/group	A significant increase in tumor incidence was not seen	Inadequate because of the short exposure duration and use of too few treatment levels	This is a limited report, and the extent of histological examination was not specified.	Viola and Caputo, 1977

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Vinylidene chloride	75-35-4	Carcinogenicity	Rats	Inhalation	Not reported	6 hours/day, 5 days/week for 12 months	0 or 55 ppm	16/sex/group	A increased incidence of hepatic hemangiosarcomas was noted, but was not significantly different from controls	Inadequate because of the short exposure duration and use of too few test animals and treatment levels	Additional groups of 4 rats/sex were sacrificed after 1, 2, 3, 6, and 9 months of treatment with similar results.	Lee et al , 1977, 1978
Vinylidene chloride	75-35-4	Carcinogenicity	Rats	Inhalation	Not reported	6 hours/day, 5 days/week for 10 months	0 or 55 ppm	16/sex/group	A significant increase in tumor incidence was not seen.	Inadequate because of the short exposure duration and use of too few test animals and treatment levels	Additional groups of 4 to 8 rats/sex were sacrificed after 1, 3, and 6 months of treatment and 12 months observation with similar results.	Hong et al , 1981
Vinylidene chloride	75-35-4	Carcinogenicity	Rats	Oral	Gavage	5 days/week for 104 weeks	0, 1, or 5 mg/kg/day in corn oil	50/sex/group	No significant increase was noted in incidence of tumors with Bonferroni correction and life table analysis; a significantly increased incidence of lymphomas was seen in female mice without the statistical corrections	Inadequate because an MTD was not achieved	Use of a maximum tolerated dose was not demonstrated.	NTP, 1982

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Vinylidene chloride	75-35-4	Carcinogenicity	Mice	Oral	Gavage	5 days/week for 104 weeks	0, 2, and 10 mg/kg/day in corn oil	50/sex/day	No significant increase was noted in incidence of tumors with Bonferroni correction and life table analysis, without these statistical corrections, there were increased incidences of adrenal pheochromocytomas, pancreatic islet-cell adenomas and carcinomas, testes interstitial cell tumors, and subcutaneous fibromas in males and pituitary adenomas in females.	Inadequate because an MTD was not achieved	Use of a maximum tolerated dose was not shown	NTP, 1982
Vinylidene chloride	75-35-4	Carcinogenicity	Rats	Oral	Drinking water	2 years	0, 7, 10, or 20 mg/kg/day (males), 0, 9, 14, or 30 (females)	48/sex/group; 80/sex in controls	Increased incidence of mammary gland fibroadenomas/ adenofibromas in low dose, but no dose-response was noted. A high incidence of these tumors was seen in controls. Mammary carcinomas were not increased; increased incidence of total tumors was seen in males.	This is an adequate carcinogenicity study.	Clear evidence of carcinogenicity was not demonstrated.	Rampy et al., 1977, 1978, Humiston et al., 1978, Quast et al., 1983
Vinylidene chloride	85-35-4	Carcinogenicity	Rats	Oral	Gavage	52 weeks	0, 5, 10, or 20 mg/kg/day in olive oil	50/sex/group, 100/sex/group in controls	No significant increase in incidence of tumors was observed	The study is inadequate because the minimum acceptable duration is not used	A longer exposure duration did not yield positive results in other oral studies.	Maltoni et al., 1985

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Vinylidene chloride	75-35-4	Carcinogenicity	Rats	Oral	Gavage	52 weeks	0 or 0.5 mg/kg/day in olive oil	50/sex/group, 77 to 82/sex/group in controls	No significant increase in incidence of tumors was observed.	The study was inadequate since only one exposure group was used and the exposure duration was too short	Data from other oral studies indicate that this dose was well below the MTD.	Maltoni et al., 1985
Vinylidene chloride	75-35-4	Carcinogenicity	Rats	Oral	Not reported, but appears to be gavage	52 to 59 weeks	0, 0.5, 5, 10 or 20 mg/kg/day in olive oil	50/sex/group, 175/sex/group in controls	Incidence of brain tumors (gliomas, meningiomas, or *ependymomas*) were not significantly increased over controls	Inadequate because of short exposure duration	Negative findings agree with other oral findings	Maltoni et al., 1982
Vinylidene chloride	75-35-4	Carcinogenicity	Rats	Oral	Gavage	1 day/week for 120 weeks	0 or 150 mg/kg on day 17 of gestation, from weaning, 0 or 50 mg/kg in olive oil	64 to 90 males and females	Exposure in utero followed by weekly treatment from weaning did not lead to a significant increase in incidence of tumors An increased prevalence of hyperplastic nodules was seen in the liver.	*Inadequate study*	Animals were treated once/week, which is not a standard TSCA guidelines regimen. Treatment has no effect on litter size or pre-weaning deaths.	Ponomarkov and Tomatis, 1980
Vinylidene chloride	75-35-4	*Carcinogenicity*	*Mice*	*Dermal*	Topical application	3 applications/ week for life	0, 40, or 121 mg/application in acetone	30 females/group	No local papillomas or carcinomas, nor significant increase in incidence of distant tumors	Inadequate study	Animals were not treated the minimum recommended 6 hours/day.	Van Duuren et al., 1979
Vinylidene chloride	75-35-4	**Carcinogenicity - Summary**								**Available data suggest a potential for carcinogenicity (HEEP, 1986).**		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Vinylidene chloride	75-35-4	Developmental Neurotoxicity	Rats	Inhalation	Not reported	23 hours/day, days 6-16 of gestation, and sacrificed on gestation day 20	0, 57, and 283 ppm (0, 230, and 1,142 mg/m^3)	13 to 18 treated and 17 control litters, with tests conducted on 2/litter/exposure group, one male and one female	Tests were conducted from postnatal day 1 to 12 or 14. No effects were observed in the following behavior tests: surface righting, pivoting, auditory startle, bar holding, righting in air, visual placing, swimming, physical maturation or activity tests	This is an adequate developmental behavioral study	A feed restricted control group was included because all treated dams ate less and had lower body weights than controls	Short et al , 1977a
Vinylidene chloride	75-35-4	**Neurotoxicity - Summary**								Some information is available that indicates neurological effects (signs of inebriation) in humans and animals after acute inhalation exposure to high concentrations of vinylidene chloride (ATSDR, 1992) A developmental behavioral study showed no effects of treatment		
Vinylidene chloride	75-35-4	Developmental toxicity	Rats	Inhalation	Not reported	7 hours/day, gestation days 6-15	0, 20, 80, and 160 ppm (0, 80, 320, and 630 mg/m^3)	30-44 presumed-pregnant females in treated groups, 20-47 in concurrent controls for each treated group	Maternal effects were decreased food consumption and decreased body weight gain (days 6-9) in the 2 highest exposure groups, and increased liver weight in the high-exposure group. Significant ($p < 0.05$) changes in the incidence of delayed skull and cervical vertebra ossification and wavy ribs were observed in the 80 and 160 ppm exposure groups.	This is an adequate developmental toxicity study	A LOAEL of 80 ppm (NOAEL = 20 ppm) for alterations in skeletal development and maternal toxicity was determined.	Murray et al , 1979

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Vinylidene chloride	75-35-4	Developmental toxicity	Rabbits	Inhalation	Not reported	7 hours/day, gestation days 6-15	0, 80, and 160 ppm (0, 320, and 630 mg/m^3)	18-22 presumed-pregnant rabbits in treated groups, 16 in control group	Maternal effects were a significant decrease in body weight gain in the 160 ppm group, and increased liver weight at 80 ppm (statistically significant) and 160 ppm (not statistically significant) groups There was an increased incidence of resorptions and skeletal alterations at 160 ppm	This is a marginally adequate developmental toxicity study Only 2 exposure levels were tested.	Maternal and developmental toxicity was seen at 160 ppm and maternal toxicity at 80 ppm	Murray et al , 1979

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Vinylidene chloride	75-35-4	Developmental toxicity	Rats	Inhalation	Not reported	23 hours/day, days 6-16 of gestation, and sacrificed on gestation day 20	0, 15, 57, 300, and 449 ppm (0, 59, 230, 1190, and 1780 mg/m^3)	Approximately 20/ exposure group, 60 in the control group	Maternal toxicity was noted at all test levels (decreased body weight gain and food consumption); 25% maternal deaths occurred at 300 ppm and higher. There was an increased incidence of resorptions at 57 and 449 ppm, a decrease in number of fetuses/dam at 300 ppm, and a decrease in fetal weight at 57, 300, and 449 ppm. The incidence of lateral ventricle hydrocephalus increased at 15 and 57 ppm (statistically significant) and also at 300 ppm (not statistically significant). Also, a significant increase in incomplete sternebrae ossification was observed in the 15, 57, and 300 ppm groups	This is a marginally adequate developmental toxicity study. A NOAEC was not identified for maternal and developmental toxicity.	No effects were observed in behavioral tests of the pups	Short et al., 1977a

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Vinylidene chloride	75-35-4	Developmental toxicity	Mice	Inhalation	Not reported	23 hours/day, days 6-16 of gestation, and sacrificed on gestation day 17	0, 15, 30, 57, 144, and 300 ppm (0, 59, 120 230, 571, and 1190 mg/m^3) 56 and 283 ppm (g d 8-20)	Approximately 20/ exposure group, 60 in the control group	Maternal mortality was 100% at 144 and 300 ppm, and decreased food consumption with decreased weight gain occurred in groups exposed to ≥ 30 ppm. There were no viable fetuses at 30 ppm or higher. Also, a significant increase in incomplete sternebrae ossification was observed in the 15 ppm group.	This is an inadequate developmental toxicity study because of severe maternal toxicity	A NOAEC was not identified for fetal effects	Short et al , 1977a
Vinylidene chloride	75-35-4	Developmental toxicity	Mice	Inhalation	Not reported	23 hours/day gestation days (g d) 6-15, 8-15, 10-15, 12-15 6-9, 9-12, 12-15, and 15-17	54 ppm (g d 6-15), 41, 54, and 74 ppm (g d 8-15), 41 ppm (g d 10-15), 54 ppm (g d 10-15 and 12-15), 56 81, and 112 ppm (g d 6-9, 9-12, 12-15, and 15-17)	Not reported	Maternal toxicity (decreased weight gain) was evidence at these shorter exposure periods, but incidences of resorption were decreased Developmental toxicity (increased incidences of cleft palate) was seen at 54 ppm levels, after treatment on gestation days 10-15 and 12-15 Delayed ossification, immature skin, and hematomas were also noted in various groups (not specified).	Inadequate study. Maternal toxicity occurred at nearly all concentrations	The authors were attempting to eliminate the severe maternal toxicity observed in other studies by treatment for shorter times during gestation, along with identifying the sensitive times during gestation	Short et al , 1977a
Vinylidene chloride	75-35-4	**Developmental toxicity - Summary**								Adequate or marginally adequate data are available for maternal and developmental effects in two species		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Vinylidene chloride	75-35-4	Reproductive toxicity	Rats	Inhalation	Not reported	6 hours/day, 5 days/week, 11 weeks premating	55 ppm, control group not reported	12 males mated with 1 or 2 females	Male fertility and the incidence of pre- and post-implantation losses in females were not affected by treatment; however, there was a significant decrease in number of pregnancies.	This is an adequate dominant lethal test, but does not fully evaluate the reproductive effects.	There were 20 mated females in the treated and 24 in the control group	Short et al., 1977b
Vinylidene chloride	75-35-4	Reproductive toxicity	Rats	Oral	Drinking water	3-generation study Parental animals were exposed for 100 days before mating (after raising one litter, they were mated again for a second litter) and F_{1b} rats were exposed after weaning. Exposure continued with the F_2 and F_3 animals	Drinking water concentrations were 0, 50, 100, or 200 ppm	Parental: 10 males, 20 females in treated groups, 15 males, 30 females in the control group. Number of animals that were bred in subsequent generations ranged from 20 to 24 in the treated group	No clear dose-related reproductive effects were observed in any generation.	These concentrations caused mild dose related lesions in the liver	A free-standing NOEL of 200 ppm for reproductive effects after oral exposure is indicated by these data.	Nitschke et al , 1983
Vinylidene chloride	75-35-4	**Reproductive toxicity - Summary**								Available information suggests low reproductive toxicity potential, although adequate inhalation studies were not located (HEEP, 1986; ATSDR, 1992).		
Vinylidene chloride	75-35-4	**Pharmacokinetics - Summary**								Data are available regarding the pharmacokinetics of inhaled or ingested vinylidene chloride. Absorption appears to be rapid and complete, pulmonary absorption appears to be biphasic with a rapid first-order phase. Distribution is primarily to the liver and kidneys, and significant accumulation does not seem to occur, up to 70-80% of absorbed oral and inhalation doses are excreted within 24 hours (HEEP, 1986)		

REFERENCES

ATSDR (Agency for Toxic Substances and Disease Registry) "Toxicological Profile on 1,1-Dichloroethene." (1992)

Carpenter, C P , Smyth, H F , and Pozzani, U C "The assay of acute vapor toxicity, and the grading and interpretation of results on ninety-six chemical compounds " *Journal of Industrial Hygiene and Toxicology* 31(6):343-346 (1949).

HEEP "Health and Environmental Effects Profile for Dichloroethenes " US Environmental Protection Agency (1986)

Hong, C B , Winston, J M , Thornburg, L P , Lee, C C , and Woods, J S "Follow-up study on the carcinogenicity of vinyl chloride and vinylidene chloride in rats and mice tumor incidence and mortality subsequent to exposure " *Journal of Toxicology and Environmental Health* 7(6):909-924 (1981)

Humiston, C G., Quast, J F , Wade, C E, Ballard, J , Beyer, J E , and Lisowe, R W "Results of a two-year toxicity and oncogenicity study with vinylidene chloride incorporated in the drinking water of rats " MCA Report No. VCD 1 3-Tox-Orl-Dow. Toxicology Research Laboratory Health and Environmental Research, Dow Chemical USA, Midland, MI (1978)

Lee, C C , Bhandari, J C , Winston, J M , House, W B , Peters, P J., Dixon, R L , and Woods, J S "Inhalation toxicity of vinyl chloride and vinylidene chloride " *Environmental Health Perspectives* 21 25-32 (1977)

Lee, C C , Bhandari J C , Winston, J M , House, W B , Dixon, R L, and Woods, J S "Carcinogenicity of vinyl chloride and vinylidene chloride " *Journal of Toxicology and Environmental Health* 4(1) 15-30 (1978)

Maltoni, C , Ciliberti A , and Carretti, D "Experimental contributions in identifying brain potential carcinogens in the petrochemical industry " *Annals of the New York Academy of Science* 381 216-249 (1982)

Maltoni, C , Lefemine, G , Chieco, P., Cotti, G., and Patella, V "Experimental research on vinylidene chloride carcinogenesis " In *Archives of Research on Industrial Carcinogenesis* Volume 3 Maltoni, C , and Mehlman, M.A , eds Princeton, NJ: Princeton Scientific Publishers pp 16-25 and 41-48 (1985)

McKenna, M J , Quast, F, Ballmer, M.F., and Rampy, L.W. "Vinylidene chloride· A chronic inhalation toxicity and oncogenicity study in rats " Chemical Manufacturers Association Report No VDC 1 3 September 8, 1982.

Murray, F J Nitschke, K D , Rampy, L, and Schwetz, B "Embryotoxicity and fetotoxicity of inhaled or ingested vinylidene chloride in rats and rabbits " *Toxicology and Applied Pharmacology* 49:189-202 (1979)

Nitschke, K D., Smith, F A , Quast, J F , Norris, J M , and Schwetz, B A "A three-generation rat reproductive toxicity study of vinylidene chloride in the drinking water " *Fundamental and Applied Toxicology* 3 75-79 (1983).

NTP, National Toxicology Program "Carcinogenesis bioassay of vinylidene chloride in F344/N rats and B6C3F1/N mice (gavage study) " NTP Technical Report No 228 (1982)

Ott, M G , Fishbeck, W A , Townsend, J C., and Shneider, E.J. 1976 "A health study of employees exposed to vinylidene chloride " *Journal of Occupational Medicine* 18(11) 735-738

Ponomarkov, V , and Tomatis, L "Long-term testing of vinylidene chloride and chloroprene in rats " *Oncology* 37(3) 136-141 (1980)

Prendergast, J A , Jones, R A , Jenkins, L.J. Jr , and Siegel, J "Effects on experimental animals of long-term inhalation of trichloroethylene, carbon tetrachloride, 1,1,1-trichloroethane, dichlorodifluoromethane, and 1,1-dichloroethylene." *Toxicology and Applied Pharmacology* 10(2):270-289 (1967)

Quast, J F., Humiston, C G., Wade, C E , et al "A chronic toxicity and oncogenicity study in rats and subchronic toxicity study in dogs on ingested vinylidene chloride " *Fundamental and Applied Toxicology* 3(1) 55-62 (1983).

Quast, J F., McKenna, M J , Rampy, L.W , and Norris, J.M "Chronic toxicity and oncogenicity study on inhaled vinylidene chloride in rats " *Fundamental and Applied Toxicology* 6.105-144 (1986)

Rampy, L W , Quast, J F , Humiston, C G., Balmer, M F , and Schwetz, B A. "Interim results of two-year toxicological studies in rats of vinylidene chloride incorporated in the drinking water or administered by repeated inhalation " *Environmental Health Perspectives* 21:33-43 (1977).

Rampy, L W Quast, J F , Humiston, C G., Balmer, M F., and Schwetz, B.A "Results of 2-year toxicological studies in rats of vinylidene chloride incorporated in the drinking water or administered by repeated inhalation." *Toxicology and Applied Pharmacology*. 45(1) 244-245 (1978)

Reitz, R H , Watanabe, P G , McKenna, M.J , Quast, J F., and Gehring, P J "Effects of vinylidene chloride on DNA synthesis and DNA repair in the rat and mouse: A comparative study with dimethylnitrosamine " *Toxicology and Applied Pharmacology* 52 357-370 (1980)

Table of Toxicity Data for HAPs (continued)

Short, R D. Jr , Minor, J L., Winston, J M , Fertuson, B , and Unger, T "Toxicity studies of selected chemicals Task II. The developmental toxicity of vinylidene chloride inhaled by rats and mice during gestation Prepared by Midwest Research Institute, Kansas City, MO for the US EPA, Washington, DC EPA-560/6-77-022 (1977a)

Short, R D Jr , Minor, J L , Winston J M , and Lee, C.-C "A dominant lethal study in male rats after repeated exposures to vinyl chloride or vinylidene chloride " *Journal of Toxicology and Environmental Health* 3 965-968 (1977b)

Siegel, J , Jones, R A , Coon, R A , and Lyon, J P "Effects on experimental animals of acute, repeated and continuous inhalation exposures to dichloroacetylene mixtures " *Toxicology and Applied Pharmacology* 18(1).168-174 (1971).

Viola, P L and Caputo, A "Carcinogenicity studies on vinylidene chloride " *Environmental Health Perspectives* 21 45-47 (1977)

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
1,1,2-Trichloroethane	79-00-5	Epidemiology (Cohort study)	Humans	Occupational	Not reported	Not reported	Not reported	58 solvents/EDC plant workers (55 males and 3 females) and 38 contractors (sex not reported)	No effect of occupational exposure to 1,1,2-trichloroethane (among at least 15 other solvents) on serum chemistry including SGPT and cholesterol was reported, as compared to an unspecified range of reference values (the source of the range was not reported).	This study was inadequate because of the lack of exposure information	This document was a sanitized summary report of a review of internal health records at Dow Chemical Co. submitted under TSCA to OPPT/EPA	Dow Chemical Company, 1991
1,1,2-Trichloroethane	79-00-5	Epidemiology (Cohort study)	Humans	Occupational	Not reported	>1 year	Not reported	270 men (28 known deceased); comparison groups were all white males in United States during 1944-1982 (28 deaths compared to 29 15 expected deaths), and all white males in Texas during 1965-1982 (24 deaths compared to 19 37 expected deaths).	Total deaths and cancer deaths were not related to occupational exposure to 1,1,2-trichloroethane (among 15 other chemicals) in 270 workers at a Texas manufacturing plant during 1944-1982.	This study was inadequate because of the lack of exposure information.	The study had 80% power to detect a 1 5-, 1.8, and 2 4-fold risk in all deaths, circulatory deaths, and cancer deaths, respectively.	Dow Chemical Company, 1989
1,1,2-Trichloroethane	79-00-5	**Epidemiology - Summary**								No adequate epidemiological studies on 1,1,2-trichloroethane were located [ATSDR, 1989, CHEMTRACK, 7/93, U.S. EPA, 1984a (HEA, Final Draft), U S EPA, 1984b (EPA 540/1-86-045), IARC, 1991; TSCATS, 9/93]		
1,1,2-Trichloroethane	79-00-5	Acute toxicity	Rats	Inhalation	Not specified	6 hours	Not reported	Males; number not specified	LC_{50} = 1654 ppm.	This study inadequately reported methods and results.	This was a brief summary of an acute toxicity study, exposure was whole-body.	Bonnet et al., 1980

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
1 1 2-Trichloroethane	79-00-5	Acute toxicity	Rats	Inhalation	Vapor	4 hours	500 ppm, control group not reported	6/group; sex not reported	1/6 rats died.	This study inadequately reported methods and results	This was a brief summary of a comparison between chemicals with respect to mortality due to inhalation; no LC_{50} or NOAEL was indicated	Union Carbide Corporation, 1987a
1,1,2-Trichloroethane	79-00-5	Acute toxicity	Rats	Inhalation	Vapor	8 hours	1000, 2000 ppm; control group not reported	6/group, sex not reported	Mortality was 3/6 in rats exposed to 1000 ppm, and 6/6 in rats exposed to 2000 ppm; all rats apparently died within the 8-hour exposure period	This study inadequately reported methods and results.	This was a brief summary of a comparison between chemicals with respect to mortality due to inhalation, no LC_{50} or NOAEL was indicated	Union Carbide Corporation, 1987d; Union Carbide Corporation, 1961
1,1 2-Trichloroethane	79-00-5	Acute toxicity	Mice	Inhalation	Not reported	6 hours	Exposure levels not specified	Number and sex not specified	LC_{50} = 416 ppm	Insufficient information is available for evaluation	This was a brief summary of an acute toxicity study, a NOAEL was not indicated.	Gradiski et al., 1978
1,1,2-Trichloroethane	79-00-5	Acute toxicity	Mice	Inhalation	Not reported	3 hours	800 ppm (control not reported)	Number and sex not specified	Transient decreases in plasma triglycerides and ATP and an increase in liver triglycerides were observed SGPT was also increased, and remained elevated through 20 hours post-dosing	Insufficient information was available for evaluation	This was a brief summary of an acute toxicity study, no NOAEL was suggested from these data, and it is not clear that all exposure levels were reported	Takahara, 1986

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
1,1,2-Trichloroethane	79-00-5	Acute toxicity	Rats	Inhalation	Not reported	7 hours	100, 250, or 500 ppm (control group not reported)	Females, number not specified	Mortality in over 50% of rats in the 250 and 500 ppm groups was reported; necropsy of survivors revealed "marked" kidney and liver damage. At 100 ppm, all survived but were not microscopically examined	Adequacy could not be evaluated, methods and results were inadequately reported	This is a summary of unpublished data, no NOAEL was suggested from these data, since no histopathology was conducted on the lowest exposure group	Torkelson and Rowe, 1981
1,1,2-Trichloroethane	79-00-5	Acute toxicity	Rats	Inhalation	Not reported	1, 2, or 4 hours	250 ppm (control group not reported)	Females, number not specified	Liver and kidney necrosis were observed after a 4-hour exposure, but "apparently" not after 1- or 2-hour exposures.	Adequacy could not be evaluated, methods and results were inadequately reported.	This is a summary of unpublished data; a NOAEL was not suggested from the data and only a single dose level and a limited number of endpoints were reported.	Torkelson and Rowe, 1981
1,1,2-Trichloroethane	79-00-5	Acute toxicity	Rats	Inhalation	Vapor	8 hours	Not specified	6 females/group	8-hour LC_{50} = 5.45 mg/L (1,000 ppm) (calculated by the moving average method).	This study was limited by a failure to report exposure levels, and insufficient endpoints examined.	A NOAEL could not be determined	Pozzani et al., 1959
1,1,2-Trichloroethane	79-00-5	Acute toxicity	Rats	Inhalation	Vapor	2 hours	0 or 890 ppm	5 males/group	No treatment-related effects were observed with respect to relative liver weight, serum glucose-6-phosphatase, SGPT, or SGOT	This study was limited by an insufficient number of exposure levels used and endpoints examined.	This study indicates a free-standing NOEL of 890 ppm for hepatotoxicity.	Carlson, 1973

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
1,1,2-Trichloroethane	79-00-5	**Acute toxicity - Summary**								No adequate acute inhalation toxicity studies were located [ATSDR, 1989; CHEMTRACK, 7/93; U.S EPA, 1984a (HEA, Final Draft); U.S EPA, 1984b (EPA 540/1-86-045); IARC, 1991, TSCATS, 9/93], however, available data indicate that acute renal and hepatic toxicity and death result from single exposures of ≥250 ppm for ≥4 hours.		
1,1,2-Trichloroethane	79-00-5	Subchronic toxicity	Rats	Inhalation	Vapor	7 hours/day, 5 days/week, 6 months	0 or 84 ppm	12 males and 12 females/group (5 replacement rats were used because of deaths in the first month)	The mortality rate among exposed rats was 62% (18/29), although severe lung infection among some treated rats confounded the interpretation. "Major" damage occurred in liver, kidney, and lung in 55%, 52%, and 59% of exposed rats, compared to respective incidences of 46%, 25%, and 29% in controls. No notable differences with the control group were observed with respect to body length, liver and kidney weights, icterus index, liver fat, and blood cytology	This is an inadequate study due to the lung infection problem and the deficiency in number of exposure levels	The replacement rats were exposed for 45 periods	Union Carbide Corporation, 1987b

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
1,1,2-Trichloroethane	79-00-5	Subchronic toxicity	Dogs	Inhalation	Vapor	7 hours/day, 5 days/week, 6 months	0 or 84 ppm	1 male/group	No notable changes from pre-exposure values were observed with respect to bromsulfalein retention, serum phosphatase level, blood urea nitrogen, and blood cytology. A "light cloudy swelling" of the liver and "light" congestion of the lungs were noted at necropsy, while liver and kidney weights were not remarkable	This is an inadequate study due to deficiency in number of exposure levels and number of dogs exposed per level	Clinical values were determined monthly except for the last month where they were determined weekly	Union Carbide Corporation, 1987b
1,1,2-Trichloroethane	79-00-5	Subchronic toxicity	Rats	Inhalation	Vapor	6 months, frequency not reported	0 or 100 ppm	4 males, 7 females in the treated group, 5 males, 6 females in the control group	Mean liver and kidney weights as a percent of the controls were 93.0% and 94.1%, respectively. No other endpoints were reported.	Methods and results were inadequately reported, only one concentration and too few animals were tested	This report consisted of excerpts of tables from a large report	Union Carbide Corporation, 1987c
1,1,2-Trichloroethane	79-00-5	Subchronic toxicity	Mice	Oral	Gavage	14 days	0, 3.8, and 38 mg/kg	8-12/sex/exposure group	Brain, thymic, and testicular weights were significantly increased in males at 38 mg/kg.	This appears to be an adequate study.	LD_{50} is 378 mg/kg for males and 491 mg/kg for females. Doses tested were 1/10 and 1/100 of LD_{50}	White et al., 1985a, White et al., 1985b
1,1,2-Trichloroethane	79-00-5	Subchronic toxicity/ Immunotoxicity	Mice	Oral	Gavage	14 days	0, 3.8, and 38 mg/kg	8-12/sex/exposure group	No alterations were noted in humoral or cell-mediated immune status.	This appears to be an adequate study.	Doses tested were 1/10 and 1/100 of LD_{50}.	Sanders et al., 1985; White et al., 1985b

