Initial Risk-Based Prioritization of High Production Volume (HPV) Chemicals

Chlorobenzenes Category

Sponsored Chemicals

Monochlorobenzene (CASRN 108-90-7)
(CA Index Name: Benzene, chloro-)

1,2-Dichlorobenzene (CASRN 95-50-1)
(CA Index Name: Benzene, 1,2-dichloro-)

1,3-Dichlorobenzene (CASRN 541-73-1)
(CA Index Name: Benzene, 1,3-dichloro-)

1,2,3-Trichlorobenzene (CASRN 87-61-6)
(CA Index Name: Benzene, 1,2,3-trichloro-)

Supporting Chemicals

1,4-Dichlorobenzene (CASRN 106-46-7)
(CA Index Name: Benzene, 1,4-dichloro-)

1,2,4-Trichlorobenzene (CASRN 120-82-1)
(CA Index Name: Benzene, 1,2,4-trichloro-)

Prioritization Decision: High Priority, CASRN 541-73-1.
Low Priority, Other Category Chemicals.

- Although the chemicals in this category present medium to high potential risk for both human health and the environment, existing regulations already governing most of these chemicals with regard to occupational exposure, environmental releases from facilities, and the presence of these chemicals in drinking water are expected to mitigate risk from most members of the category and, through ongoing reporting, are expected to be sufficient to alert the Agency to any instances of potentially unreasonable risk from these chemicals.
- **However, in order to confirm or refute the high potential risk from CASRN 541-73-1 currently based on release and exposure assumptions and on limited available exposure data, particularly concerning potential exposures to workers, consumers, children, and the general population, companies are encouraged to provide available information on a voluntary and non-confidential basis. Examples of information that would assist EPA in its analysis include, but are not limited to:**

- **Worker exposures to CASRN 541-73-1, including engineering and process controls, industrial hygiene practices, and stewardship activities that would affect the potential for exposure;**
- **Potential exposures to CASRN 541-73-1 in consumer products, including data on its presence and concentration in products and formulations, and on consumer use activity patterns, considering the frequency and duration of exposures and the potential for children to be exposed; and**
- **Other information pertinent to potential exposures to CASRN 541-73-1.**

- **No follow-up action is suggested at this time on the remaining chemicals in this category.**

Screening-level prioritizations are interim evaluations that do not constitute either final Agency determinations as to risk or final determinations as to whether sufficient data are available to characterize risk. They are based predominantly on screening-level hazard, exposure, and risk characterizations prepared by EPA using data submitted to the Agency under the HPV Challenge Program[1] and the 2006 Inventory Update Reporting (IUR)[2], and data publicly available through other selected sources. These screening-level characterizations do not constitute full risk assessments. They are intended only to support initial decisions to determine the relative priority for further assessment or risk management activities concerning HPV chemicals, and to identify data needs for individual chemicals or chemical categories. The methodology used in preparing these characterizations and prioritization decisions is available on the EPA website.[3]

Screening-Level Characterization Summary

Risk Characterization

Potential Risk to Aquatic Organisms from Environmental Releases: *MEDIUM/HIGH*. Although there is a high potential for exposure from environmental releases, the moderate acute hazard to fish suggests a medium potential risk to fish. The high potential for exposure and the high acute hazard to aquatic invertebrates and plants suggests a high potential risk to aquatic invertebrates and aquatic plants.

Potential Risk to Workers: Differences in hazard response, existing regulations, and in exposure potentials warrants different prioritizations by category member:

LOW. Although the exposure potential is high and the human health hazard is moderate for CASRNs 95-50-1 and 108-90-7, the existence of OSHA PEL's suggests a low potential risk for these chemicals.

MEDIUM. The moderate human health hazard for CASRN 87-61-6 and its medium exposure potential suggests a medium potential risk.

[1] US EPA, HPV Challenge Program information: http://www.epa.gov/hpv/.
[2] US EPA, IUR information: http://www.epa.gov/oppt/iur/index.htm.
[3] US EPA, Methodology for Risk-Based Prioritization Under ChAMP: http://www.epa.gov/champ/pubs/rbp/method.pdf.