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
1,1,2-Trichloroethane	79-00-5	Subchronic toxicity	Mice	Oral	Drinking water	90 days	0, 4 6, 46, and 305 mg/kg for males, 0, 3 9, 44, and 384 mg/kg for females	8-12/sex/exposure group	There was a concentration dependant reduction in weight gain in males and alterations in hepatic microsomal enzyme activities and serum enzyme levels in both sexes. A significant decrease in hematocrit and hemoglobin levels in females was noted.	This appears to be an adequate study	The liver was a target of toxicity in both sexes	White et al , 1985a; White et al., 1985b
1,1,2-Trichloroethane	79-00-5	Subchronic toxicity/ Immunotoxicity	Mice	Oral	Drinking water	90 days	0, 4 6, 46, and 305 mg/kg for males, 0, 3 9, 44, and 384 mg/kg for females	8-12/sex/exposure group	Cell-mediated immunity was unaltered in both sexes and humoral immune status was depressed in both sexes Spleen lymphocyte responsiveness LPS (B cell mitogen) was significantly decreased in females. Macrophage function was depressed in males.	This appears to be an adequate study	There are sex differences in the ability of 1,1,2-trichloroethane to alter immune function.	Sanders et al., 1985; White et al., 1985b
1,1,2-Trichloroethane	79-00-5	Subchronic toxicity	Rats, guinea pigs, and rabbits	Inhalation	Not reported	7 hours/day, 5 days/week, 6 months	15 ppm (control group not reported)	Males and females, number not specified	No treatment-related effects were observed with respect to growth, mortality, organ weights, hematology, clinical chemistry, and histopathology.	Inadequate because only one concentration and too few animals were tested	This is a summary of unpublished data.	Torkelson and Rowe, 1981
1,1,2-Trichloroethane	79-00-5	**Subchronic toxicity - Summary**								No adequate subchronic inhalation toxicity studies were located [ATSDR, 1989, CHEMTRACK, 7/93, U S EPA, 1984a (HEA, Final Draft), U S. EPA, 1984b (EPA 540/1-86-045), IARC, 1991, TSCATS, 9/93]		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
1,1,2-Trichloroethane	79-00-5	**Chronic toxicity - Summary**								No chronic inhalation toxicity studies on 1,1,2-trichloroethane were located [ATSDR, 1989, CHEMTRACK, 7/93; U S EPA, 1984a (HEA, Final Draft), U S EPA, 1984b (EPA 540/1-86-045); IARC, 1991, TSCATS, 9/93]		
1,1,2-Trichloroethane	79-00-5	Carcinogenicity	Mice	Oral	Gavage	5 days/week, 78 weeks; 13-week post-treatment observation period	0, 150, or 300 mg/kg/day in corn oil for 8 weeks, then 0, 200, and 400 mg/kg/day for the remaining 70 weeks (TWA 0, 195, and 390 mg/kg/day, calculated for 7 days/week); both vehicle and untreated control groups were used.	50/sex	Hepatocellular carcinomas were increased in all treated groups ($p<0.01$), adrenal pheochromocytomas were present in 8/48 and 12/43 high-dose males and females, respectively, but in no other group 50% mortality was achieved in each treated group during the period 58-90 weeks after initiation of dosing.	This assay is limited by the alteration of dose levels in mid-treatment and the brevity of the treatment period. However, the remaining methods and results appear adequate as a qualitative indicator of carcinogenicity	A single technical grade batch of the test substance was used; results of purity testing ranged between 91-99% over 1 year; impurities were not specified.	NCI, 1978
1,1,2-Trichloroethane	79-00-5	Carcinogenicity	Rats	Oral	Gavage	5 days/week, 78 weeks, 35-week post-treatment observation period	0, 35, and 70 mg/kg/day in corn oil for 20 weeks, then 0, 50, and 100 mg/kg/day for the remaining 58 weeks (TWA: 0, 46, and 92 mg/kg/day calculated for 7 days/week); both vehicle and untreated control groups were used.	50/sex	No significant increase in tumor incidence was found in males or females 50% mortality was achieved in each dose group during the period 96 to >105 weeks after initiation of dosing.	This assay is limited by the alteration of dose levels in mid-treatment and an abbreviated treatment period. However, the remaining methods and results appear adequate.	A single technical grade batch of the test substance was used, results of purity testing ranged between 91-99% over 1 year, impurities were not specified.	NCI, 1978

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
1,1,2-Trichloroethane	79-00-5	**Carcinogenicity - Summary**								Carcinogenicity was demonstrated in mice but not in rats (NCI, 1978), although the exposure levels in the rat assay are significantly lower than in the mouse assay and neither study strictly followed TSCA guidelines. A review of other sources (ATSDR, 1989, CHEMTRACK 7/93, IARC, 1991; TSCATS, 9/93) revealed no further carcinogenicity data		
1,1,2-Trichloroethane	79-00-5	Neurotoxicity	Mice	Oral	Gavage (in water/corn oil)	Once	100 mg/kg; other dose levels not specified	Male and female mice, number/group not reported	128 mg/kg caused reversible "motor impairment" in 50% of treated mice (although neither this dose level nor higher dose levels were reported in the methods). The peak effect apparently occurred 5 minutes after dosing. Results of necropsy were not reported. "Taste aversion" (not elaborated in study report) occurred in the 100 mg/kg dose group.	This study is limited by insufficient reporting of methods and results	These data do not support a NOAEL, since the dose levels were not clear.	Borzelleca, 1983
1,1,2-Trichloroethane	79-00-5	Neurotoxicity	Mice	Inhalation	Vapor	4 hours	Not reported	10 males/group	418 ppm of 1,1,2-trichloroethane was required for a 50% elevation in the clonic seizure threshold dose of pentetrazole	This study is limited by failure to report the exposure levels tested, and by the failure to examine sufficient endpoints.	This is a translation of a French study; these data do not support a NOAEL, since the dose levels were not clear	De Ceaurriz et al., 1981
1,1,2-Trichloroethane	79-00-5	**Neurotoxicity - Summary**								No adequate inhalation or oral neurotoxicity studies on 1,1,2-trichloroethane were located [ATSDR, 1989; CHEMTRACK, 7/93, U.S. EPA, 1984a (HEA, Final Draft); U.S. EPA, 1984b (EPA 540/1-86-045), IARC, 1991, TSCATS, 9/93], although available data are suggestive of neurological effects.		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
1,1,2-Trichloroethane	79-00-5	Chernoff/ Kavlock postnatal mouse screening test	Mice	Oral	Gavage	Once/day, gestation days 8-12	0 or 350 mg/kg/day in corn oil	30 timed-pregnant mice	No treatment-related effects were observed with respect maternal toxicity, number of litters born, number of litters resorbed, number live pups/litter, number dead pups/litter, pup survival, live pup weight, and pup weight gain	This is an adequate screening test, but is not adequate to evaluate developmental toxicity since malformations were not studied.	The major purpose of this study was to test the utility and accuracy of a developmental toxicity screen with numerous chemicals, including 1,1,2-trichloroethane	Seidenberg et al., 1986, Seidenberg and Becker, 1987
1,1,2-Trichloroethane	79-00-5	**Developmental toxicity - Summary**								No adequate inhalation or oral developmental toxicity studies on 1,1,2-trichloroethane were located [ATSDR, 1989, CHEMTRACK, 7/93, U.S EPA, 1984a (HEA, Final Draft); U S. EPA, 1984b (EPA 540/1-86-045); IARC, 1991; TSCATS, 9/93].		
1,1,2-Trichloroethane	79-00-5	**Reproductive toxicity - Summary**								No inhalation or oral reproductive toxicity studies on 1,1,2-trichloroethane were located [ATSDR, 1989; CHEMTRACK, 7/93; U.S. EPA, 1984a (HEA, Final Draft); U S EPA, 1984b (EPA 540/1-86-045) IARC, 1991; TSCATS, 9/93]		
1,1,2-Trichloroethane	79-00-5	***Pharmacokinetics - Summary***								The blood/gas partition coefficient of 1,1,2-trichloroethane in rats and humans is suggestive of rapid absorption after inhalation exposure (IARC, 1991); data concerning respiratory and urinary elimination of radioactive label in humans after single-breath inhalation exposure to ^{36}Cl-labelled 1,1,2-TCE are available (ATSDR, 1989, IARC, 1991). Other data are available concerning distribution, metabolism, and excretion of 1,1,2-TCE after inhalation exposure, and after exposure by other routes (ATSDR, 1989, IARC, 1991)		

REFERENCES

ATSDR. (Agency for Toxic Substances and Disease Registry). "Toxicological Profile on Trichloroethylenes " (1989).

Bonnet, P., Francin, J M., Gradiski, D., Raoult, G., and Zissu, D. "Determination of the LC_{50} of the principal chlorinated aliphatic hydrocarbons in the rat " *Arch Mal Prof* 41 317-321 (1980)

Borzelleca, J F "A review of volatile organic contaminant data." *Proceedings of the American Water Works Association Water Quality Technical Conference* pp 225-244 (1983)

Carlson G P "Effect of phenobarbital and 3-methylcholanthrene pretreatment on the hepatotoxicity of 1,1,1-trichloroethane and 1,1,2-trichloroethane " *Life Sciences* 13 67-73 (1973)

Table of Toxicity Data for HAPs (continued)

CHEMTRACK National Toxicology Program Results Report "Results, status and publication information on all NTP chemicals produced from NTP CHEMTRACK system " July (1993).

De Ceaurriz, J C , Micillino, J C , Bonnet, P , and Guenier, J P "Sensory irritation caused by various industrial airborne chemicals " *Toxicology Letters* 9:137-143 (1981)

Dow Chemical Company "Mortality among Dow Chemical employees of a Texas operations per-let manufacturing plant with cover letter dated 050389 " TSCA 8D submission 86-890000215, microfiche number OTS0516752 Washington, DC OPPT, US EPA (1989)

Dow Chemical Company. "Letter from Dow Chemical Company to USEPA submitting studies on health effects of multiple chemicals on workers at several plant sites " TSCA 8D submission 86-910000955S, microfiche Number OTS0530632 Washington, DC: OPPT, US EPA (1991).

Gradiski, D , Bonnet, P. Raoult, G , Magadur, J L , and Francin, J M "Compared acute pulmonary toxicity of the main chlorinated aliphatic solvents " *Arch Mal Prof Med Trav Secur Soc.* 39 249-257 (1978).

IARC (International Agency for Research on Cancer) Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans "Chlorinated drinking-water, chlorination by-products; some other halogenated compounds, cobalt and cobalt compounds" 52:337-359 (1991).

NCI National Cancer Institute "Bioassay of 1,1,2-trichloroethane for possible carcinogenicity " Technical Report Series Number 74 (1978)

Pozzani, U C , Weil, C S , and Carpenter, C P "The toxicological basis of threshold limit values: 5 The experimental inhalation of vapor mixtures by rats, with notes up on the relationship between single dose inhalation and single dose oral data." *American Industrial hygiene Association Journal.* 20.364-369 (1959)

Sanders, V M , White, K L , Shopp, G M , and Munson, A.E "Humoral and cell-mediated immune status of mice exposed to 1,1,2-trichloroethane." *Drug and Chemical Toxicology* 8(5) 357-372 (1985).

Seidenberg, J M , Anderson, D G., and Becker, R A. "Validation of an *in vivo* developmental toxicity screen in the mouse " *Teratogenesis Carcinogenesis, and Mutagenesis.* 6 361-374 (1986)

Seidenberg, J M , and Becker, R A "A summary of the results of 55 chemicals screened for developmental toxicity in mice " *Teratogenesis Carcinogenesis, and Mutagenesis* 7:17-28 (1987)

Takahara, K "Experimental study on toxicity of trichloroethane III Changes in liver function of mice after exposure to 1,1,1- and 1,1 2-trichloroethane " *Okayama Igakkai Zasshi* 98 1099-1109 (1986).

Torkelson, T R. and Rowe, V K "Halogenated aliphatic hydrocarbons; 1,1,2-Trichloroethane" In: *Patty's Industrial Hygiene and Toxicology* Third revised edition, Volume IIB Torkelson, T R , and Rowe, V K., eds New York, NY John Wiley and Sons pp 3510-3513 (1981).

TSCATS (Toxic Substances Control Act Test Submissions) Database (1993)

Union Carbide Corporation "Initial submission Progress report for the month ending August 31, 1961 with cover letter dated 052892 " TSCA 8E submission 88-920003273, microfiche Number OTS0536615 Washington, DC: OPPT, US EPA (1961).

Union Carbide Corporation "Acute inhalation toxicity of 1,1,2-trichloroethane and 1,1,2,2-tetrachloroethylene in rats " TSCA 8D submission 86-870001395, microfiche Number OTS0515557. Washington, DC: OPPT, US EPA (1987a)

Union Carbide Corporation "Repeated exposure of rats and dogs to vapors of eight chlorinated hydrocarbons " TSCA 8D submission 86-870001397, microfiche Number OTS0515559 Washington, DC OPPT, US EPA (1987b)

Union Carbide Corporation "Recalculation of liver and kidney weights previously reported with revised conclusions on the toxicity of eight chlorinated hydrocarbons." TSCA 8D submission 86-870001399, microfiche Number OTS0515561. Washington, DC OPPT, US EPA (1987c).

Union Carbide Corporation "Inhalation toxicity of tetrachloroethylene and 1,1,2-trichloroethane in rats and rabbit skin irritation of toluene diisocyanate " TSCA 8D submission 86-870001427, microfiche Number OTS0515589 Washington, DC OPPT, US EPA (1987d).

U S EPA (Environmental Protection Agency) "Health Effects Assessment for 1,1,2-Trichloroethane " (1984a)

U S EPA (Environmental Protection Agency) EPA document number EPA 540/1-86-045 (1984b)

White, K L , Sanders V M , Barnes, D W , Shopp G M , and Munson, A E. "Toxicology of 1,1,2-trichloroethane in the mouse " *Drug and Chemical Toxicology* 8(5) 333-355 (1985a).

White, K L., Sanders, V M., Barnes, D W., Tucker, A N., Sain, L E., Shopp, G M., Carchman, R A., and Munson, A E. "Immunotoxicological investigations in the mouse: General approach and methods." *Drug and Chemical Toxicology* 8(5) 299-331 (1985b).

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl methacrylate	80-62-6	Epidemiology (Prevalence study)	Humans	Occupational	As dental laboratory technicians	5 to 46 years (mean = 12 8 years)	2200 to 5600 $\mu g/m^3$ (0 5 to 1.4 ppm)	178 (146 males and 32 females)	Eight persons having a mean of 28 years of employment had simple pneumoconiosis. Mean values for percent predicted forced vital capacity (FVC) and forced expiratory volume (FEV) were reduced among male nonsmoker technicians compared to matched controls. Spirometric values decreased with increasing work-years.	Adequate study, but because of exposure to other materials, a clear association with methyl methacrylate could not be made	Subjects were simultaneously exposed to other potentially toxic materials, including precious metal alloys and silica	Rom et al , 1984
Methyl methacrylate	80-62-6	Epidemiology (Prevalence study)	Humans	Occupational	As dental technicians	3 to 29 years (mean = 15 6 years)	Not quantified	87 male and female respondents (number/sex not reported), 15 illustrative cases participated in the clinical analysis	Subjective responses: dermatitis in 34% of persons, finger numbness, coldness, and whitening in 25% Neurophysiological evaluation of 15 cases revealed decreased sensory conduction velocities in the fingers and occasional decreased sensory action potential amplitude associated with numbness, but not with dermatitis	Adequate study, but because of the lack of exposure data and information on other chemical exposures, a clear association with methyl methacrylate could not be made	Physiological tests accompanied subjective responses Effects were more common among persons with longer career and heavier exposure Additional studies provide supporting data.	Rajaniemi, 1986

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl methacrylate	80-62-6	Epidemiology (Cohort study)	Humans	Occupational	As commercial producers of methyl methacrylate (MMA) and ethyl acrylate (EA)	12, 36, or 39 years	Not quantified	3 cohorts 3934 men, 6548 men, 3381 men	No excess of mortality from cancer was seen in employees hired since the mid-1940s. Excess colon and rectal cancer were noted in employees exposed at least 3 years during the early 1940s to the highest levels of vapor-phase chemicals	Inadequate since exposure levels were not available	Workers were exposed to a mixture, but methyl methacrylate was estimated to be the major constituent (88 to 100%). In the early 1940s, the mix was approximately 88% MMA and 12% EA.	Walker et al., 1991
Methyl methacrylate	80-62-6	Epidemiology (Cohort study)	Humans	Occupational	As commercial producers of MMA	17 to 23 years	0.13 to 1.00 ppm, 8-hour TWA	1561 men	No effect was noted on survival or cancer mortality.	Adequate	Only 2% of the study cohort was lost to follow-up	Collins et al., 1989
Methyl methacrylate	80-62-6	Epidemiology (Retrospective cohort study)	Humans	Occupational	During plastics manufacture	Up to 29 years	Not quantified	1372 men	Total deaths or observed cancer deaths were not increased over the expected. The observed number of respiratory cancers was increased, but was not statistically significant. When grouped by year of hire, increased unspecified cancers and lymphatic cancers were noted	Inadequate. Exposure data are unavailable	Co-exposure to other possible carcinogens (workers were also exposed to ethyl acrylate) provides a confounder for this study.	Rohm and Haas, 1989c

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl methacrylate	80-62-6	Epidemiology (Retrospective cohort study)	Humans	Occupational	As commercial producers of plastics	1 to 12 years	Not quantified	3934 males	Deaths from cancer of the respiratory tract, skin, stomach, liver, bladder, and kidneys were not higher than the expected U.S. mortality rates (1528 observed; 1869 expected). Deaths from cancer of the colon and rectum were significantly increased over the expected U.S. mortality rates (52 observed; 31 2 expected, SMR = 167, p <0.01); however, the majority of these cases do not appear to be related to length of exposure or total exposure	Quantitative exposure information was not available.	Although the cohort size was large, the exposures occurred simultaneously to ethyl acrylate, and the authors concluded that it was impossible to separate exposure to ethyl acrylate from exposure to methyl methacrylate.	Rohm and Haas. 1984

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl methacrylate	80-62-6	Epidemiology (Retrospective cohort study)	Humans	Occupational	During plastics manufacture	Up to 37 years	Not quantified	6667 males at the Bristol plant, 3381 males at the Knoxville plant	At Bristol, exposure to ethyl acrylate was considered minor to exposure to methyl methacrylate No statistically significant excess of site-specific cancers was noted At Knoxville, cancers of the digestive tract, including colorectal cancer, were statistically significantly lower than predicted values. No association was seen between cumulative exposure "dose" and risk of respiratory cancer or digestive cancers including colorectal cancers	Inadequate Quantitative exposure data are unavailable, and workers were also exposed to ethyl acrylate	Exposures happened simultaneously to ethyl acrylate, and the authors concluded that it was impossible to separate exposure to ethyl acrylate from exposure to methyl methacrylate.	Rohm and Haas, 1990
Methyl methacrylate	80-62-6	Epidemiology (Case report)	Humans	Occupational	Medical, while mixing bone cement	Not reported, short time period during mixing procedure	3.8 to 7.8 mg/m^3 (0.9 to 1.9 ppm)	1 operating room nurse	Corneal ulceration occurred on repeated occasions when the nurse worked under the same conditions	Limited observations.	This effect level was considerably less than Denmark's threshold limit value of 410 mg/m^3 as reported in this article	Nissen and Corydon, 1985
Methyl methacrylate	80-62-6	**Epidemiology - Summary**								Epidemiology studies were located to identify some qualitative effects of exposure to methyl methacrylate.		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl methacrylate	80-62-6	Acute toxicity	Rats	Inhalation	Vapor	4 hours followed by a 14-day observation period	0, 1191, 2159, 2220, 4055, 4446, 4632, or 16,000 ppm	5/sex/group	Mortality occurred at 16,000 ppm. Rats gained less among higher exposure groups Compound-related hypoactivity, dyspnea, and anesthesia were noted at all doses.	Adequate range-finding test	A no-effect level is not reported in the document.	NTP, 1986
Methyl methacrylate	80-62-6	Acute toxicity	Mice	Inhalation	Vapor	4 hours followed by a 14-day observation period	0, 1191, 2159, 2220, 4055, 4446, 4632, or 16,000 ppm	5/sex/group	All high-dose mice died prior to the end of the study. Compound-related hypoactivity, dyspnea, and anesthesia were noted at all doses. No effect was evident on body weight No abnormalities were apparent at necropsy	Adequate range-finding test.	A no-effect level is not reported in the document	NTP, 1986
Methyl methacrylate	80-62-6	Acute toxicity	Rats	Inhalation	Vapor	4 hours	1086 to 2715 ppm	10 males/ concentration	LC_{50} (within 24 hours post-exposure) was 1350 (1161-1570) ppm No evidence of bleeding from any orifice was seen in any treated rats. Irritation of the eyes, nose, and respiratory tract, along with labored breathing, were apparent during treatment.	Inadequate	The study is limited by use of males, only as test animals, the use of only 2 exposure groups, and the use of only a 24-hour post exposure observation period.	Oberly and Tansy, 1985
Methyl methacrylate	80-62-6	Acute toxicity	Rats	Inhalation	Vapor	1, 2, 3, or 4 hours	96.7 ± 0.41 ppm was measured chamber concentration	4 males/group	No effects were seen at 1 hour of exposure. Interalveolar congestion and hemorrhage, pulmonary vasodilation and edema were noted in rats exposed for 2, 3, or 4 hours.	This test measured limited endpoints	This study demonstrates portal-of-entry effects at non-lethal concentrations.	Raje et al., 1985

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl methacrylate	80-62-6	Acute toxicity	Rats	Inhalation	Vapor	8 hours	11.2, 13.4, 16.0, 20.1, 25.5, 26.5, 30.0, 31.3, 33.0, 35.6, and 92.3 mg/L (2734.8, 3272.0, 3906.9, 4908.1, 6226.7, 6470.8, 7325.5, 7642.9, 8058.0, 8692.9, and 22538.1 ppm)	5-10/exposure level	Mortality was observed at 25.5 mg/L and higher, with an LC_{50} value of 30-33 mg/L; concentration-related clinical signs at 13.4 mg/L and higher included slight irritation to the upper respiratory tract, depression, increased urine flow, slight dyspnea, and mild cyanosis	This is an adequate acute toxicity study for determining an LC_{50}.	Gross necropsy findings were not reported	Haskell Laboratories, 1937
Methyl methacrylate	80-62-6	**Acute toxicity - Summary**								Other acute inhalation toxicity studies reported similar clinical signs, and indicated effects on the respiratory system (TSCATS, 1992)		
Methyl methacrylate	80-62-6	Subchronic toxicity	Rats	Inhalation	Vapor	6 hours/day, 5 days/week for 14 weeks	0, 500, 1000, 2000, and 5000 ppm	10/sex/group	Mortality occurred at 2000 ppm and higher. Decreased body weight and compound-related lesions of olfactory epithelium, kidney and liver were noted at 2000 ppm and above, and at ≥1000 ppm, females had malacia and gliosis of the brain.	Adequate range-finding study	Appropriate protocol was observed. A NOAEC and LOAEC were identified at 500 and 1000 ppm, respectively.	NTP, 1986
Methyl methacrylate	80-62-6	Subchronic toxicity	Mice	Inhalation	Vapor	6 hours/day, 5 days/week for 14 weeks	0, 500, 1000, 2000, and 5000 ppm	10/sex/group	Mortality occurred at 2000 ppm and higher. Decreased body weight and metaplasia of the nasal epithelium occurred in all treatment groups, and compound-related lesions of the kidney, olfactory epithelium, and liver were noted at 2000 ppm and higher.	Adequate range-finding study.	Appropriate protocol was observed. A LOAEC was identified, and a companion study conducted at Industrial Biotest Labs identified a NOAEC of 250 ppm	NTP, 1986

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl methacrylate	80-62-6	Subchronic toxicity	Dogs	Inhalation	Vapor	6 hours/day, 5 days/week for 3 months	0, 100, and 400 ppm	6 males/exposure level	No toxicity was observed	This study is of limited use because it only identifies a free-standing NOEL and by the use of too few animals per group.	Purity was not reported, important endpoints were examined	Rohm and Haas Company, 1979
Methyl methacrylate	80-62-6	Subchronic toxicity/ Immunotoxicity	Rats	Inhalation	Vapor	8 hours/day for 3 and 6 months	0 or 116 ppm	50 males/group	In the 3-month study, there was a marked absence of visceral and subcutaneous fat Exposed rats had significantly lower whole body (226.7 g vs. 213.7 g), lung (0.94 g vs. 0 84 g), and spleen (0.41 g vs 0.59 g) weights than controls In the 6-month study, mean body and popliteal fat pad weights and levels of serum protein, cholesterol, and blood urea nitrogen were significantly lower than controls	This study is inadequate because only one concentration level was tested	Immune function was not assessed	Tansy et al 1976
Methyl methacrylate	80-62-6	Subchronic toxicity	Rats	Inhalation	Vapor	4 hours/day, 5 days/week for 32 days	0, and 110 ± 5 ppm	Not reported	During exposure rats preened and huddled with their eyes closed. No effects were observed on survival, body or tissue weights, blood chemistry, gross metabolic performance, or spontaneous small intestinal motor activity as compared to controls	The study is limited by the use of only one test exposure level and lack of information regarding number of test animals	No histopathology was reported	Oberly and Tansy, 1985

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl methacrylate	80-62-6	Subchronic toxicity	Rats	Inhalation	Vapor	6 hours/day, 5 days/week for 97 days	0, 63, 125, 250, 500, or 1000 ppm	10/sex/exposure level	No toxicity was observed	This study is of limited use because it only identifies a free-standing NOEL, however, 1000 ppm may be at the threshold for toxicity	Purity was not reported; important endpoints were examined, a non-significant 10% decrease in body weight gain was observed at 1000 ppm.	Rohm and Haas Company, 1989a
Methyl methacrylate	80-62-6	Subchronic toxicity	Mice	Inhalation	Vapor	6 hours/day, 5 days/week for 96 days	0, 63, 125, 250, 500, or 1000 ppm	10/sex/exposure level	Decreased body weight gain at 1000 ppm	This appears to be an adequate subchronic toxicity study	Purity was not reported; important endpoints were examined.	Rohm and Haas Company, 1989a
Methyl methacrylate	80-62-6	**Subchronic toxicity - Summary**								Data on subchronic inhalation toxicity were adequate in 2 species.		
Methyl methacrylate	80-62-6	Chronic toxicity	Hamsters	Inhalation	Vapor	6 hours/day, 5 days/week for 18 months	0, 25, 100, and 400 ppm	66/sex/exposure level	Tendency (statistical significance unknown) towards a shorter life expectancy in males at 400 ppm; otherwise, no toxicity was observed	This is an adequate chronic toxicity study.	Purity was not reported, important endpoints were evaluated, this study identified a FEL of 400 ppm and a NOAEC of 100 ppm	Rohm and Haas Company, 1983

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl methacrylate	80-62-6	Chronic toxicity	Rats	Inhalation	Vapor	2 years	0, 25, 100, or 400 ppm	44-49/sex/exposure level	The two highest exposure groups showed exposure related minimal to slight changes (including inflammation, degeneration, atrophy, and hyperplasia) in the olfactory epithelium of the anterior nasal cavity There was also concentration dependant slight to moderate inflammation and hyperplasia in the respiratory epithelium of the anterior nasal cavity.	This appears to be an adequate study	Histopathologic observations were limited only to the nasal cavity. The NOEL was 25 ppm	Rohm and Haas Company, 1992
Methyl methacrylate	80-62-6	Chronic toxicity	Rats	Inhalation	Vapor	6 hours/day, 5 days/week for 104 weeks	0, 25, 100, and 400 ppm	70/sex/exposure level	Mild rhinitis was observed in treated rats; otherwise no toxicity was observed	This is an adequate chronic toxicity study.	Purity >99.6%, clinical signs and important endpoints were evaluated.	Rohm and Haas Company, 1989b
Methyl methacrylate	80-62-6	Chronic toxicity	Rats	Inhalation	Vapor	6 hours/day, 5 days/week for 102 weeks	Males: 0, 500, or 1000 ppm Females 0, 250, or 500 ppm	50/sex/group	Decreased body weight occurred in both sexes in the high-dose group. Treatment-related inflammation of the nasal cavity and degeneration of the olfactory sensory epithelium was seen in both sexes	Inadequate because a NOAEC was not identified.	Purity >99%; adequate endpoints were examined.	NTP, 1986

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl methacrylate	80-62-6	Chronic toxicity	Mice	Inhalation	Vapor	6 hours/day, 5 days/week for 102 weeks	0, 500, or 1000 ppm	50/sex/group	Treated mice had decreased body weight, treatment-related inflammation of the nasal cavity, degeneration of the olfactory sensory epithelium, and epithelial hyperplasia of the nasal cavity.	Inadequate because a NOAEC was not identified	Purity >99%, adequate endpoints were examined	NTP, 1986
Methyl methacrylate	80-62-6	**Chronic toxicity - Summary**								Data on chronic inhalation toxicity are available which suggest that the respiratory system is a target organ, but a NOAEC was not identified in these studies (NTP, 1986; TSCATS, 1992).		
Methyl methacrylate	80-62-6	Carcinogenicity	Hamsters	Inhalation	Vapor	6 hours/day, 5 days/week for 18 months	0, 25, 100, and 400 ppm	66/sex/exposure level	No evidence of carcinogenicity was observed	This is an adequate carcinogenicity study	Purity was not reported; important endpoints were evaluated.	Rohm and Haas Company, 1983
Methyl methacrylate	80-62-6	Carcinogenicity	Rats	Inhalation	Vapor	6 hours/day, 5 days/week for 104 weeks	0, 25, 100, and 400 ppm	70/sex/exposure level	No evidence of carcinogenicity was observed	This is an adequate carcinogenicity study	Purity >99 6%; clinical signs, important endpoints were evaluated	Rohm and Haas Company, 1989b
Methyl methacrylate	80-62-6	Carcinogenicity	Rats	Inhalation	Vapor	6 hours/day, 5 days/week for 102 weeks	Males: 0, 500, or 1000 ppm Females: 0, 250, or 500 ppm	50/sex/group	No evidence of carcinogenicity was observed in either sex at any treatment level	Adequate	Purity >99%; adequate endpoints were examined.	NTP, 1986
Methyl methacrylate	80-62-6	Carcinogenicity	Mice	Inhalation	Vapor	6 hours/day, 5 days/week for 102 weeks	0, 500, or 1000 ppm	50/sex/group	No evidence of carcinogenicity was observed in either sex at any treatment level.	Adequate.	Purity >99%, adequate endpoints were examined.	NTP, 1986
Methyl methacrylate	80-62-6	**Carcinogenicity - Summary**								Adequate data on carcinogenicity are available in 3 species.		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl methacrylate	80-62-6	Neurotoxicity	Rats	Oral	Gavage	Daily for 21 days	0 or 500 mg/kg/day	30 males/group	Markedly impaired locomotor activity and learning; increased biogenic amine level in brain.	The study is limited by the use of only one exposure level.	Authors suggest that the changes in regional brain biogenic amine levels may be partly responsible for altered behavior.	Husain et al., 1985
Methyl methacrylate	80-62-6	Neurotoxicity	Rats	Inhalation	Vapor	60 minutes	0 or 400 ppm	Males (number not reported)	Depression in the multiple-unit electrical activity in the lateral hypothalamus and ventral hippocampus	The study is limited by lack of information regarding number of test animals and limited scope of endpoints examined.	The study identified a LOAEL for central neuronal activity of 400 ppm	Innes and Tansy, 1981
Methyl methacrylate	80-62-6	**Neurotoxicity - Summary**								Additional neurotoxicity testing of methyl methacrylate could be required. Available information indicates a potential for neurotoxicity (TSCATS, 1992; TOXLINE, 6/93)		
Methyl methacrylate	80-62-6	Developmental toxicity	Rats	Inhalation	Vapor	2 hours/day, every 3 days on gestation days 6-18	0, 0.52, or 4.48 mg/L (0, 129.9, or 1093.9 ppm)	Not reported	No maternal toxicity was observed. Delayed ossification occurred in both treatment groups, and at 4.48 mg/L increased incidence of resorption occurred	Inadequate. The exposure regimen did not follow accepted protocol; exposures were conducted only every 3 days.	This report is in abstract form only	Luo et al., 1986
Methyl methacrylate	80-62-6	Developmental toxicity	Rats	Inhalation	Vapor	6 hours/day on gestation days 6-15	0, 99, 304, 1178, and 2028 ppm	27/exposure level	Maternal toxicity was observed at all exposure levels, no developmental toxicity was observed	This is an adequate developmental toxicity study with no developmental effects observed at levels producing maternal toxicity.	Purity 99.9%, this study identified a LOAEL of 99 ppm for maternal toxicity and a NOAEL of 2028 ppm	Rohm and Haas Company, 1991

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl methacrylate	80-62-6	Developmental toxicity	Rats	Inhalation	Vapor	5 hours/day on gestation days 6-15	0, 100, 1000 ppm (Exp I), 0, 25, 100, and 1000 ppm (Exp II)	30/exposure level	No maternal toxicity; increased number of early resorptions and incidence of retarded skeletal ossification at 1000 ppm	This is a marginally adequate developmental toxicity study with developmental effects observed at levels not producing maternal toxicity. Dams were exposed 5 hours/day, instead of 6 hours/day.	This study identified a NOAEL of 1000 ppm for maternal toxicity, and a NOAEL of 100 ppm and LOAEL of 1000 ppm for developmental toxicity.	Imperial Chemistry Industries, 1977
Methyl methacrylate	80-62-6	Developmental toxicity	Mice	Inhalation	Vapor	6 hours/day on gestation days 4-13	0, 116, or 400 ppm	18-38/exposure level	No maternal toxicity; decreased fetal body weights at 116 and 400 ppm	This is an inadequate study because exposure did not include the later stages of organogenesis, only two doses were tested, and no NOAEL was identified for developmental toxicity.	Only raw data available from a final report.	Rohm and Haas Company, 1976a; 1976b
Methyl methacrylate	80-62-6	Embryotoxicity test	White leghorn chickens	Injection into eggs	Solution in acetone	Single injection	0, 2.3, 4.5, 9, 18, and 36 µmol/egg	20-30/dose level	ED_{50} (embryotoxicity) was 22.0 (confidence limits = 9.0 to 56.0) µmol/egg Malformations, including eye, neck, back, wings, and legs were observed, but a dose-response relationship was not seen.	This is not a standard developmental test.	The relationship of these results with regard to mammalian toxicity is unclear	Korhonen, et al., 1983
Methyl methacrylate	80-62-6	**Developmental toxicity - Summary**								Adequate developmental toxicity data are available in 1 species (TSCATS, 1992)		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl methacrylate	80-62-6	**Reproductive toxicity - Summary**								No data on the reproductive toxicity of methyl methacrylate were located (TSCATS, 1992, TOXLINE, 6/93)		
Methyl methacrylate	80-62-6	**Pharmacokinetics - Summary**								Pharmacokinetics data are available for the oral and inhalation routes of exposure (HEEP, 1985, TSCATS, 1992; TOXLINE, 6/93).		

REFERENCES

Collins, J J , Page, L C , Caporossi, J C , Utidjian, H M., and Saipher, J.N. "Mortality patterns among men exposed to methyl methacrylate " *Journal of Occupational Medicine* 31(1):41-46 (1989).

Haskell Laboratories "The toxicity and potential dangers of methyl methacrylate (monomer) with attachment and cover sheet dated 061289 " TSCA 8D submission 86-890000818, microfiche number OTS0520934 Washington, DC: OPPT, US EPA (1937)

HEEP "Health and Environmental Effects Profile for Methyl methacrylate." US Environmental Protection Agency (1985)

Husain, R., Srivastava, S P., and Seth, P.K "Methyl methacrylate induced behavioural and neurochemical changes in rats " *Archives of Toxicology*. 58 33-36 (1985).

Imperial Chemistry Industries "Methyl methacrylate monomer teratogenicity studies in the rat with attachments and cover sheet dated 071789 " TSCA 8D submission 86-890001390S, microfiche number OTS0521013 Washington, DC: OPPT, US EPA (1977)

Innes, D L., and Tansy, M F "Central nervous system effects of methyl methacrylate vapor " *Neurotoxicity* 2.515-522 (1981).

Korhonen, A , Hemminki, K., and Vainio, H "Embryotoxic effects of acrolein, methacrylates, guanidines and resorcinol on three day chicken embryos " *Acta Pharmacologica et Toxicologica* 52.95-99 (1983)

Luo, S-Q , Gang, B-Q , and Sun S-Z "Study on embryotoxicity and fetotoxicity in rats by maternal inhalation of low level methyl methacrylate." *Toxicology Letters* 31(suppl) 80 (1986)

Nissen, J.N , and Corydon, L. "Corneal ulcer after exposure to vapours from bone cement (methyl methacrylate and hydroquinone)." *International Archives of Occupational Environmental Health*. 56(2).161-165 (1985).

NTP (National Toxicology Program). "NTP technical report on the toxicology and carcinogenesis studies of methyl methacrylate in F344/N rats and B6C3F1 mice (inhalation studies) " NTP TR 314 (1986)

Oberly, R , and Tansy, M F. "LC50 values for rats acutely exposed to vapors of acrylic and methacrylic acid esters." *Journal of Toxicology and Environmental Health* 16(6):811-822 (1985)

Rajaniemi, R "Clinical evaluation of occupational toxicity of methyl methacrylate monomer to dental technicians." *Journal of the Society of Occupational Medicine* 36(2) 56-59 (1986).

Raje, R R , Ahmad, S , and Weisbroth, S H "Methylmethacrylate: Tissue distribution and pulmonary damage in rats following acute inhalation " *Research Communications in Chemical Pathology and Pharmacology* 50(1) 151-154 (1985).

Rohm and Haas Company "Progress report on teratology studies of mice exposed to methyl methacrylate monomer vapor with attachments and cover sheet dated 071789 (sanitized) " TSCA 8D submission 86-890001405S, microfiche number OTS0521022 Washington, DC: OPPT, US EPA (1976a)

Rohm and Haas Company "Final report on teratology studies of mice exposed to methyl methacrylate vapor with attachments and cover sheet dated 071789 (sanitized) " TSCA 8D submission 86-890001376S, microfiche number OTS0521011 Washington, DC OPPT, US EPA (1976b).

Rohm and Haas Company "Methyl methacrylate three month subchronic vapor inhalation safety evaluation study in Beagle dogs with attachments and cover sheet dated 071789 (sanitized)." TSCA 8D submission 86-8900013775, microfiche number OTS0521012 Washington, DC OPPT, US

IPA (1979)

Rohm and Haas Company "Methyl methacrylate Subchronic, chronic and oncogenic inhalation safety evaluation studies with attachments, cover sheet and letter (sanitized)." TSCA 8D submission 86-890001441S, microfiche number OTS0521055 Washington, DC OPPT, US EPA (1983)

Rohm and Haas Company "Interim communication on the results of a mortality study of Bristol plant employees hired prior to 1946 with cover letter dated 031684 " TSCA FYI submission FYI-OTS-0384-0300 IN, microfiche number 0300 Washington, DC OPPT, US EPA (1984)

Rohm and Haas Company "Subchronic vapor inhalation study with methyl methacrylate (C50680) in F344 rats with attachments, cover sheets and letter dated 081089 (sanitized) " TSCA 8D submission 86-8900015085, microfiche number OTS0521247. Washington, DC: OPPT, US EPA (1989a)

Rohm and Haas Company "2-Year inhalation, dominant lethal assay, evaluation of colorectal cancers at the Sanford plant, mortality patterns and report on methyl methacrylate with cover letter dated 060789 " TSCA 8D submission 86-890000315, microfiche number OTS0519080 Washington, DC OPPT, US EPA (1989b)

Rohm and Haas Company "Texas plant mortality study - (1948-1978) with cover letter dated 071289 " TSCA 8D submission 86-890001317, microfiche number OTS0520821 Washington, DC OPPT, US EPA (1989c).

Rohm and Haas Company "An evaluation of mortality from cancers of the colon and rectum among workers exposed to ethyl acrylate and methyl methacrylate with cover letter dated 012990 " TSCA FYI submission FYI-OTS-0290-0300, microfiche number OTS0000300. Washington, DC: OPPT, US EPA (1990)

Rohm and Haas Company "Methyl methacrylate: Inhalation developmental toxicity study in rats (final report) with cover letter dated 041291 " TSCA 8D submission 86-910000781, microfiche number OTS0529413. Washington, DC OPPT, US EPA (1991).

Rohm and Haas Company "Histopathologic evaluation of nasal cavities from Fischer 344 rats exposed to methyl methacrylate vapor for two years " Project Number 3302 5E (1992).

Rom, W N., Lockey, J E., Lee, J S., Kimball, A.C., Bang, K M , Leaman, H., Johns, R.E., Jr , Perrota, D , and Gibbons, H L. "Pneumoconiosis and exposures of dental laboratory technicians " *American Journal of Public Health* 74(11):1252-1257 (1984)

Santavirta, S Konttinen, U T., Bergroth, V., and Gronblad, M "Lack of immune response to methyl methacrylate in lymphocyte cultures " *Acta Orthopaedica Scandinavica* 62(1) 29-32 (1991)

Tansy, M F , Kendall, F M , Benhayem, S , Hohenleitner, F.J , Landin, W.E., and Gold, M "Chronic biological effects of methyl methacrylate vapor. I Body and tissue weights, blood chemistries, and intestinal transit in the rat " *Environmental Research* 11(1).66-77 (1976)

TOXLINE National Library of Medicine Online Database. (1993).

TSCATS (Toxic Substances Control Act Test Submissions) Database (1992).

Walker, A M , Cohen A J , Loughlin, J E., Rothman, K J , and DeFonso, L R. "Mortality from cancer of the colon or rectum among workers exposed to ethyl acrylate and methyl methacrylate " *Scandanavian Journal Work Environment and Health* 17:7-19 (1991)

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Phthalic anhydride	85-44-9	Clinical evaluation	Human	Inhalation	Fumes	8 months to 25 years	Minimal (16 workers) to high (1 worker) estimated exposures	20 males total	4 Workers had elevated total antibody binding to phthalic anhydride-human serum albumin (PA-HSA) and elevated specific IgG and IgE to PA-HSA. The worker with high exposure had allergic rhinitis associated with phthalic anhydride	Adequate to demonstrate sensitization to phthalic anhydride.	Workers were also exposed to trimellitic anhydride, however, there was little cross reactivity between the specific antibodies for these anhydrides.	Bernstein et al., 1982
Phthalic anhydride	85-44-9	Clinical evaluation	Human	Inhalation	Dust	Not reported	Not reported	2 males	Ocular itching, rhinorrhea, chest tightness, and wheezing which stopped following removal from exposure. There was an increase in serum-specific IgE to PA-HSA in both workers	Adequate to demonstrate sensitization to phthalic anhydride.	Two other workers exposed to hexahydrophthalic anhydride and himic anhydride showed cross reactivity having heightened phthalic anhydride antibodies.	Bernstein et al., 1984
Phthalic anhydride	85-44-9	Epidemiology (Cross-sectional health study)	Humans	Not reported	Not reported	Not reported	Not reported	91 males and 14 females	No potential for allergenic effects were observed as screened for by an increase in eosinophils.	Inadequate because incidence and exposure data were not provided	Although the study population was 105, only 14 were exposed to phthalic anhydride.	Koppers Co Inc., 1982a
Phthalic anhydride	85-44-9	Epidemiology (Cross-sectional health study)	Humans	Not reported	Not reported	Not reported	Not reported	129 males and 10 females	No effects were observed in pulmonary function, renal function, urinalysis, or immunological findings.	Inadequate because exposure data were not provided	This plant also produced maleic anhydride, amino resins, and alkyl resins	Koppers Co Inc., 1982b
Phthalic anhydride	85-44-9	**Epidemiology - Summary**								Several epidemiology studies suggest the potential for phthalic anhydride to induce respiratory hypersensitivity (Clement, 1990d)		
Phthalic anhydride	85-44-9	**Acute toxicity - Summary**								No data on the acute inhalation toxicity of phthalic anhydride were located (Clement, 1990d, TSCATS, 1992)		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Phthalic anhydride	85-44-9	Subchronic toxicity	Rats	Inhalation	Vapor	6 hours/day for 5 days, rested for 3 weeks, then challenged with a single 6 hour exposure	500 µg/m³ (0.08 ppm)	20/exposure level	Increased numbers of hemorrhagic foci were observed, indicative of respiratory sensitization	This is not an adequate subchronic toxicity study because only one endpoint was evaluated and only one exposure level was used.	Although only one exposure level was used, this was likely the highest vapor concentration obtainable	Amoco Corporation, 1988
Phthalic anhydride	85-44-9	**Subchronic toxicity - Summary**								Additional testing could be required on the subchronic inhalation toxicity of phthalic anhydride.		
Phthalic anhydride	85-44-9	**Chronic toxicity - Summary**								No data on the chronic inhalation toxicity of phthalic anhydride were located (Clement, 1990d; TSCATS, 1992).		
Phthalic anhydride	85-44-9	Carcinogenicity	Rats	Oral	Diet	105 weeks	0, 7500 or 15,000 ppm	50/sex/group; 20 matched controls of each sex	Under the conditions of the assay, phthalic anhydride was not carcinogenic There was, however, a significant trend in alveolar/bronchiolar adenomas in female rats	This is an adequate oral study.	Survival was not affected by treatment.	NTP, 1979
Phthalic anhydride	85-44-9	Carcinogenicity	Mice	Oral	Diet	72 weeks	12,500 or 25,000 ppm for males and 6250 or 12,500 ppm for females	50/sex/group, 20 matched controls of each sex	Under the conditions of the assay, phthalic anhydride was not carcinogenic	This is an adequate oral study	Survival was not affected by treatment	NTP, 1979
Phthalic anhydride	85-44-9	**Carcinogenicity - Summary**								No data on the carcinogenicity of phthalic anhydride following inhalation exposure were located; an adequate oral study in two species is available (Clement, 1990d; TSCATS, 1992).		
Phthalic anhydride	85-44-9	**Neurotoxicity - Summary**								No data on the neurotoxicity of phthalic anhydride were located (Clement, 1990d; TSCATS, 1992).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Phthalic anhydride	85-44-9	Developmental toxicity	Mice	Injection	I.P	Administered on gestation days 8-10	0, Treatment values not reported; highest dose was reportedly within 95% confidence limits of the calculated LD_{01}.	Not reported	The compound was considered to be a "low hazard" with regard to teratogenicity	This is not an adequate developmental toxicity study because of insufficient reporting of experimental design	This study was designed to test the relative toxicity of a number of compounds as a percent of the LD_{50} dose.	Fabro et al., 1982
Phthalic anhydride	85-44-9	**Developmental toxicity - Summary**								Additional testing could be required on the developmental toxicity of phthalic anhydride		
Phthalic anhydride	85-44-9	**Reproductive toxicity - Summary**								No data on the reproductive toxicity of phthalic anhydride were located (Clement, 1990d; TSCATS, 1992).		
Phthalic anhydride	85-44-9	**Pharmacokinetics - Summary**								Limited information regarding absorption, metabolism, and excretion of phthalic anhydride were available in humans (Clement, 1990d).		

REFERENCES

Amoco Corporation Letter dated 1/28/88 from Amoco Corporation to US EPA informing that the results of the report study on phthalic anhydride will be forwarded later TSCA 8E submission 89-880000017, microfiche number OTS0513426, Washington, DC OPPT, US EPA (1988).

Clement "Draft inhalation reference dose for phthalic anhydride (85-44-9)." Prepared by Clement Associates, Inc for Environmental Criteria and Assessment Office. (1990d).

Bernstein, D I., Patterson, R., and Zeiss, C.R. 1982 Clinical and immunologic evaluation of trimellitic anhydride - and phthalic anhydride-exposed workers using a questionnaire with comparative analysis of enzyme-linked immunosorbent and radioimmunoassay studies *Journal of Allergy a Clinical Immunology*. 69 311-318

Bernstein, D I., Gallagher, J.S., D'Souza, L., and Bernstein, I L. 1984. Heterogeneity of specific-IgE responses in workers sensitized to acid anhydride compounds. *Journal of Allergy and Clinical Immunology* 74:794-801.

Fabro, S., Shull, G., and Brown, N A "The relative teratogenic index and teratogenic potency: Proposed components of developmental toxicity risk assessment " *Teratogenesis, Carcinogenesis, and Mutagenesis*. 2:61-76 (1982).

Koppers Co Inc "1979 Cross-sectional health study of workers at nine Koppers coal tar plants. Combined Report." TSCA 8D submission 87-8210574, microfiche number OTS0206278 Washington, DC OPPT, US EPA (1982a)

Koppers Co Inc. "Occupational health evaluation of the Bridgeville, Pennsylvania plant of Koppers Company Inc organic materials group Final Report " TSCA 8D submission 87-8210482, microfiche number OTS0206278, Washington, DC: OPPT, US EPA (1982b)

NTP/NCI National Toxicology Program/National Cancer Institute. "Bioassay of phthalic anhydride for possible carcinogenicity " DHEW Publication No. (NIH) 79-1715 NTP TR 159 (1979)

TSCATS (Toxic Substances Control Act Test Submissions) Database (1992)

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Naphthalene	91-20-3	Epidemiology (Cohort study)	Humans	Inhalation	Fumes or dust	≤5 years	Not reported	21 workers	Cataracts developed in 8/21 of the workers; 7/8 of the affected workers were less than 50 years old.	This is an inadequate epidemiology study because of the small population and lack of exposure information.	This study was reported in Italian with an English abstract	Ghetti and Maria 1956
Naphthalene	91-20-3	Epidemiology (Case study)	Humans	Inhalation	Vapor	Exposed to fumes from hundreds of mothballs for "several years" in the home	Air samples collected indicated 20 ppb, but levels were probably higher with fresh mothballs	8 adults and 1 child	Vomiting and abdominal pain were observed in all individuals, and anemia was reported in "several" individuals	This is an inadequate epidemiology study	This is a summary of a case history of the effects of naphthalene inhalation on the inhabitants of homes in which a large number (300-500) of mothballs were distributed.	Linick, 1983
Naphthalene	91-20-3	Epidemiology (Case study)	Humans	Oral	Not reported	≥3 months, frequency not reported	Not reported	1 pregnant 26-year old	Maternal hemolytic anemia; newborn hemolytic anemia, jaundice, lethargy, and anorexia were noted	This is an inadequate epidemiology study.	This is a case report of transplacental naphthalene poisoning	Anziulewicz et a 1959
Naphthalene	91-20-3	**Epidemiology - Summary**								No adequate epidemiology studies were located (ATSDR, 1989; TSCATS, 1992, TOXLINE, 6/93).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Naphthalene	91-20-3	Acute toxicity	Rats	Inhalation	Vapor	4 hours, then observed for 14 days	77 7 ppm	5/sex	No mortalities were observed. Lacrimation, mouth breathing, and closed eyes were the only clinical signs. No gross pathologic lesions were observed	An inadequate range of endpoints were studied No histopathology was performed	Purity was 100%; the concentration used was the highest concentration obtainable under the experimental conditions of this laboratory. This study reported signs of irritation at saturated levels of the compound.	Pharmakon Research International, 1985
Naphthalene	91-20-3	**Acute toxicity - Summary**								Adequate acute inhalation toxicity data are not available on naphthalene (TSCATS, 1992).		
Naphthalene	91-20-3	Repeated dose study	Mice	Inhalation	Vapor	6 hours/day, 5 days/week, for 2 weeks	0, 10, or 30 ppm	5/sex/group	No treatment-related effects were noted on survival, body weight or clinical signs Small but not significant alterations were noted in hematologic parameters among high-exposure females (increased leukocytes, decreased hemoglobin and mean cell volume) but not in males.	The study is inadequate for evaluating subchronic effects because animals were exposed for an insufficient duration.	Abnormally high death rates were reported in the control group.	NTP, 1992
Naphthalene	91-20-3	**Subchronic toxicity - Summary**								No adequate data on the subchronic inhalation toxicity of naphthalene were located (ATSDR, 1989, TSCATS, 1992; TOXLINE, 6/93)		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Naphthalene	91-20-3	Chronic toxicity	Mice	Inhalation	Vapor	6 hours/day, 5 days/week for 104 weeks	0, 10, and 30 ppm	75/sex/exposure level	Chronic inflammation in nose and lungs at 10 and 30 ppm, metaplasia of olfactory epithelium and hyperplasia of respiratory epithelium in nose at 10 and 30 ppm	This is an adequate chronic toxicity study	This study identified a LOAEL of 10 ppm	NTP, 1992
Naphthalene	91-20-3	**Chronic toxicity - Summary**								An adequate chronic inhalation toxicity study was located in 1 species (NTP, 1992).		
Naphthalene	91-20-3	Carcinogenicity	Mice	Inhalation	Vapor	6 hours/day, 5 days/week for 104 weeks	0, 10, and 30 ppm	75/sex/exposure level	Incidence of pulmonary alveolar/bronchiolar adenomas was increased in females at 30 ppm.	This is an adequate carcinogenicity study	The authors concluded that there was no evidence of carcinogenic activity in males and some evidence in females	NTP, 1992
Naphthalene	91-20-3	Carcinogenicity Toxicity	Mice	Inhalation	Vapor	6 hours/day, 5 days/week for 26 weeks	0, 10, and 30 ppm	30 females/ exposure level	Increased adenomas per tumor-bearing mouse lung at 10 and 30 ppm, but the number of tumors in tumor-bearing control mice was significantly lower than the pooled controls of 6 other concurrent studies on other chemicals.	This is an adequate strain A mouse bioassay, but not an adequate lifetime cancer bioassay	This is a strain A mouse study with a normally high incidence of lung tumors in controls. The authors concluded that the adenoma response was not significant.	Adkins et al , 1986.
Naphthalene	91-20-3	**Carcinogenicity - Summary**								An adequate carcinogenicity study was located in 1 species (NTP, 1992). Naphthalene has been selected for inhalation studies in the rat by NTP; gavage study was withdrawn (CHEMTRACK, 7/93)		
Naphthalene	91-20-3	**Neurotoxicity - Summary**								No data on the neurotoxicity of naphthalene were located (ATSDR, 1989; TSCATS, 1992; TOXLINE, 6/93) There is a 90-day subchronic study in progress that will be under consideration by the OPP of EPA		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Naphthalene	91-20-3	Developmental toxicity	Mice	Oral	Gavage	Daily on gestation days 7-14	0 or 300 mg/kg/day	50/exposure group	Reduced body weight gain and increased mortality were observed in dams The number of live young at birth was decreased	This study is inadequate because the young were not examined for malformations and only one dose group was used.	300 mg/kg/day was determined to be the MTD in Booth et al., 1983	Plasterer et al., 1985
Naphthalene	91-20-3	Developmental toxicity	Rats	Oral	Gavage	Daily on gestation days 6-15	0, 50, 150, and 450 mg/kg/day	25-26/exposure group	Transient clinical signs (lethargy, slow respiration, prone body posture, and rooting behavior), transient reduced food and water consumption, and reduced body weight gain were observed in all dams Significantly decreased body weight gain was seen at 150 mg/kg/day. No significant changes in fetal growth, viability, or morphological development were observed	This is an adequate developmental study.	The NOAEL for maternal effects is 50 mg/kg/day, and the LOAEL is 150 mg/kg/day, although no LOAEL was observed for fetal effects, a significant dose-related trend toward decreased fetal weight and increased malformations was noted.	Navarro et al., 1991

Table of Toxicity Data for HAPs (*continued*)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Naphthalene	91-20-3	Developmental toxicity	Rabbits	Oral	Gavage	Daily on gestation days 6-18	0, 40, 200, and 400 mg/kg/day	18/exposure group	Clinical signs (decreased activity, dyspnea, cyanosis, ocular and/or nasal discharge, and salivation) were observed in the dams from the 200 and 400 mg/kg/day groups No effects were seen on maternal survival, body weights or body weight gain. No effects were noted on reproductive parameters. No congenital abnormalities were *observed.*	This is an adequate study, although the sample size is slightly low	Purity was not reported, this study identified a NOAEL of 40 ppm and a LOAEL of 200 ppm for maternal toxicity and a NOAEL of 400 ppm for developmental toxicity	Pharmakon Research International, 1986
Naphthalene	91-20-3	Developmental toxicity	Rabbits	Oral	Gavage	Daily on gestation days 6-19	0, 20, 80, and 120 mg/kg/day	25 to 27 females/group	No effects were reported in does or fetuses	This study is inadequate because it did not test to the MTD as indicated by maternal toxicity	Doses of 150 mg/kg were determined to be lethal in a pilot study	Navarro et al., 1992
Naphthalene	91-20-3	**Developmental toxicity - Summary**								Adequate developmental toxicity data for the oral route were available in 2 species (ATSDR, 1989, Navarro et al., 1991, TSCATS, 1992)		
Naphthalene	91-20-3	Reproductive toxicity	Mice	Oral	Gavage	Daily for 14 days	0 or 267 mg/kg/day	40 to 112/sex/group	No effects on testicular weights.	Inadequate	These data were from a subchronic study.	Shopp et al , 1984
Naphthalene	91-20-3	Reproductive toxicity	Mice	Oral	Gavage	Daily for 90 days	0 or 133 mg/kg/day	40 to 112/sex/group	No effects on testicular weights.	Inadequate	These data were from a subchronic study.	Shopp et al., 1984

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Naphthalene	91-20-3	Short-term reproductive toxicity	Mice	Oral	Gavage	Daily on gestation days 7-14	0 or 300 (pre-determined MTD) mg/kg/day	50 sperm-positive females	Decreased maternal survival and decreased body weight gain Significantly decreased number of live pups and litter weight, but not significantly decreased weight/pup	Adequate reproductive short-term screen.	Results show developmental effects.	Booth et al., 1983
Naphthalene	91-20-3	**Reproductive toxicity - Summary**								Data on the reproductive toxicity of naphthalene were inadequate.		
Naphthalene	91-20-3	**Pharmacokinetics - Summary**								Limited information is available regarding the distribution, metabolism, and excretion, of orally administered naphthalene in animals (ATSDR, 1989; Iyer et al., 1991), as well as the mechanism of action of pulmonary necrosis (Buckpitt and Franklin, 1989).		

REFERENCES

Adkins, B., Jr., Van Stee, E W., Simmons, J E., and Eustis S.L. "Oncogenic response of strain A/J mice to inhaled chemicals." *Journal of Toxicology and Environmental Health* 17 311-322 (1986)

Anziulewicz, J A., Dick, H J., and Chiarulli, E E. "Transplacental naphthalene poisoning." *American Journal of Obstetrics and Gynecology* 78(3) 519-521 (1959)

ATSDR (Agency for Toxic Substances and Disease Registry) "Toxicological Profile on Naphthalene." (1989)

Buckpitt, A R., and Franklin, R B. "Relationship of naphthalene and 2-methylnaphthalene metabolism to pulmonary bronchiolar epithelial cell necrosis." *Pharmacology and Therapeutics 41.393-410* (1989)

CHEMTRACK National Toxicology Program Results Report "Results, status and publication information on all NTP chemicals produced from NTP CHEMTRACK system." July (1993).

Booth, G M., Bradshaw, W S., and Carter, M W. "Screening of priority chemicals for potential reproductive hazard (final report)." NTIS PB83-213017 (1983)

Ghetti, G., and Mariani, I. "Alterazioni oculari da naftalina." *Medicini del Lavoro.* 47(10):533-538 (1956).

Iyer, P., Martin, J E., and Irvin, T R. "Role of biotransformation in the *in vitro* preimplantation embryotoxicity of naphthalene." *Toxicology* 66 257-270 (1991)

Linick, M. "Illness associated with exposure to naphthalene in mothballs-Indiana." *MMWR* 32(2):34-35 (1983)

Navarro, H A., Price, C J., Marr, M C., Myers, C.B., Heindel, J J., and Schwetz, B A. "Developmental toxicity of naphthalene in Sprague-Dawley (CD) rats on gestational days 6 through 15 (final study report and appendix)." NTIS PB92-135623, Report No. RTI-376 December 5 (1991).

Navarro, H A., Price, C J., Marr, M C., Myers, C B., and Heindel, J J. "Final report on the developmental toxicity of naphthalene (CAS no. 91-20-3) in New Zealand White (trade name) rabbits." NTP, NTIS/PB92-219831 (1992)

NTP (National Toxicology Program) "NTP technical report on the toxicology and carcinogenesis studies of naphthalene in B6C3F1 mice " NTP TR 410 (1992)

Pharmakon Research International, Inc "Naphthalene acute inhalation toxicity study " TSCA 8D submission 86-870000558, microfiche number OTS0513636 Washington, DC OPPT, US EPA (1985).

Pharmakon Research International "Developmental toxicity study in rabbits using test article 5601-56-1 " TSCA 8D submission 86-870000563, microfiche number OTS0513641 Washington, DC OPPT, US EPA (1986)

Plasterer, M R , Bradshaw, W S , Booth, G.M., Carter, M W , Schuler, R L , and Hardin, B D "Developmental toxicity of nine selected compounds following prenatal exposure in the mouse Naphthalene, *p*-nitrophenol, sodium selenite, dimethyl phthalate, ethylene thiourea, and four glycol ether derivatives " *Journal of Toxicology and Environmental Health* 15 25-38 (1985)

Shopp, G M , White, K L , Jr , Holsapple, M P , Barnes, D W , Duke, S S., Anderson, A C , Condie, L W , Jr , Hayes, J R , and Borzelleca, J F "Naphthalene toxicity in CD-1 mice General toxicology and immunotoxicology." *Fundamental and Applied Toxicology*. 4 406-419 (1984).

TOXLINE National Library of Medicine Online Database (1993)

TSCATS (Toxic Substances Control Act Test Submissions). Database (1992)

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
1,1'-Biphenyl	92-52-4	Epidemiology (Case studies)	Humans	Inhalation	Occupational	Approximately 100 days/year for 11 years	4.4 to 128 mg/m³ (0.7 to 20.3 ppm)	33 (32 men and 1 woman)	Complaints attributed to biphenyl exposure include headache, gastrointestinal discomfort, polyneuritic symptoms, and general fatigue. 1 man died as a result of acute yellow liver atrophy and 8 workers had evidence of hepatic and nervous system toxicity which the authors concluded were related to exposure	Inadequate because there were no controls used and detailed reference rates were not provided.	Workers were preparing biphenyl impregnated paper for wrapping fruit.	Hakkinen et al., 1973
1,1'-Biphenyl	92-52-4	**Epidemiology - Summary**								Adequate epidemiology data were not located for inhaled 1,1'-biphenyl (HEED, 1990; TSCATS, 1992).		
1,1'-Biphenyl	92-52-4	Acute toxicity	Rats	Inhalation	Vapor	6 hours	0.2 ppm	6 males	0/6 mortalities; no toxic signs; gross autopsy revealed normal-appearing viscera.	Inadequate.	Only one exposure level was used; an effect level was not identified.	Monsanto Co., 1983
1,1'-Biphenyl	92-52-4	Acute toxicity	Mice	Inhalation	Vapor	4 hours	14, 38, and 43 ppm	10/sex/group	LC_{50} >43 ppm; hyperactivity and mild respiratory discomfort noted during exposure, and gross pathology indicated mild lung congestion at all exposures	Inadequate because histopathology was not studied.	No effect level was identified.	Sun Co., 1983a
1,1'-Biphenyl	92-52-4	**Acute toxicity - Summary**								Adequate acute inhalation toxicity data on 1,1'-biphenyl were not located (HEED, 1990; TSCATS, 1992).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
1,1'-Biphenyl	92-52-4	Subchronic toxicity (range finding)	Mice	Inhalation	Vapor	7 hours/day, 5 days/week for 2 weeks	0, 24 80, and 54 75 ppm (mean measured)	10/sex/group	Hyperactivity during exposure; no histopathological effects in lungs, trachea, liver, kidneys, or spleen.	This appears to be a range-finding study with a duration too short to assess subchronic toxicity.	The concentration tested is likely the highest concentration obtainable	Sun Co , 1983b
1,1'-Biphenyl	92-52-4	Subchronic toxicity	Mice	Inhalation	Vapor	7 hours/day, 5 days/week for 13 weeks	0, 25, and 50 ppm (nominal)	50/sex/group	Treatment-related hyperplasia of tracheal epithelia was noted, along with congestion of the lung, liver, and kidney.	Inadequate because only 2 dose levels were used; a NOAEL was not identified	The tracheal effect may have resulted from irritating effects of the chemical.	Sun Co., 1983c
1,1'-Biphenyl	92-52-4	**Subchronic toxicity - Summary**								Adequate subchronic inhalation data on 1,1'-biphenyl were not located (HEED, 1990; TSCATS, 1992).		
1,1'-Biphenyl	92-52-4	**Chronic toxicity - Summary**								Chronic inhalation data on 1,1'-biphenyl were not located Evidence of chronic effects in humans has been reported (see Epidemiology section above) (HEED, 1990, TSCATS, 1992).		
1,1'-Biphenyl	92-52-4	Carcinogenicity	Rats	Oral	Diet	700 days	0, 0 001, 0.005, 0 01, 0 05, 0 1, 0 5, or 1%	15/sex/dose group	Histopathological examination revealed no treatment related incidence of tumors	Inadequate because insufficient numbers of test animals were used.	Reversible kidney lesions were observed at 0.5 and 1% and food consumption was decreased at 1%.	Ambrose et al , 1960
1,1'-Biphenyl	92-52-4	**Carcinogenicity - Summary**								Carcinogenicity data on inhaled 1,1'-biphenyl were not located, adequate oral data were not located (HEEP, 1984; TSCATS, 1992; CHEMTRACK, 7/93).		
1,1'-Biphenyl	92-52-4	**Neurotoxicity - Summary**								Neurotoxicity data on inhaled 1,1'-biphenyl were not located (HEEP, 1984; HEED, 1990; TSCATS, 1992).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
1,1'-Biphenyl	92-52-4	Developmental toxicity	Rats	Oral	Gavage	Gestation days 6-15	0, 125, 250, 500, or 1000 mg/kg/day	18 to 20 mated females/group	Maternal and embryotoxicity occurred at 1000 mg/kg/day (mortality of 5 dams during the treatment period, preceded by a sharp reduction in body weight and diarrhea), increased resorptions, and 5 dams were found not to be pregnant, possibly due to interference with implantation). No effects were noted on dams or development of offspring in the other test groups.	Adequate study.	An appropriate range of test levels and number of test animals were used, appropriate endpoints were examined.	Khera et al , 1979
1,1'-Biphenyl	92-52-4	**Developmental toxicity - Summary**								Developmental inhalation toxicity data on 1,1-biphenyl were not located (HEEP, 1984; HEED, 1990; TSCATS, 1992) An adequate study conducted by the oral route is available in rats.		
1,1'-Biphenyl	92-52-4	3-Generation reproductive toxicity	Rats	Oral	Feeding	F_0 parents from age 4 months through mating, gestation, lactation; continuous dosing of F_1 and F_2 parent generations	0, 0.01, 0.1, or 1.0% dietary levels	3 males; 9 females/group	Decreased fertility and litter size of high-dose females and decreased growth rate of pups in the high-dose group There was no evidence of cumulative toxicity over 3 generations.	Inadequate because too few animals were used and histopathology was not performed.	The authors attributed the effects in the high dose group to a decrease in food consumption.	Dow Chemical Co., 1983
1,1'-Biphenyl	92-52-4	***Reproductive toxicity - Summary***								Reproductive inhalation toxicity data were not located. Adequate oral data are available for 1 species (HEEP, 1984, HEED, 1990; TSCATS, 1992).		
1,1'-Biphenyl	92-52-4	**Pharmacokinetics - Summary**								Pharmacokinetics data on inhaled 1,1-biphenyl were not located. (HEEP, 1984, HEED, 1990, TSCATS, 1992).		

REFERENCES

Ambrose, A M , Booth, A N , DeEDs, F , and Cox, A J., Jr "A toxicological study of biphenyl, a citrus fungistat " *Food Research* 25 328-336 (1960)

CHEMTRACK National Toxicology Program Results Report "Results, status and publication information on all NTP chemicals produced from NTP CHEMTRACK system " July (1993)

Dow Chemical Company "Toxicological study of diphenyl in citrus wraps with cover letter " TSCA 8D submission 878213721, microfiche number OTS0206456 Washington, DC OPPT, US EPA (1983)

Hakkinen, I , Siltanen, E , Hernberg, S., Seppalainen, A M , Karli, P., and Vikkula, E "Diphenyl poisoning in fruit paper production " *Archives of Environmental Health* 26.70-74 (1973)

IRIS "Health and Environmental Effects Document for 1,1'-Biphenyl " US Environmental Protection Agency (1990)

HEEP. "Health and Environmental Effects Profile for 1,1'-Biphenyl." US Environmental Protection Agency (1984)

Khera, K S , Whalen, C , Angers, G , and Trivett, G "Assessment of the teratogenic potential of piperonyl butoxide, biphenyl, and phosalone in the rat." *Toxicology and Applied Pharmacology*. 47:353-358 (1979)

Monsanto Company "Toxicological investigation of biphenyl." TSCA 8D submission 878213572, microfiche number OTS0206411 Washington, DC OPPT, US EPA (1983)

Sun Company Inc. "Acute inhalation toxicity of biphenyl with cover letter." TSCA 8D submission 878213530, microfiche number OTS0206401 Washington, DC OPPT, US EPA (1983a)

Sun Company Inc. "Subacute inhalation toxicity of biphenyl " TSCA 8D submission 878213531 microfiche number OTS0206401 Washington, DC OPPT, US EPA (1983b)

Sun Company Inc "90-Day inhalation toxicity study of biphenyl (99 + % purity) in CD_1 mice " TSCA 8D submission 878213532, microfiche number OTS0206401 Washington, DC OPPT, US EPA (1983c)

TSCATS (Toxic Substances Control Act Test Submissions) Database (1992)

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylbenzene	100-41-4	Epidemiology (Cohort study)	Humans	Occupational	Commercial production of ethylbenzene	29 years	Not reported	200 males	No effects were noted on complete blood count, hemoglobin concentration, or blood chemistry values Urinalysis indicated mandelic acid, phenol, and mercapturates were within maximum allowable concentration (MAC) range.	Marginal. Quantification of exposure levels was not reported	Workers were also exposed to benzene.	Bardodej and Cirek, 1988
Ethylbenzene	100-41-4	Epidemiology (Controlled human experimental)	Humans	Inhalation	Vapor	8 hours	100 ppm	18 volunteers	There were no adverse health effects. Only traces of ethylbenzene were found in expired air and only negligible amounts were excreted in the urine; at unspecified higher concentrations, irritation of the eyes and respiratory tract occurred and subjects developed headaches and fatigue	The study is inadequate because it was designed only as a biotransformation study of ethylbenzene and thus, only a limited number of endpoints were measured	This study identifies a *NOAEL of 100* ppm for subjective symptoms in humans.	Bardodej and Bardodejova, 1970
Ethylbenzene	100-41-4	**Epidemiology - Summary**								Adverse effects have been reported in workers exposed to ethylbenzene vapor; however, concomitant exposure to other compounds limits interpretation of these studies (Clement, 1990g).		
Ethylbenzene	100-41-4	Acute toxicity	Rats	Inhalation	Vapor	4 hours	2000, 4000, and 8000 ppm, and saturated vapors	6/group	Mortalities were 0/6, 3/6, 6/6, and 6/6 for 2000 ppm, 4000 ppm, 8000 ppm, and saturated vapors, respectively	This is not an adequate acute toxicity study because only one sex was tested	Purity was not reported; clinical signs were not reported and LC_{50} was not calculated	Union Carbide Corporation, 1987

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylbenzene	100-41-4	Acute toxicity	Mice	Inhalation	Vapor	30 minutes	410, 860, 1875 3970, and 9640 ppm	4 males/group	Decrease in respiratory rate was observed at all concentrations and sedation occurred at 9640 ppm	Inadequate The group size was small and the only effect examined was respiratory rate.	At the lower exposures, the onset of respiratory depression was slow.	Nielsen and Alarie, 1982
Ethylbenzene	100-41-4	**Acute toxicity - Summary**								Additional testing could be required on the acute inhalation toxicity of ethylbenzene because of the limited range of endpoints reported.		
Ethylbenzene	100-41-4	Subchronic toxicity	Rats	Inhalation	Vapor	6 hours/day, 5 days/week for 2, 5, 9, or 16 weeks	0, 50, 300, and 600 ppm	5 males/group	No effect was noted on weight gain. Increased relative kidney weight was noted at 2 and 9 weeks in high-dose animals, but not at 16 weeks. Other effects noted at 600 ppm included changes in hepatocyte ultrastructure, but no necrosis; altered liver and kidney metabolizing enzymes, slightly increased excretion of kidney GSH, but no change in hepatic glutathione	This is not an adequate study because of the small group size, use of only males, and the limited endpoints examined.	This study provides evidence that ethylbenzene can induce drug metabolizing enzymes	Elovaara et al., 1985

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylbenzene	100-41-4	Short-term exposure	Rats, mice, and rabbits	Inhalation	Vapor	6 hours/day for 4 days	0, 400, 1200, and 2400 ppm	5 male rats and mice and 4 male rabbits/exposure level	Mortality of rats (2400 ppm) and mice (1200 and 2400 ppm), with lacrimation, shallow breathing, and prostration prior to death. Congestion of the nasal mucosa, lungs, liver, and kidneys in rats (2400 ppm) and mice (1200 and 2400 ppm) was observed in animals that died and may not be treatment related Transient increased lacrimation was observed in rabbits at all exposure levels.	This study is inadequate because of the small group size and the use of only male animals	No histopathology was performed This study identifies a FEL of 1200 ppm for mice and of 2400 ppm for rats, and a NOAEL of 2400 ppm for rabbits. This study demonstrates possible portal-of-entry effects, however, since effects on the lungs were observed only in animals that died, the congestion may be merely related to not being bled.	Biodynamics Inc., 1987
Ethylbenzene	100-41-4	Subchronic toxicity	Rats, mice, and rabbits	Inhalation	Vapor	6 hours/day 5 days/week for 4 weeks	0, 99, 382, and 782 ppm (rats and mice); 0, 383, 782, or 1610 ppm (rabbits)	5/sex/exposure level	Salivation, lacrimation, and increased relative liver weights in rats at 382 ppm and greater; hematological effects in rats at 782 ppm and greater; no adverse effects in mice, decreased body weight gains in rabbits at 782 and 1610 ppm.	This is an inadequate study Too few animals per group were used and exposure was for a short duration.	Purity 99.7%; most important endpoints were evaluated, this study identifies a NOAEL of 382 ppm and a LOAEL of 782 in rats and rabbits, and a NOAEL of 1610 ppm in mice	Cragg et al , 1989

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylbenzene	100-41-4	Subchronic toxicity	Rats	Inhalation	Vapor	6 hours/day, 5 days/week for 90 days	0, 100, 250, 500, 750, and 1000 ppm	10/sex/exposure level	Dose-related increased incidence and severity of regeneration of renal tubules, increased relative kidney (500 ppm and higher) and liver weights (250 ppm and higher)	This is an adequate subchronic toxicity study	Purity >99.5%; this study identified a NOAEL of 100 ppm and a LOAEL of 250 ppm for increased relative liver weights No histological evidence of effects was observed in the spleen or thymus.	NTP, 1992
Ethylbenzene	100-41-4	Subchronic toxicity	Mice	Inhalation	Vapor	6 hours/day, 5 days/week for 90 days	0, 100, 250, 500, 750, and 1000 ppm	10/sex/exposure level	Increased relative liver (750 ppm and higher) and kidney weights (1000 ppm)	This is an adequate subchronic toxicity study.	Purity >99.5%; this study identified a NOAEL of 500 ppm and a LOAEL of 750 ppm for increased relative liver weights, no corresponding histological evidence of adverse effects was observed in the liver, spleen, thymus, or kidney.	NTP, 1992
Ethylbenzene	100-41-4	**Subchronic toxicity - Summary**								Adequate inhalation subchronic data were available (Clement, 1990g; NTP, 1992).		
Ethylbenzene	100-41-4	Chronic toxicity	Not reported	Inhalation	Not reported	2 years	Not reported	Not reported	A 13-week study has been completed, the 2-year histopathology evaluation is in progress.	The study is not available to be evaluated.	This test is currently in progress	CHEMTRACK, 1994
Ethylbenzene	100-41-4	**Chronic toxicity - Summary**								No data on the chronic inhalation toxicity of ethylbenzene were available; however, NTP is conducting an inhalation bioassay (Clement, 1990g; TSCATS, 1992; TOXLINE, 6/93)		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylbenzene	100-41-4	Carcinogenicity	Not reported	Inhalation	Not reported	2 years	Not reported	Not reported	A 13-week study has been completed, the 2-year histopathology evaluation is in progress	The study is not available to be evaluated	This test is currently in progress	CHEMTRACK, 1994
Ethylbenzene	100-41-4	**Carcinogenicity - Summary**								No data on the carcinogenicity of ethylbenzene were located (Clement, 1990g, TSCATS, 1992). Histopathology is being evaluated in an NTP inhalation carcinogenicity study in rats and mice (CHEMTRACK, 1994).		
Ethylbenzene	100-41-4	Neurotoxicity	Rats	Inhalation	Vapor	14 hours/day, 7 days/week for 1 week	0, 1500, 2000, or 3000 ppm for 1 5 hours, 0, 1000, 1500, or 2500 ppm for 2 more hours, and 0, 500, 1000, or 1500 ppm until the end of the study (The concentration was reduced because of overt toxicity)	12 males/group	In all but the group exposed to 1500 followed by 500 ppm, there was a clear impairment of auditory sensitivity which was more noticeable at 16 kHz than 8 kHz.	This is an inadequate since the concentration was reduced during the study to mitigate overt toxicity.	This study was part of a study of a large group of solvents that indicated that many solvents produce ototoxic effects.	Pryor and Rebert, 1993
Ethylbenzene	100-41-4	Brain chemistry assay	Rabbits	Inhalation	Vapor	12 hours/day, 7 days	0 or 750 ppm	8 males/group	Marked depletion of striatal and tuberoinfundibular dopamine was noted in treated animals	Not a standard neurotoxicity test	Results suggest that dopamine metabolism is a toxicity target for ethylbenzene.	Romanelli et al., 1986, Mutti et al., 1988
Ethylbenzene	100-41-4	**Neurotoxicity - Summary**								Ototoxic effects in rats indicate the potential for ethylbenzene to be a neurotoxic agent.		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylbenzene	100-41-4	Developmental toxicity	Rats	Inhalation	Vapor	6 hours/day or continuous exposure on gestation days 7-15	6 hours/day: 0 or 600 ppm; or Continuous exposure. 0, 600, 1200, and 2400 mg/m^3 (0, 138 2, 276 3, and 552 6 ppm)	17 or 19/exposure level	All dams survived, no other maternal effects were reported In the 6 hour/day exposure group, no embryonic or fetal effects were noted. In the continuous exposure group, significantly ($p<0$ 05) increased percent dead or resorbed fetuses and skeletal retardation was seen at 600 mg/m^3 and higher, and at 2400 mg/m^3, decreased fetal weight and increased incidence of extra ribs and skeletal malformations were seen.	Marginally adequate study The TSCA guidelines require 20 animals/group	It is unclear whether effects were seen in the dams. The tabular presentation included survival of dams, but no other maternal endpoint	Ungvary and Tatrai, 1985
Ethylbenzene	100-41-4	Developmental toxicity	Mice	Inhalation	Vapor	Continuous exposure on gestation days 6-15	0 and 500 mg/m^3 (0 and 115 1 ppm)	20/group	No effects were noted on maternal survival. Increased incidence of anomalies of the uropoietic apparatus occurred in treated mice. No other effects were reported.	Inadequate because only one exposure level was used.	Results were presented in summary form	Ungvary and Tatrai, 1985
Ethylbenzene	100-41-4	Developmental toxicity	Rabbits	Inhalation	Vapor	Continuous exposure on gestation days 7-20	0, 500, and 1000 mg/m^3 (0, 115.1, and 230 3 ppm)	60, 9, and 3 respectively	No effects were noted on maternal survival, weight gain, or relative liver weight. Decreased fetal body weight occurred at 500 mg/m^3, and all dams aborted at 1,000 mg/m^3.	Inadequate, the number of animals exposed was too small.	The study suggests that abortions are induced at concentrations that are not toxic to the dams.	Ungvary and Tatrai, 1985

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylbenzene	100-41-4	Developmental toxicity	Rats	Inhalation	Vapor	7 hours/day on gestation days 1-19	0, 100, or 1000 ppm	Not reported, target number of litters/group was 30	Maternal (increased liver, kidney, and spleen weights [relative or absolute not reported]) and developmental toxicity (increased incidence of extra ribs) at 1000 ppm.	This is a marginally adequate study.	Purity was not reported. This study identified a NOAEL of 100 ppm and a LOAEL of 1000 ppm for maternal and developmental toxicity.	Hardin et al , 1981
Ethylbenzene	100-41-4	Developmental toxicity	Rabbits	Inhalation	Vapor	7 hours/day on gestation days 1-24	0, 100, and 1000 ppm	29-30/exposure level	No maternal or developmental toxicity was observed (increased maternal liver weight and slightly decreased number of live kits/litter at *100 and 1000 ppm* were not considered treatment-related)	This study is inadequate because no toxicity was produced	Purity was not reported in Hardin et al., 1981, but in the Andrew et al , 1981 report, it is reported as >99% purity	Andrew et al., 1981
Ethylbenzene	100-41-4	Developmental toxicity	Rats	Inhalation	Vapor	7 hours/day, 5 days/week for 3 weeks, followed by mating, then exposure daily through 19 days of gestation	0, 100, and 1000 ppm	38 sperm positive	Maternal toxicity (increased relative liver, kidney, and spleen weights; reduced number of sperm-positive rats that were pregnant following pregestational exposures) at high-dose Developmental toxicity (increased incidence of supernumerary ribs and decreased *crown-rump* length) at 1000 ppm	Adequate study.	Purity >99%. Although only 2 exposure levels were used, a NOAEL (100 ppm) and LOAEL (1000 ppm) were identified for both maternal and developmental toxicity.	Andrew et al , 1981
Ethylbenzene	100-41-4	**Developmental toxicity - Summary**								Adequate developmental toxicity data were located in 1 species (Hardin et al., 1981; Andrew et al., 1981).		
Ethylbenzene	100-41-4	**Reproductive toxicity - Summary**								No data on the reproductive toxicity of ethylbenzene were located (Clement, 1990g; TSCATS, 1992; TOXLINE, 6/93).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylbenzene	100-41-4	**Pharmacokinetics - Summary**									Information on the absorption, metabolism, and excretion of inhaled ethylbenzene is available in humans and animals; pharmacokinetics information on orally administered ethylbenzene is available for animals (Clement, 1990g)	

REFERENCES

Andrew, F D , Buschbom, R L , Cannon, W C , Miller, R A , Montgomery, L F., Phelps, D W , and Sikov, M R "Teratologic assessment of ethylbenzene and 2-ethoxyethanol " Prepared for NIOSH (National Institute for Occupational Safety and Health) Contract No 210-79-0037. NTIS PB83-20807 (1981)

Bardodej, Z , and Cirek, A. "Long-term study on workers occupationally exposed to ethylbenzene " *Journal of Hygiene, Epidemiology, Microbiology and Immunology* 32(1) 1-5 (1988)

Bardodej, Z , and Bardodejova, E. "Biotransformation of ethyl benzene, styrene, and alpha-methylstyrene in man." *American Industrial Hygiene Association Journal*. pp 206-209, March-April (1970).

Biodynamics, Inc. "A four-day inhalation study of ethylbenzene in the rat, mouse, and rabbit." TSCA 8D submission 86870000423, microfiche number OTS0513170 Washington, DC: OPPT, US EPA (1987)

CHEMTRACK. National Toxicology Program Results Report "Results, status and publication information on all NTP chemicals produced from NTP CHEMTRACK system " (1994).

Clement "Draft inhalation reference dose for ethylbenzene (100-41-4) " Prepared by Clement Associates, Inc for Environmental Criteria and Assessment Office (1990g)

Cragg, S T , Clarke, E A , Daly, I W., Miller, R R , Terrill, J B , and Ouellette, R E "Subchronic inhalation toxicity of ethylbenzene in mice, rats, and rabbits." *Fundamental and Applied Toxicology*. 13(3) 399-408 (1989)

Elovaara, E , Engstrom, K , Nickels, J., Aitio, A., and Vainios, H. "Biochemical and morphological effects of long-term inhalation exposure of rats to ethylbenzene." *Xenobiotica* 15(4):299-308 (1985)

Hardin, B D , Bond, G P , Sikov, M R , Andrew, F D , Beliles, R P., and Niemeier, R W "Testing of selected workplace chemicals for teratogenic potential " *Scandanavian Journal of Work Environment and Health* 7(suppl 4):66-75 (1981).

Mutti, A , Falzoi, M., Romanelli, A., Bocchi, M C., Ferroni, C , and Franchini, I "Brain dopamine as a target for solvent toxicity Effects of some monocyclic aromatic hydrocarbons " *Toxicology* 49 77-82 (1988)

Nielsen, G D , and Alarie, Y. "Sensory irritation, pulmonary irritation, and respiratory stimulation by airborne benzene and alkylbenzenes Prediction of safe industrial exposure levels and correlation with their thermodynamic properties." *Toxicology and Applied Pharmacology*. 65:459-477 1982)

NTP (National Toxicology Program) "Toxicity studies of ethylbenzene in F344/N rats and B6C3F1 mice (inhalation studies) " NIH Publication No. 92-3129 (1992)

Pryor, G T., and Rebert, C S "Neurotoxicity of inhaled substances." SRI International Final Report LSU-1644; Prepared under contract No 271-90-7202 (1993)

Romanelli, A , Falzoi, M , Mutti, A , Bergamaschi, E., and Franchini, I "Effects of some monocyclic aromatic solvents and their metabolites on brain dopamine in rabbits " *Journal of Applied Toxicology*. 6(6) 431-435 (1986)

TOXLINE National Library of Medicine Online Database (1993)

TSCATS (Toxic Substances Control Act Test Submissions) Database (1992)

Ungvary, G., and Tatrai, E "On the embryotoxic effects of benzene and its alkyl derivatives in mice, rats and rabbits " *Archives of Toxicology Supplement* 8 425-430 (1985)

Union Carbide Corporation "Range finding tests on m-xylene and ethyl benzene." TSCA 8D submission 86-870001406, microfiche number OTS0515568 Washington, DC OPPT, US EPA (1987).

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene dichloride	107-06-2	Epidemiology (Health surveys)	Humans	Occupational exposure	Aircraft industry workers, soft tank producers	Up to approximately 4 years	TWA 10-15 ppm	83 workers	Liver and gall bladder disease, nervous system dysfunction, and gastrointestinal disorders were observed	Inadequate because controls were not utilized.	This is a translation of a Russian study.	Kozik, 1957
Ethylene dichloride	107-06-2	Epidemiology (Case reports)	Humans	Occupational exposure	Oil refinery workers	Not reported	10 to 200 ppm	16 males	Burning sensation in the eyes, lacrimation, dizziness, fatigue, drowsiness, nausea, occasional vomiting, constipation, loss of appetite, liver, and G I tract effects were noted	This study provides qualitative information on effects of ethylene dichloride.	Symptoms disappeared upon change of workplace, but reappeared upon re-exposure	Cetnarowicz, 1959
Ethylene dichloride	107-06-2	**Epidemiology - Summary**								Epidemiological data are available regarding exposure to mixtures containing ethylene dichloride (TSCATS, 9/93) Numerous accounts of acute and repeated occupational exposures report fatal and non-fatal outcomes; none provide exposure data, and subjects were usually simultaneously exposed to other potentially hazardous materials Death was generally attributed to respiratory and circulatory failure (HAD, 1984).		
Ethylene dichloride	107-06-2	Acute immuno-toxicity	Rats	Inhalation	Vapor	3 hours (5 hours for bactericidal activity assays)	0, 100, and 200 ppm	Males; number not reported	No effects were seen on pulmonary bactericidal activity, nor on alveolar microphage *in vitro* phagocytosis of chicken red blood cells, cytostasis, or cytolysis of tumor target cells. Lymphocyte function was not affected.	Inadequate. Only limited specialized endpoints were studied	This study evaluated the effects of ethylene dichloride on pulmonary defense mechanisms	Sherwood et al , 1987

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene dichloride	107-06-2	Acute immuno-toxicity	Mice	Inhalation	Vapor	3 hours (5 hours for bactericidal activity assays)	0, 2.5, 5, and 10 ppm	18-36 females/ group	Increased susceptibility to pulmonary bacterial infection was noted at 5 ppm; no effects were noted on this parameter or on survival at 2 5 ppm.	Inadequate Only limited specialized endpoints were studied.	This study evaluated the effects of ethylene dichloride on pulmonary defense mechanisms	Sherwood et al., 1987
Ethylene dichloride	107-06-2	Acute upper respiratory tract irritation study	Rats	Inhalation	Vapor, head only	10 minute	8 concentrations ranging from 640 to 12,000 ppm	4 males/group	No appreciable respiratory rate depression was observed and an RD_{50} could not be determined.	This is not a standard acute toxicity test.	This substance does not appear to be an irritant to the upper respiratory tract.	E I. DuPont de Nemours & Co , 1982
Ethylene dichloride	107-06-2	Acute toxicity	Mice, rats, and rabbits	Inhalation	Vapor	1 hour	200 ppm	10/group	4/10 mice died; no mortalities were seen in rats or rabbits.	Inadequate Only one exposure level was used and limited endpoints appear to have been examined.	This is a brief summary of a study; no supporting data are provided.	Union Carbide Corp , 1987
Ethylene dichloride	107-06-2	Acute toxicity	Rats	Inhalation	Vapor	4 hours	1000 ppm	6 males or females	4/6 died during the 14 day observation period.	Inadequate. Use of controls was not reported, and the number of exposure levels and animals/group is unclear	Graded concentrations were tested, but only data on 1000 ppm were provided.	Carpenter et al., 1949
Ethylene dichloride	107-06-2	Acute toxicity	Rats	Inhalation	Vapor	0 1 to 7.0 hours to decreasing concentrations	200 to 12,000 ppm	4-6/group (sex not reported)	Adverse effects (not described) occurred with exposure to 200 ppm for 5 5 hours up to 12,000 ppm for 0 1 hour.	Inadequate Exposure was not for a set duration, and low numbers of test animals were used.	CNS depression occurred prior to death.	Spencer et al , 1951
Ethylene dichloride	107-06-2	Acute toxicity	Rats	Inhalation	Vapor	0 5 to 8 hours	6 concentrations from 300 to 3000 ppm	10 to 44 males/exposure level	Mortality occurred in all treatment groups except 300 ppm for 7 hours.	Inadequate. Exposure times varied and use of controls was not reported	Liver and kidney appeared to be target organs.	Spencer et al., 1951

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene dichloride	107-06-2	Acute toxicity	Rats, mice, guinea pigs, rabbits, cats, hogs, and raccoons	Inhalation	Vapor	1.5 to 7 hours	1500 and 3000 ppm	13-20 rats, 20-23 mice, 12-14 guinea pigs, 16 rabbits, 3 cats, 2 hogs, and 2 raccoons	Mortality occurred at 3000 ppm in all species except raccoons; 4/20 rats and 20/20 mice died after exposure to 1500 ppm for 7 hours	Inadequate. Exposure times varied, only 2 exposure levels were used, and use of controls was not reported.	Lungs and kidney appeared to be target organs.	Heppel et al., 19
Ethylene dichloride	107-06-2	**Acute toxicity - Summary**								Adequate acute inhalation toxicity data were not located, but available animal data support findings in humans; acute toxicity signs include squinting and lacrimation of the eyes, rubbing of th nose, vertigo, static and motor ataxia, unconsciousness, incoordination of extremities, and congestion of the liver, spleen lungs, adrenal glands, and kidneys. Death was usually ascribed respiratory and circulatory failure (HAD, 1984).		
Ethylene dichloride	107-06-2	Subchronic toxicity	Rabbits	Inhalation	Vapor	2 hours/day, 5 days/week, 90 days	3000 ppm	10 (sex not reported)	Anemia, granuloblastic, and erythroblastic hyperplasia of bone marrow, altered liver and kidney function, and vascular degeneration and focal necrosis of the liver and kidney were observed.	This study is limited by use of only one test exposure and no reported use of controls	Results suggest that ethylene dichloride affects formed elements of the blood	Lioia and Elmin 1959
Ethylene dichloride	107-06-2	Subchronic toxicity	Rats, guinea pigs, rabbits, and cats	Inhalation	Vapor	6 hours/day, 5 days/week, 6 weeks	0, 100, and 500 ppm	10 (rats and guinea pigs) and 4 (rabbits and cats), sexes not reported	Mortality was high in all species following exposure at 500 ppm; necropsy revealed lesions in the liver, kidney, adrenals, heart, and lungs. At 100 ppm, cats had decreased weight gain. No other effects were noted in animals exposed to 100 ppm.	This study is limited by the use of only 2 test levels.	A NOAEL of 100 ppm was identified for rats, guinea pigs, and rabbits; a NOAEL was not identified for cats	Hofmann et al., 1971

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene dichloride	107-06-2	Subchronic toxicity	Rats, guinea pigs, rabbits, and cats	Inhalation	Vapor	6 hours/day, 5 days/week for 26 weeks	0 and 500 ppm for 13 weeks, followed by 1000 ppm for an additional 13 weeks	4 cats, 4 rabbits, 10 guinea pigs, and 10 rats equally divided by sex	No adverse effects were seen after 13 weeks at 500 ppm, so animals were exposed for an additional 13 weeks to 1000 ppm. No evidence of toxicity was seen in rats, guinea pigs, or rabbits. In cats, renal injury with histological alterations and increased blood urea developed after the additional high-exposure	This is not a standard protocol for subchronic toxicity because exposure levels were changed during the study	Ethylene dichloride was not toxic to rats, guinea pigs, or rabbits at high levels of exposure; A LOAEL of 1000 ppm was identified in cats	Hofmann et al., 1971
Ethylene dichloride	107-06-2	Repeated exposure; pulmonary defense evaluation	Rats	Inhalation	Vapor	5 hours/day, 5 days/week for 12 exposures	0, 10, 20, 50, or 100 ppm	Males, number not reported	No effects were seen on pulmonary bactericidal activity, nor on alveolar microphage *in vitro* phagocytosis of chicken red blood cells, cytostasis, or cytolysis of tumor target cells. Lymphocyte function was not affected.	This is not a standard subchronic toxicity test.	Limited endpoints were examined.	Sherwood et al., 1987
Ethylene dichloride	107-06-2	Repeated exposure, pulmonary defense evaluation	Mice	Inhalation	Vapor	5 hours/day for 5 days	0 or 2 5 ppm	18-36 females/ group	No effects were noted on survival or bactericidal activity at 2 5 ppm.	This is not a standard subchronic toxicity test	Limited endpoints were examined.	Sherwood et al., 1987
Ethylene dichloride	107-06-2	**Subchronic toxicity - Summary**								Adequate subchronic inhalation toxicity data were not located (TSCATS, 9/93; HEEP, 1985; HAD, 1984) Limited available da in 5 species suggest ethylene dichloride is moderately toxic and th the liver and kidneys are the primary targets.		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene dichloride	107-06-2	Chronic toxicity	Rats	Inhalation	Vapor	7 hours/day, 5 days/week for 78 weeks	0, 5, 10, and 50 ppm, and 250 ppm reduced to 150 ppm	90/sex/group	A high incidence of mortality in the 250 ppm group led to reduced concentration of 150 ppm from week 10 to the end of the study Increased SGPT, τ-glutamine transpeptidase (females only), blood glucose and uric acid levels were noted at 50 and 150 ppm, and SGOT and cholesterol levels were depressed at these levels.	Adequate study, adequate test levels were used over an adequate lifespan.	Animals were observed for life.	Maltoni et al., 1980 (also presented as an abbreviated report in Dow Chemical Co., 1987)
Ethylene dichloride	107-06-2	Chronic toxicity	Mice	Inhalation	Vapor	7 hours/day, 5 days/week for 78 weeks	0, 5, 10, and 50 ppm, and 250 ppm reduced to 150 ppm	90/sex/group	A high incidence of mortality in the 250 ppm group led to reduced concentration of 150 ppm from a few days (not quantified) to end of the study. No treatment-related increases in incidence of tumors were observed	Adequate study using adequate test levels over an appropriate duration	The report indicates a NOAEL of 150 ppm was identified.	Maltoni et al., 1980 (also presented as an abbreviated report in Dow Chemical Co., 1987)
Ethylene dichloride	107-06-2	Chronic toxicity	Rats, guinea pigs, rabbits, and monkeys	Inhalation	Vapor	7 hours/day, 5 days/week for 170 to 248 days	100, 200 (rats and guinea pigs only), and 400 ppm (all species)	15/sex rats, 8/sex guinea pigs, 2 male, 1 female rabbit; and 2 male monkeys	400 ppm = NOAEL in rabbits, 200 ppm = NOAEL in rats, 100 ppm = NOAEL in other species Guinea pigs showed decreased body weight, increased relative liver weight and slight hepatic degeneration at 200 ppm. Mortality occurred in all species but in rabbits at 400 ppm.	This study is inadequate because of the short duration of exposure	Data suggest that guinea pigs may be more sensitive to inhaled ethyl dichloride than rats, but use of small numbers of test animals weakens this conclusion.	Spencer et al., 1951

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene dichloride	107-06-2	**Chronic toxicity - Summary**								Adequate chronic inhalation toxicity data are available in two species, with the liver as an apparent target organ.		
Ethylene dichloride	107-06-2	Carcinogenicity	Rats	Inhalation	Vapor	7 hours/day, 5 days/week for 78 weeks	0, 5, 10, and 50 ppm, and 250 ppm reduced to 150 ppm	90/sex/group	A high incidence of mortality in the 250 ppm group led to reduced concentration of 150 ppm from week 10 to end of the study No treatment-related increases in incidence of tumors was observed; however, a non-significant, non-concentration-related increase in benign mammary tumors (fibromas and fibroadenomas) was noted in treated animals.	Adequate study examining appropriate endpoints	Clear evidence of carcinogenicity was not observed during the lifetime of the rats.	Maltoni et al , 1980 (also presented as an abbreviated report in Dow Chemical Co., 1987)
Ethylene dichloride	107-06-2	Carcinogenicity	Mice	Inhalation	Vapor	7 hours/day, 5 days/week for 78 weeks	0, 5, 10, and 50 ppm, and 250 ppm reduced to 150 ppm	90/sex/group	A high incidence of mortality in the 250 ppm group led to reduced concentration of 150 ppm from a few days (not quantified) to end of the study. No treatment-related increases in incidence of tumors was observed.	Adequate study examining appropriate endpoints.	Evidence of carcinogenicity was not observed during the lifetime of the mice	Maltoni et al , 1980 (also presented as an abbreviated report in Dow Chemical Co , 1987)

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene dichloride	107-06-2	Carcinogenicity	Rats	Inhalation	Vapor	7 hours/day, 5 days/week for 24 months	0 and 50 ppm	50/sex/group	There were no significant changes in body weight or tumor incidence.	This study is inadequate because only one exposure level was used and this was not the highest concentration that could be tested	Addition of disulfiram to the diet, which produced higher ethylene dichlorsde levels, resulted in increases in liver, mammary gland (females) and testicular tumors	Cheever et al., 1990
Ethylene dichloride	107-06-2	Carcinogenicity	Rats	Oral	Gavage	5 days/week for 78 weeks	0, TWA 47, and 95 mg/kg/day	50/sex/treatment group, 20/sex/control group	Increased mortality occurred at 47 mg/kg/day and higher. Dose-related increased incidence of squamous cell carcinoma of the forestomach, hemangiosarcomas of the circulatory system, and subcutaneous fibromas occurred in treated male rats. Incidence of combined mammary fibromas and adenocarcinomas was also dose-related in females	Adequate.	Evidence of carcinogenicity was seen in both sexes.	NCI, 1978

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene dichloride	107-06-2	Carcinogenicity	Mice	Oral	Gavage	5 days/week, 78 weeks	0, TWA for males = 97 and 195 mg/kg/day; TWA for females = 149 and 299 mg/kg/day	50/sex/treatment group; 20/sex/control group	Increased mortality occurred in high-dose females; no other effects on survival were reported. Increased mammary adenocarcinomas and endometrial stromal polyps and sarcomas were seen in females, increased hepatocellular carcinomas were seen in males, and increased alveolar/bronchiolar adenomas were seen in both sexes.	Adequate	Evidence of carcinogenicity was seen in both sexes	NCI, 1978
Ethylene dichloride	107-06-2	**Carcinogenicity - Summary**								An adequate carcinogenicity study is available for rats and mice (Maltoni et al. 1980), and oral gavage and drinking water 13-week studies have been completed in rats and mice (NTP, 1991), no indication of continuing studies by NTP was reported (CHEMTRACK, 1993).		
Ethylene dichloride	107-06-2	**Neurotoxicity - Summary**								Neurotoxicity data on ethylene dichloride were not located in the available literature (TSCATS, 9/93; HEEP, 1985; HAD, 1984).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene dichloride	107-06-2	Developmental toxicity	Rats	Inhalation	Vapor	7 hours/day, gestation days 6 through 15	0, 100, and 300 ppm	16 to 30 bred females/group	Maternal mortality (two-thirds of exposed dams) occurred at 300 ppm. No evidence of maternal or developmental toxicity was seen at 100 ppm	This study is inadequate because only 2 test concentrations were used, and because there was an insufficient number of pregnant rats at 100 ppm	A threshold for maternal toxicity was not identified The NOAEL for maternal toxicity was 100 ppm. There was extreme maternal toxicity at 300 ppm (including ataxia and lethargy) and 10/16 rats died. In addition, there were no pups born to the surviving dams.	Shell Oil Co., 1979 (also cited in Rao et al , 1980)
Ethylene dichloride	107-06-2	Developmental toxicity	Rabbits	Inhalation	Vapor	7 hours/day, gestation days 6 through 18	0, 100, and 300 ppm	19-21 bred females/group	Maternal mortality occurred at both treatment levels No developmental effects were noted at any treatment level	This study is marginally adequate because only 2 test concentrations were used.	A maternal NOAEL was not identified	Shell Oil Co., 1979 (also cited in Rao et al., 1980)
Ethylene dichloride	107-06-2	**Developmental toxicity - Summary**								Adequate inhalation or oral developmental toxicity studies were not located in the available literature (HAD, 1984; HEEP, 1985, TSCATS, 9/93)		
Ethylene dichloride	107-06-2	Single generation reproduction study	Rats	Inhalation	Vapor	6 hours/day, 5 days/week during a pre-breeding period of 12 weeks through breeding, gestation, and lactation	0, 25, 75, and 150 ppm	30/sex/group	No observable signs of toxicity were seen at any treatment level in dosed parents or offspring.	This study is limited by lack of identification of an effect level	A free-standing NOEL of 150 ppm was identified.	Rao et al., 1980 Murray et al , 1980

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene dichloride	107-06-2	Multi-generation reproduction study	Mice	Oral	Drinking water	Continuous among P_0 generation for 5 weeks pre-mating through 2 weeks after weaning; F1 generation for 11 weeks pre-mating through gestation	0, 30, 90, and 290 mg/L	10 males and 30 females/group	No observable signs of toxicity were seen at any treatment level in dosed parents or offspring of either generation	This study is limited by lack of identification of an effect level in either generation.	A free-standing NOEL of 290 mg/L in drinking water was identified.	Lane et al., 1982
Ethylene dichloride	107-06-2	**Reproductive toxicity - Summary**								Adequate reproductive toxicity data were not located in the available literature (HAD, 1984; HEEP, 1985, TSCATS, 9/93).		
Ethylene dichloride	107-06-2	**Pharmacokinetics - Summary**								Data regarding absorption, distribution, metabolism, and excretion of inhaled and orally ingested ethylene dichloride are available and indicate that this substance is rapidly absorbed, distributed throughout body tissues, metabolized by hepatic microsomal systems, and eliminated primarily by urinary excretion or exhalation via the lungs (HEEP, 1985).		

REFERENCES

Carpenter, C.P., Smyth, H.P., and Pozzani, D.C. "The assay of acute vapor toxicity, and the grading and interpretation of results on ninety-six chemical compounds." *Journal of Industrial Hygiene and Toxicology*. 31(6):343-346 (1949).

Cetnarowicz, J. "Experimental and clinical investigations into the actions of dichloroethane." *Folia Medica Cracov*. 1:169-192 (Polish article summarized from English translation) (1959)

Cheever, K.L., Cholakis, J.M., El-Hawari, A.M., Kovatch, R.M., and Weisburger, E.K. "Ethylene dichloride: The influence of disulfiram or ethanol on oncogenicity, metabolism, and DNA covalent binding in rats." *Fundamental and Applied Toxicology*. 14:243-261 (1990).

CHEMTRACK National Toxicology Program Results Report "Results, status and publication information on all NTP chemicals produced from NTP CHEMTRACK system." July (1993).

Dow Chemical Co. "Studies on long-term effects on rats and mice of ethylene dichloride, administered by inhalation." TSCA 8D submission 86-870002194, microfiche number OTS0515984. Washington, DC: OPPT, US EPA (1987).

E.I. DuPont de Nemours & Co. "Upper respiratory tract irritation in rats." TSCA 8D submission 86-87001042, microfiche Number OTS0514944. Washington, DC: OPPT US EPA (1982)

HAD. "Health Assessment Document for 1,2-Dichloroethane." US Environmental Protection Agency. (1984)

IRIP "Health and Environmental Effects Profile for Dichloroethenes " US Environmental Protection Agency (1985)

Heppel, L A , Neal, P A , Perrin, T L , Endicott, K M , and Porterfield, V T "The toxicology of 1,2-dichloroethane (ethylene dichloride) III Its acute toxicity and the effect of protective agents " *Journal of Experimental Pharmacology and Therapy*. 83.53-63 (1945).

Hofmann, H T , Birnstiel, H , and Jobst, P "Inhalation toxicity of 1,1-and 1,2-dichloroethane " *Archives of Toxicology* 27(3):248-265 (1971)

Kozik, I V "Problems of industrial hygiene in using dichloroethane in the aircraft industry " *Gigiena de Truda i Professionalnye Zabolevania* 1:31-38 (1957).

Lane, R.W , Riddle, B L , and Borzelleca, J F "Effects of 1,2-dichloroethane and 1,1,1-trichloroethane in drinking water on reproduction and development in mice " *Toxicology and Applied Pharmacology* 63 409-421 (1982).

Lioia, N., and Elmino, O "Toxicity of 1,2-dichloroethane I Behavior of the formed elements of the blood and marrow " *Folia Medica* 42 1238-1254 (1959)

Maltoni, C , Valgimigli, L., and Scarnato, C. "Long-term carcinogenic bioassays on ethylene dichloride administered by inhalation to rats and mice " In. *Banbury Report No. 5*. Ames, B , Infante, P , and Reitz, R , eds. Cold Spring Harbor Laboratory pp 3-33 (1980)

Murray, J S , Rao, K S , Young, J T , Calhoun, L.L., Hanley, T R Jr., Deacon, M.M., Pilny, M.K , and John, J A "Ethylene dichloride Single generation inhalation reproduction study in rats with cover letter " TSCA FYI submission FYI-AX-0680-0078, microfiche number OTS000078 Washington, DC OPPT, US EPA (1980)

NCI. National Cancer Institute. "Bioassay of 1,2-dichloroethane for possible carcinogenicity " Technical Report Series Number 55 (1978)

Rao, K.S , Murray, J S , Deacon, M M , John, J A., Calhoun, L.L , and Young, J.T "Teratogenicity and reproduction studies in animals inhaling ethylene dichloride " *Banbury Report*. 5 149-166 (1980)

Shell Oil Co. "The effects of inhaled ethylene dichloride on the embryonal and fetal development in rats and rabbits with attachments " TSCA 8D submission 86-870001578, microfiche number OTS0516159. Washington, DC OPPT, US EPA (1979)

Sherwood, R L., O'Shea, W., Thomas, P T., Ratajczak, H V., Aranyi, C., and Graham, J A. "Effects of inhalation of ethylene dichloride on pulmonary defenses of mice and rats " *Toxicology and Applied Pharmacology* 91:491-496 (1987).

Spencer, H C., Rowe, V K , Adams, E M , McCollister, D D , and Irish, D.D "Vapor toxicity of ethylene dichloride determined by experiments on laboratory animals." *Journal of Industrial Hygiene and Occupational Medicine*. 4.482-493 (1951)

TSCATS (Toxic Substances Control Act Test Submissions) Database (1993)

Union Carbide Corporation "The toxicity of ethylene dichloride " TSCA 8D submission 86-870001403, microfiche Number OTS0515565 Washington, DC OPPT US EPA (1987)

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene glycol	107-21-1	Epidemiology (Human acute exposure)	Humans	Inhalation	Aerosol	Not reported	3, 67, 140, and 200 mg/m³ (1.2, 26.4, 55.1, and 78.8 ppm)	Not reported	Subjective reports of irritation at 140 mg/m³ and intolerable at 200 mg/m³; no effects were reported at 3 or 67 mg/m³.	There are no guidelines for acute toxicity studies in humans	This study reported only subjective responses, no controls were reported	Wills et al., 1974
Ethylene glycol	107-21-1	Epidemiology (Human repeated exposure)	Humans	Inhalation	Aerosol	20-22 hours/day for 7 or 30 days	0 or 30 mg/m³ (0 or 11.8 ppm)	4 men/preliminary exposure group 20 men/main study group	No effects on hematology, clinical chemistry, urinalysis, EKG, EEG, psychological testing of *reaction time*, visual-motor coordination, perception, or mental ability	Studies of experimental exposures of humans are note required under TSCA.	This study identifies a NOAEL of 30 mg/m³.	Wills et al., 1974
Ethylene glycol	107-21-1	**Epidemiology - Summary**								A limited study in humans indicates that ethylene glycol is irritating (not further defined) to intolerable. No other epidemiology studies were located (HEA, 1987; SRC, 1987; TSCATS, 1992).		
Ethylene glycol	107-21-1	**Acute toxicity - Summary**								No data from animal studies on the acute inhalation toxicity of ethylene glycol were located (HEA, 1987; SRC, 1987; TSCATS, 1992; NTP, 1993).		
Ethylene glycol	107-21-1	Subchronic toxicity	Rats, guinea pigs, rabbits, monkeys, and dogs	Inhalation	Vapor	Continuously for 90 days	0 or 12 mg/m³ (0 or 4.7 ppm)	15 rats/sex/ exposure group; 15 guinea pigs/sex/ exposure group; 3 male rabbits/ exposure group; 3 male monkeys/ exposure group; and 2 male dogs/ exposure group	Mortality was observed in 1/15 rats, 3/15 guinea pigs, and 1/3 rabbits; increased pulmonary inflammation was observed in all species; ocular irritation and edema was observed in rabbits, and 2 rats became blind	A limited number of endpoints were evaluated; however, this study demonstrates portal-of entry effects.	This study identifies a LOAEL (and possibly a FEL) of 12 mg/m³ for rats, guinea pigs, rabbits, monkeys, and dogs	Coon et al., 1970

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene glycol	107-21-1	Subchronic toxicity	Rats, guinea pigs, rabbits, monkeys, and dogs	Inhalation	Vapor	8 hours/day, 5 days/week for 6 weeks	0, 10, or 57 mg/m^3 (0, 3.9, or 22.4 ppm)	15 rats/sex/ exposure group; 15 guinea pigs/sex/ exposure group, 3 male rabbits/ exposure group, 3 male monkeys/ exposure group, and 2 male dogs/ exposure group	No mortality was observed, nonspecific inflammatory changes in the hearts and lungs were observed in all species at 57 mg/m^3, but not at 10 mg/m^3	A limited number of endpoints were evaluated, however, this study demonstrates portal-of entry effects.	This study identifies a NOAEL of 10 mg/m^3 and a LOAEL of 57 mg/m^3 for rats, guinea pigs, rabbits, monkeys, and dogs.	Coon et al., 1970
Ethylene glycol	107-21-1	**Subchronic toxicity - Summary**								Inadequate data are available for evaluating the subchronic inhalation toxicity of ethylene glycol. The available data indicate a potential for portal-of-entry effects (HEA, 1987; SRC, 1987).		
Ethylene glycol	107-21-1	**Chronic toxicity - Summary**								No data on the chronic inhalation toxicity of ethylene glycol were located (HEA, 1987, SRC, 1987; TSCATS, 1992, NTP, 1993). Chronic oral toxicity data indicate that ethylene glycol is toxic to mice and that target organs are liver, lungs, and kidneys (NTP, 1993).		
Ethylene glycol	107-21-1	Carcinogenicity	Mice	Oral	Diet	2 years	Males 0, 6250, 12,500, or 25,000 ppm (approximately 1500, 3000, or 6000 mg/kg/day) Females 0, 12,500, 25,000, or 50,000 ppm (approximately 3000, 6000, or 12,000 mg/kg/day)	60/sex/group	No chemical-related neoplasms were seen in mice of either sex at any treatment level. The range of exposures encompassed levels that produced systemic toxicity	This is an adequate dietary study; appropriate endpoints were examined following an acceptable protocol.	No effect was noted on survival of either sex at any dose	NTP, 1993

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene glycol	107-21-1	Carcinogenicity	Rats	Oral	Diet	24 months	0.04, 0.2, or 1.0 g/kg bw/day	26/sex/group	There was no statistically significant increase in tumor incidence in rats	This appears to be a well conducted study, although group size was only half of that recommended in the TSCA test guidelines.	The high dose was the maximum tolerated dose, with all of the males at this dose dying by 18 months.	DePass et al. 1986a
Ethylene glycol	107-21-1	Carcinogenicity	Mice	Oral	Diet	24 months	0.04, 0.2, or 1.0 g/kg bw/day	16/sex/group	There was no statistically significant increase in tumor incidence in mice	This appears to be a well conducted study, although only 16 animals/ sex/group were used rather than the 50 recommended in the TSCA test guidelines.	There was a non-statistically significant increase in lymphosarcomas in the high dose females by 1 of 3 tests used. The tumors appeared to develop earlier in this group.	DePass et al. 1986a
Ethylene glycol	107-21-1	**Carcinogenicity - Summary**								No data on the carcinogenicity of ethylene glycol following inhalation exposure were located (HEA, 1987; SRC, 1987; TSCATS, 1992). Adequate oral dietary carcinogenicity studies conducted in mice provided no evidence of carcinogenic activity of ethylene glycol. This compound was withdrawn from NTP feeding bioassay (CHEMTRACK, 7/93).		
Ethylene glycol	107-21-1	**Neurotoxicity - Summary**								No neurotoxicity data on ethylene glycol were located (HEA, 1987; SRC, 1987, TSCATS, 1992).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene glycol	107-21-1	Developmental toxicity	Rats	Inhalation	Aerosol	6 hours/day on gestation days 6-15	0, 60, 400, and 1000 ppm (0, 150, 1000, and 2500 mg/m^3)	25/exposure group	Increased maternal absolute and relative liver weights (this may not be a toxic effect) at 1000 ppm, increased delayed ossification in the fetal hindlimbs at 400 and 1000 ppm	This is an adequate study, although assessment of concentration-effects relationships may be difficult	The author concluded that, due to grooming, oral intake was greater than inhaled intake of the compound; this study identified a NOAEL of 1000 ppm (2500 mg/m^3) for maternal toxicity, and a NOAEL of 60 ppm (150 mg/m^3) and a LOAEL of 400 ppm (1000 mg/m^3) for developmental toxicity.	Union Carbide Corp., 1985
Ethylene glycol	107-21-1	Developmental toxicity	Mice	Inhalation	Aerosol	6 hours/day on gestation days 6-15	0, 60, 400, and 1000 ppm (0, 150, 1000 and 2500 mg/m^3)	25/exposure group	Decreased maternal body weight at 400 and 1000 ppm; developmental toxicity observed at 400 and 1000 ppm included increased number of late resorptions and increased incidence of external, visceral, and skeletal malformations	This is an adequate study, although assessment of concentration-effects relationships may be difficult.	The author concluded that, due to grooming, oral intake was greater than inhaled intake of the compound; this study identifies a NOAEL of 60 ppm (150 mg/m^3) and a LOAEL of 400 ppm (1000 mg/m^3) for maternal and developmental toxicity.	Union Carbide Corp., 1985

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene glycol	107-21-1	Developmental toxicity	Mice	Inhalation (nose-only exposure or whole-body exposure)	Aerosol	6 hours/day on gestation days 6-15	Nose-only: 0, 500, 1000, and 2500 mg/m³ (0, 196.9, 393.8, and 984.6 ppm) Whole-body, as positive control: 0 and 2100 mg/m³ (0 and 827.1 ppm)	30/exposure group	Maternal kidney weights were increased at 1000 and 2500 mg/m³ (no *accompanying histologic* changes were seen). Developmental toxicity (decreased fetal body weights and increased incidence of skeletal variations) was observed at 2500 mg/m³.	This appears to be an adequate study Appendices *containing* individual animal data were not submitted with the report, but averages for all data points were presented in 12 accompanying tables.	This study identifies a NOAEL of 2500 mg/m³ for maternal *toxicity, and a* NOAEL of 1000 mg/m³ and a LOAEL of 2500 mg/m³ for developmental toxicity.	Tyl, 1988
Ethylene glycol	107-21-1	Developmental toxicity	Mice	Inhalation (nose-only or whole-body exposure)	Aerosol	6 hours/day on gestation day 6	Nose-only 2500 mg/m³ (984.6 ppm) Whole-body 2100 mg/m³ (827.1 ppm)	5/exposure group	These satellite females were sacrificed immediately after one exposure and washed in hot water to determine the amount of ethylene glycol on the fur. The quantity available for potential ingestion following whole-body exposure to 2100 mg/m³ was 1390 mg/kg, and after nose-only exposure to 2500 mg/m³ was 330 mg/kg.	This appears to be an adequate study	This is a useful satellite study that may explain the relatively greater severity of effects following whole-body exposure.	Tyl, 1988
Ethylene glycol	107-21-1	Developmental toxicity	Rats	Oral	Dietary	Gestation days 6-15	0, 40, 200, 1000 mg/kg/day	20 females/group	No maternal toxicity was seen at any treatment level Slightly increased preimplantation loss and significantly increased *incidence of poorly* ossified and unossified vertebral centra were noted at 1000 mg/kg/day	Adequate.	This study identified a maternal NOAEL of 1000 mg/kg/day and a *developmental* LOAEL of 1000 mg/kg/day.	Maronpot et al., 1983

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene glycol	107-21-1	Developmental toxicity screen	Mice	Oral	Gavage	1 dose/day on gestation days 7-14	0 or 11090 mg/kg/day (maximum tolerated dose)	50/exposure group	Decreased maternal body weight gain, fetal weight, and litter viability were seen in treated mice	Inadequate because only one exposure group was used and a NOAEL was not identified.	Developmental screen	Hazelton, 1987 (a NIOSH report, also reported as Schuler et al., 1983)
Ethylene glycol	107-21-1	Developmental toxicity	Mice	Oral	Gavage	1 dose/day on gestation days 6-15	0, 750, 1500, and 3000 mg/kg/day	23-24/exposure group	Maternal toxicity was noted at mid- and high-dose (decreased body weight gain and gravid uterine weight) Developmental toxicity (decreased average fetal body weight/litter) was noted in all treatment groups, and number of live fetuses/litter was decreased at high-dose. Malformation incidence (gross, visceral, and skeletal) was increased at all treatment levels	Inadequate because a NOAEL for developmental effects was not identified	A maternal NOAEL of 750 mg/kg/day was identified, but developmental effects were noted at all treatment levels. A similar study by Price et al., (1984b) found a decrease in number of live fetuses/litter and a decreased average fetal body weight/litter at 2500 mg/kg/day and higher	Price et al., 1984

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene glycol	107-21-1	Developmental toxicity	Rats	Oral	Gavage	1 dose/day on gestation days 6-20	0, 250, 1250, and 2250 mg/kg/day	16-20/exposure (4-5/replicate)	Maternal toxicity was observed at 1250 mg/kg/day and above (treatment-related renal pathology) At 2250 mg/kg/day, decreased body weight, body weight gain, and decreased absolute and relative kidney and postpartum uterine weights were observed Developmental toxicity occurred at 2250 mg/kg/day (decreased live litter size, neonatal pup body weight, and increased mortality)	Adequate	Maternal NOAEL was 250 mg/kg/day and LOAEL was 1250 mg/kg/day. Developmental NOAEL was 1250 mg/kg/day and LOAEL was 2250 mg/kg/day	Price et al , 1988
Ethylene glycol	107-21-1	Developmental toxicity, pilot study	Rabbits	Oral	Gavage	1 dose/day on gestation days 6-19	0, 100, 500, 1000, and 2000 mg/kg/day	23-24/group	Maternal toxicity was observed at 2000 mg/kg/day (42% mortality, early deliveries and spontaneous abortion, renal pathology). No evidence of embryotoxicity or teratogenicity was noted at any treatment level	Adequate	Although rabbits appear more sensitive to maternal toxicity than other species tested, they seem to be more resistant to developmental toxicity.	Tyl et al , 1991
Ethylene glycol	107-21-1	**Developmental toxicity - Summary**								Adequate developmental studies are available Inhalation developmental toxicity studies were available in 2 species (TSCATS, 1992).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene glycol	107-21-1	Multigeneration reproductive toxicity	Rats	Oral	Diet	Continuously for 3 generations	0, 40, 200, and 1000 mg/kg/day	10-20/sex/ exposure group/ generation	No general toxicity effects were observed, nor were there effects on fertility index, gestation in F_0, F_1, or F_2 rats, histopathology of testes, epididymis, accessory sex glands, uterus, or ovaries in any generation through F_2 rats.	This study is of limited use since there was no evidence of general toxicity in any treatment group, and thus, the dose levels may not have been adequate	This study identifies a NOAEL of 1000 mg/kg for parental and reproductive toxicity	DePass et al., 1986b
Ethylene glycol	107-21-1	Continuous breeding study	Mice	Oral	Drinking water	Continuously for 2 generations	0, 0.25%, 0.5% and 1.0% Authors estimated doses of 0, 0.41, 0.84 and 1.64 g/kg.	20/sex/generation	No effects were observed in the 0.25% groups. At the 1% level, there was a decrease in the number of litters/fetal pairs, live pups/litter, and live pup weight (this also occurred in the 0.5% group). In the 1% level, there was an increase in facial and skeletal abnormalities.	Adequate data indicate that ethylene glycol is a reproductive toxicant when administered continuously to mice in drinking water	A pilot study indicated that levels of 2.5% and 5.0% were lethal.	Lamb et al., 1985
Ethylene glycol	107-21-1	Continuous breeding study	Mice	Oral	Drinking water	Continuously for 2 generations	0, 0.5%, 1.0% and 1.5% Authors estimated doses of 0, 0.9, 1.8, 2.8 g/kg	20/sex/generation	At the 1.5% level, there was decreased fertility index, female pups/litter, pup weight, and increased pup death during weaning. At 1.0% and higher, there was facial abnormalities, and ablepharon. In the high dose males, sperm mobility was decreased, the number of abnormal sperm increased, and there was degeneration of the testes	Adequate data indicate that ethylene glycol is a reproductive toxicant when administered continuously to mice in drinking water.	The NOAEL level was 0.5%	Gulati et al., 1986

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Ethylene glycol	107-21-1	**Reproductive toxicity - Summary**								Sufficient evidence is available to indicate that ethylene glycol is a reproductive toxicant in male mice exposed continuously to ≥1% test material by the oral route in drinking water. Reproductive toxicity in female mice has not been ruled out.		
Ethylene glycol	107-21-1	**Pharmacokinetics - Summary**								Information on pharmacokinetics of oral and inhaled ethylene glycol is available in humans and animals (HEA, 1987; TSCATS, 1992; NTP, 1993). It is rapidly absorbed, metabolized, and eliminated in all species tested, and rates vary with dose and route of exposure.		

REFERENCES

CHEMTRACK National Toxicology Program Results Report "Results, status and publication information on all NTP chemicals produced from NTP CHEMTRACK system." July (1993)

Coon, R A , Jones, R A., Jenkins, L J , Jr , and Siegel, J "Animal inhalation studies on ammonia, ethylene glycol, formaldehyde, dimethylamine, and ethanol " *Toxicology and Applied Pharmacology*. 16:646-655 (1970).

DePass, L R , Garman, R H , Woodside, M D , Giddens, W E , Maronpot, R R , and Weil, C S "Chronic toxicity and oncogenicity studies of ethylene glycol in rats and mice " *Fundamental and Applied Toxicology* 7:547-565 (1986a)

DePass, L R , Woodside, M D , Maronpot, R R , and Weil, C.S "Three-generation reproduction and dominant lethal mutagenesis studies of ethylene glycol in the rat " *Fundamental and Applied Toxicology*. 7:566-572 (1986b)

Dow Chemical Corporation "Initial submission Developmental toxicity evaluation of ethylene glycol in mice by nose only or whole body exposure with cover letter dated 050792 " TSCA 8ECP submission 88-920002497, microfiche number OTS0537307 Washington, DC: OPPT, US EPA (1992)

Gulati, D.K , Hommel-Barnes, L., Welch, M., Russell, S , Poonacha, K B., and Lamb, J.C "Final report ethylene glycol- Reproduction and fertility assessment in CD-1 mice when administered in drinking water " Prepared for the National Toxicology Program. (1986).

Hazelton Labs "Screening of priority chemicals for potential reproductive hazard " Prepared for NIOSH, Cincinnati, OH (1987)

HEA "Health Effects Assessment for Ethylene Glycol " US Environmental Protection Agency (1987).

Lamb, J C , IV, Maronpot, R R , Gulati, D K , Russell, V S , Hommel-Barnes, L , and Sabharwal, P.S "Reproductive and developmental toxicity of ethylene glycol in the mouse " *Toxicology and Applied Pharmacology* 81 100-112 (1985)

Maronpot, R R., Zelenak, J P , Weaver, E.V , and Smith, N J. "Teratogenicity study of ethylene glycol in rats." *Drug Chemistry and Toxicology*. 6(6) 579-594 (1983).

NTP (National Toxicology Program) "NTP technical report on the toxicology and carcinogenesis studies of ethylene glycol in B6C3F$_1$ mice (feed studies) " NTP TR 413 (1993)

Price, C J , Tyl, R W , Piserchia, P.V , Feldman, D B , DeWoskin, R B , and Marr, M C "Teratologic evaluation of ethylene glycol administered to CD-1 mice on gestational days 6 through 15 " Prepared for National Center for Toxicological Research, Jefferson, Arkansas (1984)

Price C J., George, J D , Marr, M C., Kimmel, C A , Schwetz, B A , and Morrissey, R E "Developmental toxicity evaluation of ethylene glycol in CD rats " Prepared for National Center for Toxicological Research, Jefferson, Arkansas (1988)

SRC (Syracuse Research Corporation) "Reference doses (RfDs) for inhalation exposure, ethylene glycol " SRC TR 87-122 (1987)

TSCATS (Toxic Substances Control Act Test Submissions) Database (1992)

Tyl, R W , Fisher, L C , Kubena, M F., Vrbanic, M A., and Losco, P E "Developmental toxicity evaluation of ethylene glycol (EG) applied cutaneously to CD-1 mice. *Teratology Society Abstracts* p 498 (1988)

Tyl, R W , Price, C J , Marr, M C , Myers, C B., Heindel, J J , and Schwetz, B.A "Final report on the developmental toxicity of ethylene glycol in New Zealand white rabbits " Prepared for U S Department of Health and Human Services (1991)

Union Carbide Corporation "Summarized results of study to determine the teratogenic potential of ethylene glycol by exposure of CD rats and CD-1 mice to an aerosol of ethylene " TSCA FYI submission OTS-1085-0323 SU, microfiche number 0323. Washington, DC: OPPT, US EPA (1985)

Union Carbide Corporation. "Initial submission Ethylene glycol Developmental toxicity evaluation of the aerosol in CD-1 mice by nose only or whole body exposure (final report) with cover letter dated 103191 " TSCA 8ECP submission 88-9200000119, microfiche number OTSO534569. Washington, DC. OPPT, US EPA (1991)

Wills, J H , Coulston, F , Harris, E S , McChesney, E W , Russell, J.C , and Serrone, D.M. "Inhalation of aerosolized ethylene glycol by man " *Clinical Toxicology* 7(5):463-476 (1974)

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl isobutyl ketone	108-10-1	Epidemiology (Case studies)	Humans	Inhalation	Vapor	20-30 minutes of high-exposure; low-exposure for rest of work day	80 ppm (low exposure) and 500 ppm (high-exposure)	19 workers	Over 50% of the workers complained of nausea, headache, burning in the eyes, and weakness Somnolence, insomnia, and intestinal pain were also reported. 4 of the workers had enlarged livers.	This study indicates a potential for neurotoxicity, but it is inadequate for determining a NOAEL or LOAEL.	A LOAEL could not be determined because the effects may have resulted from short-duration exposures to high levels or from long-duration exposure to low levels	Linari et al., 1964
Methyl isobutyl ketone	108-10-1	Epidemiology (Case studies)	Humans	Inhalation	Vapor	15-30 minutes of high-exposure, low-exposure for rest of work day	50 ppm (low exposure) and 100-105 ppm (high-exposure)	14 cases	A few workers complained of gastrointestinal and CNS symptoms 2 of the workers had enlarged livers.	This study indicates a potential for neurotoxicity, but it is inadequate for determining a NOAEL or LOAEL.	This was a subgroup of the 19 workers studied by Linari et al., 1964 five years later	Armeli et al., 1968
Methyl isobutyl ketone	108-10-1	Epidemiology (Case studies)	Humans	Inhalation	Vapor	2 hours with exercise	10, 100, and 200 mg/m^3 (2 4, 24.4, and 48 8 ppm) MIBK; or 100 mg/m^3 (24.4 ppm) MIBK plus 150 mg/m^3 (39 6 ppm) toluene	8 males exposed to various concentrations in sequence	Irritation ($p = 0$ 066) and undefined CNS symptoms ($p = 0$ 101) were reported. Effects from MIBK alone were noted at all treatment levels and showed an exposure-related trend. Effects were greater from exposure to a mixture of MIBK and toluene than to the single substance. No effects were noted on simple reaction time, ability to do mental arithmetic, or mood	There are no guidelines for tests in humans	The small number of subjects and borderline statistical significance limits these data.	Hjelm et al., 1990
Methyl isobutyl ketone	108-10-1	**Epidemiology - Summary**								Another study briefly reported headache, nausea, and respiratory irritation in workers exposed to 100 ppm (Elkins, 1959)		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl isobutyl ketone	108-10-1	Acute toxicity	Mice	Inhalation	Vapor	30 minutes	19,500 and >20,000 ppm	10/exposure group	Anesthesia was produced in 7/10 animals at 19,500 ppm, however, all recovered normally following removal. Deep anesthesia was observed in mice at >20,000 ppm, and these mice did not recover. Mice dying had some congestion of the lungs.	This study demonstrated the anesthetic effects of methyl isobutyl ketone following acute exposure to high levels; however, only a limited number of endpoints were evaluated.	This study identified a LOAEL of 19,500 for anesthesia from acute exposure	E I DuPont de Nemours, 1983
Methyl isobutyl ketone	108-10-1	**Acute toxicity - Summary**								Data on the acute inhalation toxicity of methyl isobutyl ketone were inadequate (HEA, 1987, TSCATS, 1992).		
Methyl isobutyl ketone	108-10-1	Subchronic toxicity	Rats, dogs, mice, and monkeys	Inhalation	Vapor	Continuously for 2 weeks	0, 100, and 200 ppm	50 rats/exposure group, 40 mice/ exposure group, 8 dogs/exposure group; 4 monkeys/ exposure group	Increased relative kidney weights at 100 and 200 ppm, and increased relative liver weights at 200 ppm	This is an adequate range-finding study.	This study did not identify a NOAEL for rats, mice, dogs, and monkeys	MacEwen et al., 1971
Methyl isobutyl ketone	108-10-1	Subchronic toxicity	Rats, dogs, mice, and monkeys	Inhalation	Vapor	Continuously for 90 days	0 or 410 ppm	100 male rats/ exposure group, 8 male dogs/ exposure group, 2 male monkeys/ exposure group	No effects were observed in dogs and monkeys, rats had increased relative liver and kidney weights, and hyaline droplet degeneration of the proximal tubules with occasional tubular necrosis	These results are of questionable relevance because of the specialized conditions used in the study	This study was carried out under unusual conditions (oxygen-rich environment and low atmospheric pressure). This study identified a LOAEL of 410 ppm for rats and a NOAEL of 410 ppm for dogs and monkeys	MacEwen et al., 1971

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl isobutyl ketone	108-10-1	Subchronic toxicity	Rats	Inhalation	Vapor	6 hours/day, 5 days/week for 14 weeks	0, 50, 250, and 1000 ppm	14/sex/exposure level	Increased absolute and relative liver weights and total urinary protein in males at 1000 ppm, increased serum cholesterol and urinary glucose in males at 250 and 1000 ppm; increased incidence of hyaline droplets in renal proximal tubules in males at 250 and 1000 ppm.	This is an adequate subchronic toxicity study	This study identifies a NOAEL of 50 ppm and a LOAEL of 250 ppm for increased serum cholesterol and urinary glucose.	Phillips et al., 198
Methyl isobutyl ketone	108-10-1	Subchronic toxicity	Mice	Inhalation	Vapor	6 hours/day, 5 days/week for 14 weeks	0, 50, 250, and 1000 ppm	14/sex/exposure level	Increased absolute liver weight was seen in males at 250 ppm and higher, and increased relative liver weights in males at 1000 ppm.	This is an adequate subchronic toxicity study.	This study identified a NOAEL of 250 ppm	Phillips et al., 1987
Methyl isobutyl ketone	108-10-1	**Subchronic toxicity - Summary**								Adequate subchronic inhalation toxicity studies were available in 2 species.		
Methyl isobutyl ketone	108-10-1	**Chronic toxicity - Summary**								No data on the chronic inhalation toxicity of methyl isobutyl ketone were located (HEA, 1987; TSCATS, 1992).		
Methyl isobutyl ketone	108-10-1	***Carcinogenicity - Summary***								*No data on the carcinogenicity of methyl isobutyl ketone were* located (HEA, 1987, TSCATS, 1992). Methyl isobutyl ketone has been nominated for NTP testing; the route was not specified (CHEMTRACK, 7/93).		
Methyl isobutyl ketone	108-10-1	Neurotoxicity	Baboons	Inhalation	Vapor	Continuously for 7 days	0 or 50 ppm	4 juvenile males	Minimal effects in accuracy were observed in a delayed match-to-sample discrimination task, but response time was slowed.	This study reported equivocal effects for neurotoxicity following short-term exposure	This study identified a LOAEL of 50 ppm for behavioral changes	Geller et al., 1979

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl isobutyl ketone	108-10-1	Neurotoxicity	Hens	Inhalation	Vapor	Continuously for 90 days, followed by a 30-day observation period	0 or 1000 ppm	5/exposure level	Leg weakness was observed during exposure, followed by subsequent recovery	This is an inadequate study because only one exposure level was used and the group size was small	This study identifies a LOAEL of 1000 ppm.	Abou-Donia et al., 1985
Methyl isobutyl ketone	108-10-1	**Neurotoxicity - Summary**								Available data indicate a potential for neurotoxicity (see also developmental toxicity studies) (HEA, 1987) TSCA Section 4 inhalation neurotoxicity studies in rats are in progress (US EPA, 1993)		
Methyl isobutyl ketone	108-10-1	Developmental toxicity	Mice	Inhalation	Vapor	6 hours/day on gestation days 6-15	0, 300, 1000, and 3000 ppm	25/exposure level	Maternal toxicity (decreased body weight gain, loss of coordination, negative tail and toe pinch, partial paralysis, muscular weakness in hindlimbs, piloerection, lacrimation, and red perioral encrustation) was observed at 3000 ppm; decreased fetal body weights and increased incidence of unossified skeletal elements at 3000 ppm	This is an adequate study.	This study identified a NOAEL of 1000 ppm and a LOAEL of 3000 ppm for maternal and developmental toxicity	Union Carbide, 1984

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Methyl isobutyl ketone	108-10-1	Developmental toxicity	Rats	Inhalation	Vapor	6 hours/day on gestation days 6-15	0, 300, 1000, and 3000 ppm	25/exposure level	Maternal toxicity (decreased body weight gain, loss of coordination, negative tail and toe pinch, partial paralysis, muscular weakness in hindlimbs, piloerection, lacrimation, and red perioral encrustation) was observed at 3000 ppm, decreased fetal body weights and increased incidence of unossified skeletal elements at 3000 ppm	This is an adequate study	This study identifies a NOAEL of 1000 ppm and a LOAEL of 3000 ppm for maternal and developmental toxicity.	Union Carbide, 1984
Methyl isobutyl ketone	108-10-1	**Developmental toxicity - Summary**								Adequate developmental toxicity studies are available in 2 speci (HEA, 1987, TSCATS, 1992; TOXLINE, 1992).		
Methyl isobutyl ketone	108-10-1	**Reproductive toxicity - Summary**								No data on the reproductive toxicity of methyl isobutyl ketone w located (HEA, 1987; TSCATS, 1992; TOXLINE, 1992).		
Methyl isobutyl ketone	108-10-1	**Pharmacokinetics - Summary**								Limited information on the absorption and excretion of methyl isobutyl ketone was available in animals for the oral and inhalati routes (HEA, 1987, TSCATS, 1992; TOXLINE, 1992).		

REFERENCES

Abou-Donia, M B., Lapadula, D.M , Campbell, G., and Timmons, P R "The synergism of n-hexane-induced neurotoxicity by methyl isobutyl ketone following subchronic (90 days) inhalation in hens Induction of hepatic microsomal cytochrome P-450 " *Toxicology and Applied Pharmacol* 81 1-16 (1985)

Arneli, G , Linari, F , and Martorano, G "Rilievi clinici ed ematochimici in operai esposti all'azione di un chetone superiore (MIBK) ripetuti a distanza di 5 anni " *Lavoro Umano* 20 418-424 (1968)

CHEMTRACK National Toxicology Program Results Report "Results, status and publication information on all NTP chemicals produced from NTP CHEMTRACK system " July (1993)

E I DuPont de Nemours "Industrial Hygiene Bulletin" -- prepared by Shell Chemical Corporation with cover letter. TSCA 8D submission 878211796, microfiche number OTS205872 Washington, DC OPPT, US EPA (1983)

Elkins, H B "The Chemistry of Industrial Toxicology" Second Edition. New York, NY John Wiley and Sons p 121 (1959).

Geller, I., Gause, F., Kaplan, H., and Hartmann, R.J. "Effects of acetone, methyl ethyl ketone and methyl isobutyl ketone on a match-to-sample task in the baboon." *Pharmacology Biochemistry and Behavior* 11:401-406 (1979)

IRIS "Health Effects Assessment for Methyl Isobutyl Ketone." US Environmental Protection Agency (1987)

Hjelm, E.W., Hagberg, M., Iregren, A., and Lof, A. "Exposure to methyl isobutyl ketone. Toxicokinetics and occurrence of irritative and CNS symptoms in man." *International Archives of Occupational Environmental Health* 62:19-26 (1990)

Linari, F., Coscia, G.C., Mariorano, G., and Perrelli, G. "L'aminoaciduria nella intossicazione professionale da piombo." *Archives of Science and Medicine*. 116:336-347 (1964)

MacEwen, J.D., Vernot, E.H., and Haun, C.C. "Effect of 90-day continuous exposure to methylisobutylketone on dogs, monkeys and rats (final report)." Prepared for the Aerospace Medical Research Laboratory. (1971)

Phillips, R.D., Morgan, E.J., Dodd, D.E., Fowler, E.H., Kary, C.D., and O'Donoghue, J. "A 14-week vapor inhalation toxicity study of methyl isobutyl ketone." *Fundamental and Applied Toxicology* 9(3):380-388 (1987)

TOXLINE. National Library of Medicine Online Database. (1993)

TSCATS (Toxic Substances Control Act Test Submissions) Database (1992)

Union Carbide Corporation. "Teratologic evaluation of methyl isobutyl ketone in Fischer 344 rats and CD-1 mice following inhalation exposure (final report) Part 1 and 2 with cover letter and abstract dated 100584." TSCA 4d submission 40-8444071, microfiche number OTS0507469. Washington, DC: OPPT, US EPA (1984)

US EPA (U.S. Environmental Protection Agency). "Multi-substance rule for testing of neurotoxicity; Final Rule." *Federal Register* 56FR40262. July 27 (1993)

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Maleic anhydride	108-31-6	Epidemiology (Case study)	Humans	Inhalation	Aerosol	1 month	Not reported	1 male	A 64 year old man developed a cough, rhinitis, breathlessness, and wheezing He had a positive patch test for MA, and he developed an asthmatic reaction starting 2 minutes after exposure to 0 09 mg/m³ of respirable MA dust	This was an acceptable bronchial provocation test	Purity = 98%	Lee et al., 1991
Maleic anhydride	108-31-6	Epidemiology (Acute toxicity)	Humans	Inhalation	Aerosol	5 minutes, 1 hour, and 4 hours	2 5, 4 5, 10, 20, and 30 ppm for 5 minute exposure, 6 ppm for 1 hour exposure; 5 ppm for 4 hour exposure	5-10 subjects/ exposure group	Greater than slight eye irritation was observed at 20 ppm and higher; greater than slight nose irritation and pulmonary discomfort was observed at 30 ppm and higher, no effect on CNS or respiratory function	This study demonstrates the irritative properties to humans of maleic anhydride following acute exposure.	Purity >99%; this study identifies a NOAEL of 10 ppm and a LOAEL of 20 ppm	Chevron Chemical Company, 1984
Maleic anhydride	108-31-6	**Epidemiology - Summary**								Several studies indicated that occupational exposure to maleic anhydride in the workplace adversely affects respiratory organs, skin, and eyes (ACGIH, 1986).		
Maleic anhydride	108-31-6	**Acute toxicity - Summary**								*Additional acute inhalation toxicity testing of maleic anhydride* could be required. Limited available acute toxicity data indicate irritative portal-of-entry effects		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Maleic anhydride	108-31-6	Subchronic toxicity	Rats, hamsters, and rhesus monkeys	Inhalation	Aerosol	6 hours/day, 5 days/week for 6 months	1, 3, or 10 mg/m^3 (0.2, 0.7, or 2.5 ppm)	15/sex/group (rats and hamsters) 3/sex/group (monkeys)	There were no treatment related deaths. There were intermittent reduced body weights in the mid dose rats and reduced body weights from day 40 to the end of the study in male rats. There was no effect on body weight in the other species. Nasal and ocular irritations were observed in all groups; this was considered reversible. There were no treatment-related hematological or clinical chemistry, urinalysis, or pulmonary function effects	The study appears to be adequate in rats and hamsters.	Portal-of-entry effects are observed	Short et al., 1988
Maleic anhydride	108-31-6	Subchronic toxicity	Rats	Inhalation	Aerosol	6 hours/day, 5 days/week for 21-22 exposures (≈30 days)	0, 0.012, 0.032, and 0.0860 mg/L (12, 32, and 86 mg/m^3) (0, 2.9, 7.9, and 21.4 ppm)	10/sex/exposure group	Reduced body weights at 0.032, and 0.0860 mg/L, numerous upper respiratory lesions were observed at 0.012, 0.032, and 0.0860 mg/L, and numerous lung lesions were observed at 0.032 and 0.0860 mg/L	This is an inadequate study since a NOAEL was not identified.	This study identifies a LOAEL of 0.012 mg/L. This study demonstrates portal-of-entry effects following short-term exposure	Goldenthal et al., 1984a

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Maleic anhydride	108-31-6	Subchronic toxicity	Rats	Inhalation	Aerosol	6 hours/day, 5 days/week for 6 months	0, 0 0011, 0 0033, and 0 010 mg/L (0, 0.3, 0 8, and 2 5 ppm)	15/sex/exposure group	Reduced body weights at 0.0033 and 0.010 mg/L. Dose-related red-tinged nasal discharge and sneezing. Brain cholinesterase was increased at 0 0033 and 0.010 mg/L, however the authors did not consider this effect to be treatment related. No histological evidence of damage to the respiratory tract was observed	This appears to be an adequate subchronic toxicity study	This study identifies a NOAEL of 0 0011 and a LOAEL of 0 0033 mg/L	Ulrich et al., 1984
Maleic anhydride	108-31-6	Subchronic toxicity	Hamsters	Inhalation	Aerosol	6 hours/day, 5 days/week for 6 months	0, 0.0011, 0 0033, and 0 010 mg/L (0, 0 3, 0 8, and 2 5 ppm)	15/sex/exposure group	Nasal discharge, ocular irritation, dyspnea, and gasping were observed at 0.010 mg/L Brain cholinesterase was increased at 0 010 mg/L. No histological evidence of damage to the respiratory tract was observed.	This appears to be an adequate subchronic toxicity study	This study identifies a NOAEL of 0 0033 and a LOAEL of 0.010 mg/L.	Ulrich et al., 1984
Maleic anhydride	108-31-6	Subchronic toxicity	Monkeys	Inhalation	Aerosol	6 hours/day, 5 days/week for 6 months	0, 0 0011, 0 0033, and 0 010 mg/L (0, 0 3, 0 8, and 2 5 ppm)	3/sex/exposure group	Nasal and ocular irritation, and slight dyspnea with coughing and sneezing were observed at 0.010 mg/L. No histological evidence of damage to the respiratory tract was observed	This subchronic toxicity study is not adequate because of the small numbers of animals used/ treated group	This study identifies a NOAEL of 0 0033 and a LOAEL of 0 010 mg/L	Ulrich et al., 1984
Maleic anhydride	108-31-6	**Subchronic toxicity - Summary**								Subchronic inhalation toxicity studies in several species reported primarily respiratory effects (HEEP, 1986).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Maleic anhydride	108-31-6	**Chronic toxicity - Summary**								No data on the chronic inhalation toxicity of maleic anhydride were located (HEEP, 1986, TSCATS, 1992).		
Maleic anhydride	108-31-6	Carcinogenicity	Rats	Oral	Diet	2 years	0, 10, 32, and 100 mg/kg/day	126/sex/group	No treatment-related increased incidence of neoplastic lesions was noted.	Inadequate	Retrospective analysis indicates that the doses received ranged from 44 to 92% of the target doses; some uncertainty exists as to whether animals received anhydride or whether it was converted in the feed to acid.	CIIT, 1984
Maleic anhydride	108-31-6	**Carcinogenicity - Summary**								No data on the inhalation carcinogenicity of maleic anhydride were located, adequate oral data were not located (HEEP, 1986, TSCATS, 1992; CHEMTRACK, 7/93).		
Maleic anhydride	108-31-6	**Neurotoxicity - Summary**								No data on the neurotoxicity of maleic anhydride were located (HEEP, 1986, TSCATS, 1992).		
Maleic anhydride	108-31-6	Developmental toxicity	Rats	Oral	Gavage	Daily on gestation days 6-15	0, 30, 90, and 140 mg/kg/day	25/exposure group	Reduced body weight gain was observed in dams at all exposure levels. No developmental toxicity was observed.	This is an adequate study	This study identifies a LOAEL of 30 mg/kg for maternal toxicity and a NOAEL of 140 mg/kg for developmental toxicity.	Goldenthal et al., 1984b
Maleic anhydride	108-31-6	**Developmental toxicity - Summary**								An adequate developmental toxicity study using the oral route was available in 1 species; no developmental toxicity studies on inhaled maleic anhydride were available (HEEP, 1986, TSCATS, 1992).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Maleic anhydride	108-31-6	Reproductive toxicity	Rats	Oral	Gavage	Daily during an 80-day premating period, mating, gestation, and lactation for 2-generations	0, 20, 55, and 150 mg/kg/day	10-20/sex/ exposure group/ generation	65 and 100% mortality in males and females, respectively, reduced body weight gain, and renal cortical necrosis was observed at the high-dose level. Pup growth was decreased at 150 mg/kg. The high mortality was the result of gavage errors	This is an adequate 2-generation study, reporting reproductive toxicity at dose levels producing parental toxicity	This study identified a NOAEL of 55 mg/kg and a LOAEL of 150 mg/kg for parental and reproductive toxicity	Monsanto Co., 1984
Maleic anhydride	108-31-6	**Reproductive toxicity - Summary**								An adequate 2-generation reproductive toxicity study using the oral route was available in 1 species; no reproductive toxicity studies on inhaled maleic anhydride were available (HEEP, 1986, TSCATS, 1992)		
Maleic anhydride	108-31-6	**Pharmacokinetics - Summary**								Limited data on the absorption and distribution of orally administered maleic anhydride were available in dogs (HEEP, 1986, TSCATS, 1992)		

REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists) "Documentation of the threshold limit values and biological exposure indices." Cincinnati, OH p 353 (1986)

CHEMTRACK National Toxicology Program Results Report "Results, status and publication information on all NTP chemicals produced from NTP CHEMTRACK system " July (1993).

Chevron Chemical Company, Inc "Sensory threshold studies on maleic anhydride " TSCA 8D submission 878214794, microfiche number OTS0206657 Washington, DC OPPT, US EPA (1984).

CIIT Chemical Industry Institute of Toxicology "Chronic dietary administration of maleic anhydride. Volume I Narrative " TSCA FYI submission FYI-1283-0277, microfice number OTS0000277-0. Washington, DC: OPPT, US EPA (1983)

Goldenthal, E I , Jessup, D C., Geil, R G., and Leong, B.K.J "Four-week inhalation study in rats (IRD-77-108), with cover memo " TSCA 8D submission 878214771, microfiche number OTS0206655 Washington, DC: OPPT, US EPA (1984a).

Goldenthal, E I , Jessup, D C , and Rodwell, D E. "Teratology study in rats (IRD-77-110) with cover memo " TSCA 8D submission 878214774, microfiche number OTS0206655. Washington, DC OPPT, US EPA (1984b)

HEEP "Health and Environmental Effects Profile for Maleic Anhydride " US Environmental Protection Agency (1986)

Lee, H S , Wang, Y T , Cheong, T H , Tan, K.T , Chee, B E , and Narendran, K. "Occupational asthma due to maleic anhydride " *British Journal of Industrial Medicine* 48 283-285 (1991)

Monsanto Company "Three-generation reproduction study in rats (modified to a two-generation study) volume 1 of 3 " TSCA 8D submission 878214777 microfiche number OTS0206655. Washington, DC OPPT, US EPA (1984)

Short, R.D., Johannsen, F.R., and Ulrich, C.E. "A 6-month multispecies inhalation study with maleic anhydride." *Fundamental and Applied Toxicology* 10: 517-524 (1988)

TSCATS (Toxic Substances Control Act Test Submissions) Database (1992)

Ulrich, C.E., Blair, M., Rop, D.A., and Arceo, R.J. "Six-month multispecies inhalation toxicity study (IRD-77-109) with cover memo." TSCA 8D submission 878214772, microfiche number OTS0206655. Washington, DC: OPPT, US EPA (1984)

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Chlorobenzene	108-90-7	**Epidemiology - Summary**								One study reported neurotoxicity in humans occupationally exposed to chlorobenzene, however, this study did not report exposure levels (Rozenbaum et al., 1947).		
Chlorobenzene	108-90-7	Acute toxicity	Mice and guinea pigs	Inhalation	Vapor	2 hours	Not reported	Not reported	LC_{50} in guinea pig was 50 mg/m^3 LC_{50} in mice was 20,000 mg/m^3	Incomplete report of data.	Insufficient information was provided regarding number of animals tested and exposure levels.	Lecca-Radu, 1959 (English translation not available, as cited in Willhite 1990)
Chlorobenzene	108-90-7	Acute toxicity	Rats and guinea pigs	Inhalation	Vapor	30 minutes	0, 2990, 5850, and 7970 ppm	5/sex/exposure level	Slight eye and nasal irritation at 2990 ppm, narcotic effects at 5850 and 7970 ppm, no mortality	This study demonstrates neurotoxicity following acute exposure.	Purity was not reported; this study identifies a NOAEL of 2990 ppm and a LOAEL of 5850 ppm for rats and guinea pigs	UBTL, 1991
Chlorobenzene	108-90-7	**Acute toxicity - Summary**								Adequate acute inhalation toxicity data are not available for chlorobenzene. One study indicates a potential for acute neurotoxicity (TSCATS, 1992).		
Chlorobenzene	108-90-7	Subchronic toxicity	Rats, rabbits, and guinea pigs	Inhalation	Vapor	7 hours/day, 5 days/week for 44 days	475 or 1000 ppm	Not reported	At low exposure, liver, kidney, and lung lesions were observed in guinea pigs. These signs were observed in all species at the high exposure level.	Tests were conducted for an inadequate duration at only two exposure levels. It is not known how many test animals were used.	Hard copy of original study was not available for review.	Deichmann, 1981

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Chlorobenzene	108-90-7	Subchronic toxicity	Mice	Inhalation	Vapor	7 hours/day, 7 days/week for 3 months	0 1 mg/L (22 ppm)	5 males and 5 females/exposure group	Agitation and increased movement were noted in treated animals, but no other changes in behavior. Leukopenia and lymphocytosis were noted	Inadequate This study examined limited endpoints and only one test exposure level was used	Effects were similar to those of benzene	Zub, 1978
Chlorobenzene	108-90-7	Subchronic toxicity	Mice	Inhalation	Vapor	7 hours/day, 7 days/week for 3 weeks	0 and 2 5 mg/L (0 and 543 ppm)	5 males and 5 females/exposure group	Half of the animals died after dosing. Loss of appetite, general emaciation, neutropenia, and marked somnolence were observed. There was a statistically significant drop in WBC and an indication that there was damage to the bone marrow.	Inadequate This study examined limited endpoints and only one test exposure level was used.	At twice this concentration, all animals died.	Zub, 1978
Chlorobenzene	108-90-7	Subchronic toxicity	Rats	Inhalation	Vapor	7 hours/day, 5 days/week for 24 weeks	0, 73, or 248 ppm	32 males/group	Microscopic lesions in adrenal cortex, kidney, liver congestion, and decreased SGOT at 73 and 248 ppm.	The study is limited by use of only 2 exposure levels and treatment of males only	Purity = 99% chlorobenzene; this study identifies a LOAEL of 73 ppm	Dilley, 1977
Chlorobenzene	108-90-7	Subchronic toxicity	Rabbits	Inhalation	Vapor	7 hours/day, 5 days/week for 24 weeks	0, 73, or 248 ppm	32 males/group	Decreased LDH and liver congestion at 73 and 248 ppm	The study is limited by use of only 2 exposure levels and treatment of males only.	Purity = 99% chlorobenzene, this study identifies a LOAEL of 73 ppm	Dilley, 1977
Chlorobenzene	108-90-7	**Subchronic toxicity - Summary**								Adequate subchronic inhalation toxicity data are not available Studies available suggest a potential for liver and kidney effects (ATSDR, 1990; SRC, 1990).		
Chlorobenzene	108-90-7	**Chronic toxicity - Summary**								No data on the chronic inhalation toxicity chlorobenzene were located (ATSDR, 1990, SRC, 1990; TSCATS, 1992).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Chlorobenzene	108-90-7	Carcinogenicity	Rats	Oral	Gavage	5 days/week for 103 weeks	0, 60, or 120 mg/kg	50/sex	Small increase in neoplastic nodules in male rats of the high dose group.	Adequate oral study	Considered equivocal evidence of carcinogenicity	NTP, 1985
Chlorobenzene	108-90-7	Carcinogenicity	Mice	Oral	Gavage	5 days/week for 103 weeks	0, 60, or 120 mg/kg (females), or 0, 30, or 60 mg/kg (males)	50/sex	No increased incidence of tumors.	Adequate oral study.	Considered non-carcinogenic in mice	NTP, 1985
Chlorobenzene	108-90-7	***Carcinogenicity - Summary***								No data on the inhalation carcinogenicity of chlorobenzene were located (TSCATS, 1992). Adequate oral data indicate equivocal evidence of carcinogenicity (NTP, 1985).		
Chlorobenzene	108-90-7	Neurotoxicity	Rats	Inhalation	Vapor	14 hours/day, 7 days/week for 1 weeks	0, 1500, 2000, or 3000 ppm for 2 hours, 0, 500, 1500, or 2000 ppm for the remaining 5 hours and after the 5th day; 0, 500, 1000, or 1500 ppm on the 6th day, and 0, 500, 1000, or 250 ppm on the 7th day, respectively. (The *concentration* was reduced because of overt toxicity)	12/males/group	In all but the group exposed to 1500 followed by 500 ppm, there was a clear impairment of auditory sensitivity which was more noticeable at 16 kHz than 8 kHz	This is an inadequate since the concentration was reduced during the study to mitigate overt toxicity	This study was part of a study of a large group of solvents that indicated that many solvents produce ototoxic effects.	Pryor and Rebert, 1993
Chlorobenzene	108-90-7	**Neurotoxicity - Summary**								Ototoxic effects in rats indicate the potential for chlorobenzene to be a neurotoxic agent		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Chlorobenzene	108-90-7	Developmental toxicity	Rats	Inhalation	Vapor	6 hours/day on gestation days 6-15	0, 75, 210, or 590 ppm	32-33/exposure group	Decreased maternal body weight gain (only for days 6-8), and increased absolute and relative liver weights at 590 ppm, increased incidence of skeletal abnormalities (delayed ossification, bilobed centra, and cervical spurs) at 590 ppm	This is an adequate study, reporting developmental toxicity at an exposure level producing minimal maternal toxicity	Purity 99 9% The LOAEL for maternal and developmental toxicity was 590 ppm and the NOAEL for both effects was 210 ppm.	John et al , 1984; Dow Chemical Co , 1982
Chlorobenzene	108-90-7	Developmental toxicity	Rabbits	Inhalation	Vapor	6 hours/day on gestation days 6-18	0, 75, 210, or 590 ppm	30/exposure group	Maternal toxicity in the form of increased absolute and relative liver weight at 210 ppm; increased resorption rate and number of malformed fetuses at 590 ppm	This is an adequate study, reporting developmental toxicity at exposure levels producing maternal toxicity	Purity 99.9%; this study identifies a LOAEL of 590 ppm for maternal and developmental toxicity A number of malformations were observed in other concentration groups, but there was no concentration-related trends	John et al., 1984, Dow Chemical Co , 1982
Chlorobenzene	108-90-7	Developmental toxicity	Rabbits	Inhalation	Vapor	6 hours/day on gestation days 6-18	0, 10, 30, 75, or 590 ppm	29-32/exposure group	Maternal toxicity in the form of increased liver weight at 590 ppm, and there was a significant increase in resorption in this group	This is an adequate study, reporting developmental toxicity at exposure levels producing maternal toxicity.	There was an increase in extra ribs at the lowest concentration that was not considered biologically significant.	John et al , 1984, Dow Chemical Co , 1982
Chlorobenzene	108-90-7	**Developmental toxicity - Summary**								**Adequate developmental toxicity data were available in 2 species (ATSDR, 1990; TSCATS, 1992); therefore, no additional developmental toxicity data are needed.**		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Chlorobenzene	108-90-7	Reproductive toxicity	Rats	Inhalation	Vapor	6 hours/day, 7 days/week for 2 generations	0, 50, 150, or 450 ppm	30/sex/group/ generation	Parental toxicity (hepatocellular hypertrophy, renal degeneration, and testicular degeneration of the germinal epithelium) at 150 and 450 ppm; other than affect on the testis, no reproductive parameters were affected	This is an adequate 2-generation reproductive toxicity study	This study identified a NOAEL of 50 ppm and a LOAEL of 150 ppm for liver and kidney effects; however, the authors considered the observed effects on the liver to be equivocal	Nair et al , 1987
Chlorobenzene	108-90-7	**Reproductive toxicity - Summary**								An adequate 2-generation reproductive toxicity study was available in rats (ATSDR, 1990; TSCATS, 1992).		
Chlorobenzene	108-90-7	**Pharmacokinetics - Summary**								Information on absorption, metabolism, and excretion of chlorobenzene was available in humans and rats for the oral and inhalation routes of exposure (ATSDR, 1990).		

REFERENCES

ATSDR (Agency for Toxic Substances and Disease Registry) "Toxicological Profile on Chlorobenzene " (1990).

Deichmann, W B "Halogenated cyclic hydrocarbons." In *Patty's Industrial Hygiene and Toxicology*. Third revised edition. Vol 2B, Clayton, G D., and Clayton, F E., editors. New York: John Wiley and Sons, pp. 3603-3611 (1981)

Dilley, J V , "Toxic evaluation of inhaled chlorobenzene (monochlorobenzene) (final report) " PB 276 623 Prepared for NIOSH (1977).

Dow Chemical Company "Monochlorobenzene - Inhalation teratology study in rats and rabbits " TSCA 8D submission 87-8211237, microfiche number OTS0206148 Washington, DC OPPT, US EPA (1982).

John, J.A , Hayes, W C , Hanley, T R , Jr , Johnson, K.A., Gushow, T.S., and Rao, K S "Inhalation teratology study on monochlorobenzene in rats and rabbits." *Toxicology and Applied Pharmacology* 76.365-373 (1984).

Lecca-Radu, R "Modifications of blood carbonic anhydrase and leucocytic indophenol oxidase in chronic benzene and monochlorobenzene intoxication " *Igiena*. 8 231-240 (1959)

Nair, R S , Barter, J A., Schroeder, R E., Knezevich, A , and Stack, C R "A two-generation reproduction study with monochlorobenzene vapor in rats." *Fundamental and Applied Toxicology*. 9 678-686 (1987).

NTP (National Toxicology Program). "NTP technical report on the toxicology and carcinogenesis studies of chlorobenzene in F344/N rats and B6C3F1 mice (gavage studies) " PB86-149714 NTP TR 261 (1985).

Pryor, G T , and Rebert, C S "Neurotoxicity of inhaled substances " SRI International Final Report LSU-1644; Prepared under contract No 271-90-7202 (1993)

Rozenbaum, N D , Block, R S , Kremneva, S N , Ginzburg, S L , and Pozhatiskii, I V "Use of chlorobenzene as a solvent from the standpoint of industrial hygiene." *Gigiena i Sanitaria* 12 21-24 (1947)

SRC (Syracuse Research Corporation) "Interaction Profile on Chlorobenzene " SRC TR 90-061 (1990)

TSCATS (Toxic Substances Control Act Test Submissions) Database (1992)

UBTL Inc "Initial submission A Utah biomedical test laboratory report on NIOSH sponsored inhalation study for IDHL values (final report) with cover letter dated 102291 " TSCA 8ECP submission 88-920000156, microfiche number OTS0534605 Washington, DC: OPPT, US EPA (circa 1991)

Zub, M "Reactivity of the white blood cell system to toxic action benzene and its derivatives " *Acta Biologica Cracoviensia* 21 163-174 (1978)

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Phenol	108-95-2	Epidemiology (Case report)	Humans	Inhalation and dermal	Not reported	Intermittent exposure for an unspecified length of time	Not reported	1 male	Muscle pain and weakness that may represent a neurological effect	Inadequate.	This is not a controlled neurotoxicity study.	Merliss, 1972
Phenol	108-95-2	**Epidemiology - Summary**								Adequate epidemiology data for inhaled phenol were not located in the available literature (ATSDR, 1989; TSCATS, 1992).		
Phenol	108-95-2	Acute toxicity/ Immunotoxicity	Mice	Inhalation	Vapor	5 replicate challenges of single 3-hour exposures	approximately 5.6 ppm	appoximately 30/group for the streptococcus infectivity study and 18/group for the pulmonary bactericidal activity assay.	Phenol did not produce significant changes in mortality from streptococcal challenge. There were no significant effects on bactericidal activity	Inadequate. The exposure level was too low and the exposure time was too short to be an adequate study of immunotoxicity		
Phenol	108-95-2	Acute toxicity	Rats	Inhalation	Not reported	24 hours/day for 15 days	0 and 26 ppm	Males and females; number/group not reported	Increased activity, motor disorders, involuntary muscle twitching, especially in the neck region, during treatment; and increased plasma potassium and magnesium levels.	Inadequate. Number of test animals was not reported and an insufficient number of exposure levels was used.	Effects were observed after 3 days of exposure.	Dalin and Kristoffersson, 1974
Phenol	108-95-2	Acute toxicity	Mice	Inhalation	Not reported	4 exposure level (concentration not reported) for 5 minutes	Not reported	Males, number/ group not reported	0.1 RD_{50} (50% decrease in respiratory rate) was 17 ppm and irritation of the upper respiratory tract was observed.	Inadequate Number of test animals and range of exposure levels is unknown	The authors estimated that 17 ppm would be an uncomfortable concentration for humans	De Ceaurriz et al., 1981
Phenol	108-95-2	**Acute toxicity - Summary**								Adequate acute inhalation toxicity data were not located for phenol (ATSDR, 1989, TSCATS, 1992).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Phenol	108-95-2	Subchronic toxicity	Rats	Inhalation	Vapor	7 hours/day, 5 days/week for 74 days	26 ppm	15/group, sex not reported	No effects noted on survival, clinical signs, nor gross or histopathology	Inadequate. No controls were used, sex of test animals is not known, and an insufficient number of test concentrations was used.	26 ppm represents a free standing NOAEL.	Deichmann et al., 1944
Phenol	108-95-2	Subchronic toxicity	Rabbits	Inhalation	Vapor	7 hours/day, 5 days/week for 88 days	26 ppm	6/group, sex not reported	Pulmonary congestion and hyperplasia, myocardial degeneration, centrolobular degeneration of the liver, and edema of the liver	Inadequate. No controls were used, sex of test animals is not known, and an insufficient number of test concentrations was used	Only frank effects were reported	Deichmann et al., 1944
Phenol	108-95-2	Subchronic toxicity	Guinea pigs	Inhalation	Vapor	7 hours/day, 5 days/week for 74 days	26 ppm	12/group; sex not reported	5 animals died after 20 exposures; liver and heart necrosis, pneumonia, renal cortical injury, and hind limb paralysis were noted.	Inadequate. No controls were used, sex of test animals is not known, and an insufficient number of test concentrations was used	Only frank effects were reported.	Deichmann et al., 1944
Phenol	108-95-2	Subchronic toxicity	Rats, mice, and monkeys	Inhalation	Vapor	Continuous exposure for 90 days	0 and 5 ppm	50 rats, 100 mice, and 10 monkeys; all males	No effects on survival, hematology, or pathology were noted in any species.	Inadequate. Only one test concentration was used.	There were some very minimal histopathological changes in the lungs of mice, but the authors did not consider them meaningful.	Sandage, 1961
Phenol	108-95-2	Subchronic toxicity	Not reported	Inhalation	Not reported	Not reported	Not reported	Not reported	Results are not yet available	Adequacy cannot be determined	This study is currently in progress.	US EPA, 1993

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Phenol	108-95-2	**Subchronic toxicity - Summary**								Adequate subchronic inhalation toxicity data were not located for phenol (ATSDR, 1989; TSCATS, 1992). Subchronic toxicity testing is currently being required under NPRM (US EPA, 1993)		
Phenol	108-95-2	**Chronic toxicity - Summary**								Chronic inhalation toxicity data were not located for phenol (ATSDR, 1989; TSCATS, 1992).		
Phenol	108-95-2	Carcinogenicity	Rats	Oral	Drinking water	105 weeks	0, 2500, or 5000 ppm	50/sex/day	Equivocal evidence of carcinogenicity. At the low dose, but not the high dose, there was an increased incidence of leukemia, lymphoma, and pheochromocytomas in the adrenals of male rats.	Inadequate because the control groups had an unusually high spontaneous tumor incidence.	A dose-response effect was not found.	NCI, 1980
Phenol	108-95-2	Carcinogenicity	Mice	Oral	Drinking water	105 weeks	0, 2500, or 5000 ppm	50/sex/day	Increased uterine endometrial stromal polyps relative to matched controls were observed in high-dose females (5/48), but this did not exceed those observed in historical controls (frequency not reported)	Inadequate since it was concluded that a toxic dose was not obtained.	No tumors could be clearly associated with phenol	NCI, 1980
Phenol	108-95-2	**Carcinogenicity - Summary**								Carcinogenicity data for inhaled phenol were not located; adequate oral data were not found (ATSDR, 1989, TSCATS, 1992); phenol has been nominated for study by NTP, route not specified (CHEMTRACK, 7/93).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Phenol	108-95-2	Neurotoxicity	Rats	Inhalation	Not reported	24 hours/day for 15 days	0 and 26 ppm	Males and females tested number not reported	Increased activity and involuntary muscle twitching, especially in the neck region, during treatment.	Inadequate Insufficient endpoints were examined, number of animals is unknown, and insufficient exposure levels were tested.	Effects first observed after 3 days	Dalin and Kristoffersson, 1974
Phenol	108-95-2	Neurotoxicity	Guinea pigs	Inhalation	Vapor	7 hours/day, 5 days/week for 74 days	26 ppm	12/group; sex not reported	5 animals died after 20 exposures Hind limb paralysis was noted	Inadequate No controls were used, sex of test animals is not known, and an insufficient number of test concentrations used	The study was terminated after 29 exposures because of poor condition of the animals.	Deichmann et al., 1944
Phenol	108-95-2	Neurotoxicity	Rats	Oral	Gavage	1 exposure	207 mg/kg	Males, number not reported	Twitching around the eyes and ear muscles immediately after exposure, followed by convulsions and coma. Violent clonic spasms of the whole body persisted for 15 to 30 minutes	Inadequate. Number of test animals is unknown, only one exposure level was tested, and insufficient endpoints were examined	This study was primarily designed to assess the tissue distribution of phenol.	Liao and Oehme, 1981
Phenol	108-95-2	Neurotoxicity-acute and subchronic	Not reported	Inhalation	Not reported	Not reported	Not reported	Not reported	Results are not yet reported.	Adequacy cannot be determined	These studies are currently in progress.	US EPA, 1993
Phenol	108-95-2	Neurotoxicity - Summary								Adequate neurotoxicity data were not located for phenol (ATSDR, 1989; TSCATS, 1992). Acute and subchronic inhalation neurotoxicity testing is currently being required under NPRM (US EPA, 1993)		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Phenol	108-95-2	Developmental toxicity	Rats	Oral	Gavage	Gestation days 6-15	0, 30, 60, and 120 mg/kg/day	20 to 22 pregnant females/group	No statistically significant signs of maternal toxicity were observed. There was an increased proportion of litters with resorption sites in the 30 and 60 mg/kg/day groups, but not in the 120 mg/kg/day group. A dose-related decrease in mean live fetal body weight was statistically significant at 120 mg/kg/day	Adequate.	The NOAEL for maternal toxicity was 120 mg/kg/day. For determining the NOAEL and LOAEL for developmental toxicity, it may be necessary to review the raw data from this study in order to determine the significance of the effects on resorption. At a minimum, the LOAEL is 120 mg/kg/day and the NOAEL is 60 mg/kg/day. However, upon further review of the resorption data, the LOAEL may be 30 mg/kg/day, the lowest level tested.	Jones-Price et al., 1983a
Phenol	108-95-2	Developmental toxicity	Mice	Oral	Gavage	Gestation days 6-15	0, 70, 140, and 280 mg/kg/day	5 to 27 pregnant females/group	Dose-related decreased maternal weight gain and fetal growth retardation and an apparent, though not statistically significant, dose-related increase in cleft palate were observed	Adequate.	Appropriate endpoints were evaluated.	Jones-Price et al., 1983b
Phenol	108-95-2	Developmental toxicity	Not reported	Oral	Gavage	Not reported	Not reported	Not reported	Results are not yet reported	Adequacy cannot be determined.	This study is currently in progress.	US EPA, 1993

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Phenol	108-95-2	**Developmental toxicity - Summary**								No inhalation developmental toxicity studies on phenol were located. Adequate oral developmental toxicity studies in 2 species were located (ATSDR, 1989, TSCATS, 1992). *Developmental* neurotoxicity testing is currently being required under NPRM (US EPA, 1993).		
Phenol	108-95-2	Multi-generation reproductive toxicity	Rats	Oral	Drinking water	2-5 generations	100, 500, or 1000 ppm (5 generations); 3000 or 5000 ppm (3 generations), 7000 or 8000 ppm (2 generations)	Not reported	No effects were noted in any generation until 10,000 ppm where reproduction was "retarded". There was no reproduction at 12,000 ppm.	Inadequate. The number of test animals was not reported and test doses did not lead to effects	The authors attributed some of the observed effects on the animals not drinking the water.	Heller and Pursell, 1938
Phenol	108-95-2	Reproductive toxicity	Not reported	Inhalation	Not reported	Not reported	Not reported	Not reported	Results are not yet reported	Adequacy cannot be determined.	This study is currently in progress.	US EPA, 1993
Phenol	108-95-2	**Reproductive toxicity - Summary**								No inhalation reproductive toxicity studies on phenol were located. Adequate oral studies were not located (ATSDR, 1989, TSCATS, 1992). Reproductive toxicity testing is currently being required under NPRM (US EPA, 1993)		
Phenol	108-95-2	**Pharmacokinetics - Summary**								Information on absorption, metabolism, and elimination of inhaled phenol is available for humans and animals (ATSDR, 1989, HEEP, 1987)		

REFERENCES

ATSDR (Agency for Toxic Substances and Disease Registry) "Toxicological Profile on Phenol." (1989)

CHEMTRACK National Toxicology Program Results Report "Results, status and publication information on all NTP chemicals produced from NTP CHEMTRACK system." July (1993)

Dalin, N.M. and Kristoffersson, R. "Physiological effects of a sublethal concentration of inhaled phenol on the rat." *Ann Zool Fennici* 11 193-199 (1974).

De Ceaurriz, J.C., Micillino, J.C., Bonnet, P., and Guenier, J.P. "Sensory irritation caused by various industrial airborne chemicals." *Toxicology Letters* 9:137-143 (1981).

Deichmann, W.B., Kitzmiller, K.V., and Witherup, B.S. "Phenol studies VII. Chronic phenol poisoning, with special reference to the effects upon experimental animals of the inhalation of phenol vapor." *American Journal of Clinical Pathology* 14 273-277 (1944).

Table of Toxicity Data for HAPs (continued)

Heller, V G , and Pursell, L. "Phenol-contaminated waters and their physiological action." *Journal of Pharmacology and Experimental Therapy* 63 99-107 (1938)

Jones-Price, C , Ledoux, T A , Reel, J R., Fisher, P W , Langhoff-Paschke, L , Marr, M C., and Kimmel, C A "Teratologic evaluation of phenol (CAS No. 108-95-2) in CD rats Research Triangle Park, NC Research Triangle Institute NTIS PB83247726 (1983a).

Jones-Price, C., Ledoux, T A., Reel, J R , Langhoff-Paschke, L , Marr, M C , and Kimmel, C A "Teratologic evaluation of phenol (CAS No. 108-95-2) in CD-1 mice Laboratory study, September 18, 1980 to January 12, 1981 Research Triangle Park, NC: Research Triangle Institute NTIS PB85104461 (1983b)

Liao, T F , and Oehme, F W "Tissue distribution and plasma protein binding of [^{14}C] phenol in rats *Toxicology and Applied Pharmacology* 57 220-225 (1981)

Merliss, R R "Phenol marasmus " *Occupational Medicine*. 14 55-56 (1972)

NCI, National Cancer Institute "Bioassay of phenol for possible carcinogenicity." Technical Report Series No 203 (1980)

Sandage, C "Tolerance criteria for continuous inhalation exposure to toxic material. I. Effects on animals of 90-day exposure to phenol, CCl_4 and a mixture of indole, skatole, H_2S and methyl mercaptan." Wright-Patterson Air Force Base, OH U S. Air Force systems command, Aeronautical Systems Division, ASD technical report 61-519 (1961)

TSCATS (Toxic Substances Control Act Test Submissions) Database (1992)

US EPA. "Acetophenone, phenol, N,N-dimethylaniline, ethyl acetate, and 2,6-dimethylphenol, Proposed test rule, notice of opportunity to initiate negotiations for TSCA Section 4 testing consent agreements " *Federal Register* 58(223) 61654-61671 November 22 (1993)

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Diethanolamine	111-42-2	**Epidemiology - Summary**								No epidemiology data on diethanolamine were located (Clement, 1991a, TSCATS, 1992, TOXLINE, 6/93).		
Diethanolamine	111-42-2	Acute toxicity	Rats	Inhalation	Vapor or aerosol	Short-term (no further information provided)	200 ppm vapor or 1400 ppm aerosol	Not reported	Respiratory difficulties and some deaths occurred (no further information provided).	Inadequate. Exposure levels, number of test animals, exposure duration identification of no-effect-level were not reported	This is an abstract	Hartung et al , 1970
Diethanolamine	111-42-2	**Acute toxicity - Summary**								Adequate acute inhalation toxicity data on diethanolamine were not located (Clement, 1991a, TSCATS, 1992, TOXLINE, 6/93)		
Diethanolamine	111-42-2	Range-finding test	Rats	Inhalation	Not reported	Continuous exposure for 9 days	0 or 25 ppm	Not reported	Increased liver weight, elevated SGOT, increased kidney weight, and elevated BUN were noted	Inadequate Protocol *information critical* to assessing the study is not reported (for example, number of test animals, other exposure levels, if any)	This is an abstract.	Hartung et al., 1970
Diethanolamine	111-42-2	Subchronic toxicity	Rats	Inhalation	Not reported	A "workday schedule" for 13 weeks	0 or 6 ppm	Not reported	*Effects included* depression of growth rate, increased lung and kidney weights, and some deaths among male rats.	Inadequate Protocol information critical to assessing the study is not reported (for example, number of test animals, other exposure levels, if any).	This is an abstract.	Hartung et al , 1970

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Diethanolamine	111-42-2	Subchronic toxicity	Rats, guinea pigs, and dogs	Inhalation	Vapor	6 hours/day, 5 days/week for 9 weeks	0 or 0.5 ppm	10 rats, 6 guinea pigs, 3 dogs/ exposure group, all males	No signs of toxicity were noted. Histopathological examination of a wide variety of tissues including sections of the cerebrum, cerebellum, and eye showed no lesions.	This study is inadequate because duration of exposure was less than 90 days	The concentration test was likely the highest vapor concentration obtainable. Purity 99%; most endpoints were evaluated.	Eastman Kodak Company, 1989
Diethanolamine	111-42-2	Subchronic toxicity	Rats, guinea pigs, and dogs	Inhalation	Vapor	Continuously for 90 days	0 or 0.26 ppm	10 rats, 5 guinea pigs, 2 dogs/sex/ exposure group, all males	No toxicity was observed in guinea pigs or dogs; equivocal histological evidence of slight lung effects in rats.	This study is inadequate since high aerosol exposure may occur	The concentration test was likely the highest vapor concentration obtainable Purity was not reported; most endpoints were evaluated	Eastman Kodak Company, 1989
Diethanolamine	111-42-2	**Subchronic toxicity - Summary**								Additional testing could be required on subchronic inhalation toxicity of inhaled diethanolamine. Oral subchronic toxicity testing has been completed by NTP (CHEMTRACK, 7/93).		
Diethanolamine	111-42-2	**Chronic toxicity - Summary**								No data on the chronic inhalation toxicity of diethanolamine were located (Clement, 1991a; TSCATS, 1992; TOXLINE, 3/93).		
Diethanolamine	111-42-2	Skin painting assay	Not reported	Topical	Not reported	Not reported	Not reported	Not reported	Results are not available yet	This test is in progress presently.	The histopathology portion of the study is under review.	NTP, no date
Diethanolamine	111-42-2	**Carcinogenicity - Summary**								No data on the carcinogenicity of diethanolamine were located (Clement, 1991a, TSCATS, 1992, CHEMTRACK, 7/93). Studies by the oral (dietary) and dermal routes have been initiated by NTP; the subchronic study is complete (NTP Report #20).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Diethanolamine	111-42-2	Neurotoxicity	Rats	Oral	Drinking water	13 weeks	0, 0.16, 0.32 0.63, 1.25, 2.5, and 5.0 mg/mL (doses were 28-288 mg/kg for males and 15-240 mg/kg for females)	10/sex/exposure level	Demyelination of brain and spinal cord at 2.5 and 5.0 mg/mL	This was a subchronic toxicity study showing neurotoxic effects	Purity was not reported, this study identified a NOAEL of 1.25 and a LOAEL of 2.5 for neurotoxicity	Battelle Columbus Lab, 1989
Diethanolamine	111-42-2	**Neurotoxicity - Summary**								Available evidence for diethanolamine suggests a potential for neurotoxicity (TSCATS, 1992) However, the available study was not designed specifically to determine neurotoxicity; thus, more neurotoxicity studies could be required for diethanolamine		
Diethanolamine	111-42-2	Chernoff/ Kavlock post-natal mouse screening test	Mice	Oral	Gavage	Daily on gestation days 6-15	0 and 450 mg/kg/day	50 mated females/group	No maternal toxicity, despite exposure to the predicted LD_{10}. Developmental toxicity occurred (decreased neonatal survival, $p=0.001$, increased gestation length, $p<0.01$) and neonatal weight gain, $p \leq 0.001$)	This is an adequate screening test, but is not adequate to evaluate developmental toxicity since malformations were not studied	The Chernoff/ Kavlock preliminary screen score was 19, which represents high priority for testing in a conventional developmental toxicity test. This is an acceptable screening test; compound identity was confirmed by gas chromatography using a flame ionization detector	NIOSH, 1987

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
Diethanolamine	111-42-2	Chernoff/ Kavlock preliminary developmental toxicity	Mice	Oral	Gavage	Daily on gestation days 6-15	450 mg/kg/day	34/exposure level	No maternal toxicity Developmental toxicity was noted (decreased number of viable litters, percent survival of pups, and weight gained by pups)	This is an adequate screening test, but is not adequate to evaluate developmental toxicity since malformations were not studied	This may be a report on the NIOSH, 1987, test, but if so, some information was lacking in this presentation. Purity was not reported (purest grade commercially available); only one exposure level used; did not measure *many parameters of* developmental toxicity.	Union Carbide Corp., 1990
Diethanolamine	111-42-2	**Developmental toxicity - Summary**								Additional testing could be required on the developmental toxicity of diethanolamine Developmental screening tests completed by NIOSH suggest the substance is a developmental toxicant, and results place it in a high-priority category for testing		
Diethanolamine	111-42-2	Subchronic toxicity	Rats	Oral	Drinking water	13 weeks	0, 0 16, 0.32, 0 63, 1.25, 2 5, and 5 0 mg/mL (doses were 28-288 mg/kg for males and 15-240 mg/kg for females)	10/sex/exposure level	Atrophy of the prostate at 5.0 mg/mL; atrophy of seminal vesicle, hypospermia in the epididymis, and spermatic arrest in the testis at 2.5 and 5.0 mg/mL.	This was a subchronic toxicity study which identified reproductive effects.	Purity was not reported; this study identifies a NOAEL of 1.25 mg/mL and a LOAEL of 2.50 mg/mL for reproductive effects in males.	Battelle Columbus Lab, 1989
Diethanolamine	111-42-2	**Reproductive toxicity - Summary**								Available evidence for diethanolamine suggests a potential for reproductive toxicity in males (TSCATS, 1992). However, the available study was not designed specifically to determine reproductive toxicity, thus, more reproductive toxicity studies could be required for diethanolamine		
Diethanolamine	111-42-2	**Pharmacokinetics - Summary**								The only pharmacokinetics study located for diethanolamine used intravenous administration in dogs (TSCATS, 1992).		

REFERENCES

Battelle Columbus Lab "Diethanolamine Subchronic dosed water and dermal studies in F344 rats and B6C3F1 mice -- Final report for prechronic dosed water study of diethanolamine in Fischer 344 rats." TSCA FYI submission OTS1189-0721, microfiche number OTS0000721. Washington, DC OPPT, US EPA (1989)

CHEMTRACK National Toxicology Program Results Report "Results, status and publication information on all NTP chemicals produced from NTP CHEMTRACK system." July (1993)

Clement. "Draft inhalation reference dose for diethanolamine (111-42-2)." Prepared by Clement Associates, Inc. for Environmental Criteria and Assessment Office (1991a).

Eastman Kodak Company. "Subacute inhalation toxicity of diethanolamine and bimat imbibant (485K)." TSCA 8D submission 86-890000205, microfiche number OTSO516742. Washington, DC OPPT, US EPA (1989).

Hartung, R., Rigas, L.K , and Cornish, H.H. "Acute and chronic toxicity of diethanolamine." *Toxicology and Applied Pharmacology*. 17:308 (1970)

NIOSH "Screening of priority chemicals for reproductive hazards - Monoethanolamine (CAS. No. 141-43-5); Diethanolamine (CAS. No 111-42-2); Triethanolamine (CAS. No 102-71-6) " Prepared for National Institute for Occupational Safety and Health (NIOSH) NTIS Document No. PB89-139067 (1987)

NTP (National Toxicology Program). "NTP Technical Report on Toxicity Studies of Diethanolamine (CAS No. 111-42-2) Administered Topically and in Drinking Water to F344/N Rats." Technical Report Series #20 (1992).

TOXLINE. National Library of Medicine Online Database. (1993).

TSCATS (Toxic Substances Control Act Test Submissions) Database (1992).

Union Carbide Corporation. "Screening of priority chemicals for reproductive hazards final report Monoethanolamine, diethanolamine, triethanolamine with cover letter." TSCA 8D submission Old Doc ID 86-900000423, microfiche number OTS0526003. Washington, DC: OPPT, US EPA (1990).

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
1,2,4-Trichlorobenzene	120-82-1	**Epidemiology - Summary**								No epidemiological studies were located (HAD, 1985; HEA, 1987, TSCATS, 1992).		
1,2,4-Trichlorobenzene	120-82-1	Acute toxicity	Rats	Inhalation	Vapor	4 hours, then observed for 14 days	418 ppm	6 males	No mortality; lacrimation, salivation, pink ears, labored breathing, and discoordination were observed; body weights decreased 16%, then recovered normally.	This is an inadequate acute toxicity study because only males were used and only one concentration was tested.	No LC_{50} could be calculated.	E.I. DuPont de Nemours, 1982
1,2,4-Trichlorobenzene	120-82-1	**Acute toxicity - Summary**								Data on the acute inhalation toxicity of 1,2,4-trichlorobenzene were inadequate (HAD, 1985; HEA, 1987; TSCATS, 1992).		
1,2,4-Trichlorobenzene	120-82-1	Subchronic toxicity	Rats	Inhalation	Vapor	7 hours/day, 5 days/week for 44 days	0, 30, or 100 ppm	20 males/exposure group	Increased urinary excretion of porphyrin at 30 and 100 ppm, no gross or histologic effects.	This study is limited since only male test animals were used.	This study identified a LOAEL of 30 ppm; however, the authors indicated that the observed effect might not be toxic.	Kociba, 1981
1,2,4-Trichlorobenzene	120-82-1	Subchronic toxicity	Rats	Inhalation	Vapor	6 hours/day, 5 days/week for 3 months	0, 3, and 10 ppm	10-26/sex/ exposure group	Increased urinary excretion of porphyrin at 10 ppm.	A limited number of parameters were examined.	This study identified a LOAEL of 10 ppm; however, the authors indicated that the observed effect might not be toxic.	Watanabe et al , 1978
1,2,4-Trichlorobenzene	120-82-1	**Subchronic toxicity - Summary**								Subchronic inhalation toxicity studies were located; however, an unequivocal LOAEL was identified (HAD, 1985; HEA, 1987; TSCATS, 1992).		

Table of Toxicity Data for HAPs (continued)

Chemical Name	CAS Number	Study Type	Species	Route of Administration	Type of Exposure	Duration	Exposure levels	Number studied/ exposure level	Response	Study Adequacy	Comments	Reference
1,2,4-Trichlorobenzene	120-82-1	Chronic toxicity	Rats	Inhalation	Vapor	Continuous exposure for 26 weeks	0, 25, 50, and 100 ppm	30 males/group	No effects were noted on survival, body weight, ophthalmic condition, hematological or serum biochemistry, pulmonary function or operant behavior. Histopathological examination revealed transient mild hepatomegaly and vacuolation in liver parenchymal cells, and hyaline degeneration in the renal cortex in all test groups at 4 and 13 weeks of exposure. These changes were not apparent at 26 weeks of exposure.	Inadequate. Only male test animals were used.	The increase in size and vacuolation of the cytoplasm of hepatocytes may reflect an increase in the amount of endoplasmic reticulum needed to increase detoxifying enzymes.	Coate et al., 1977
1,2,4-Trichlorobenzene	120-82-1	Chronic toxicity	Rabbits	Inhalation	Vapor	Continuous exposure for 26 weeks	0, 25, 50, and 100 ppm	16 males/group	No effects were noted on survival, body weight, ophthalmic condition, hematological or serum biochemistry, pulmonary function, operant	Inadequate. Only male test animals were used.	It is not known whether transient changes such as those found in rats occurred here, since interim sacrifices	Coate et al , 1977