HIGH. The high human health hazard for CASRN 541-73-1 and its high exposure potential suggests a high potential risk.

Potential Risk to the General Population and to Consumers: Differences in hazard response warrants different prioritizations by category member:

MEDIUM. Although the exposure potential is high, the moderate human health hazard for CASRNs 87-61-6, 95-50-1, and 108-90-7 suggests a medium potential risk for these chemicals.

HIGH. The high human health hazard and high potential exposure for CASRN 541-73-1 suggests a high potential risk for this chemical.

Potential Risk to Children: *MEDIUM.* Although available data with postnatal exposures in animals suggest a low hazard for two category members (CASRNs 95-50-1 and 108-90-7), the data in adult animals for all category members suggest either a moderate (CASRNs 87-61-6, 95-50-1, and 108-90-7) or high (CASRN 541-73-1) human health hazard potential. The moderate/high hazard and the medium potential for children's exposure to these chemicals (based on possible exposure through the use of household products) suggests a medium potential risk.

Production Volume, Use, and Release Information

The ranges reported below are based on 2006 IUR submissions. CASRNs 95-50-1 and 108-90-7 are HPV chemicals and CASRNs 87-61-6 and 541-73-1 are Moderate Production Volume (MPV) chemicals.

- CASRNs 95-50-1 and 108-90-7: ≥ 10 million and < 50 million lbs.
- CASRNs 87-61-6 and 541-73-1: ≥ 10,000 and < 500,000 lbs.

Non-confidential IUR information for members of this category indicates that the industrial processing and uses include intermediates and solvents for plastics manufacturing and basic organic chemicals manufacturing, and pesticide and other agricultural chemical manufacturing. Hazardous Substance Data Bank (HSDB) information for the members of this category states that they are used primarily as pesticides, solvents, heat transfer medium, and chemical intermediates, as well as many other uses. However, HSDB information for CASRN 95-50-1 states that it is no longer contained in any registered pesticide products.

All members of this category are on the Toxics Release Inventory, except CASRN 87-61-6. Release information from the 2006 TRI reporting year follows. No additional data on releases were available from other sources.

- CASRN 108-90-7
  - Total releases: 706,124 lbs.
    - Air releases: 468,409 lbs.
    - On-site water releases: 667 lbs.
    - Remaining releases were deep-well injected or sent to off-site landfills.

- CASRN 95-50-1
  - Total releases: 106,925 lbs.
    - Air releases: 42,580 lbs.
    - On-site water releases: 892 lbs.
    - Most of the remaining releases were deep-well injected.

- CASRN 541-73-1
  - Total releases: 267,540 lbs.
    - Air releases: 1,040 lbs.
    - On-site water releases: 293 lbs.
    - Most of the remaining releases were deep-well injected or disposed to on-site landfills.

Hazard Characterization Summary

The chemicals in this category are solids or liquids with moderate water solubility and moderate to high vapor pressure. They are expected to have moderate mobility in soil. Volatilization of the chemicals in this category is considered high based on their Henry's Law constants. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered negligible to slow. CASRNs 95-50-1, 108-90-7, and 541-73-1 are expected to have moderate persistence (P2) and low bioaccumulation potential (B1). CASRN 87-61-6 is expected to have high persistence (P3) and moderate bioaccumulation potential (B2).

The evaluation of available toxicity data for fish, aquatic invertebrates, and aquatic plants for the chemicals in this category indicates that the potential acute hazard is moderate for fish and high for aquatic invertebrates and aquatic plants. A trend of increasing toxicity with increasing chlorine substitution is observed in aquatic organisms.

The acute oral toxicity for the members of this category to rats, mice, rabbits, and guinea-pigs is low. Acute dermal toxicity to rats and rabbits is low. Acute inhalation toxicity to rats and mice is moderate. CASRN 95-50-1 is slightly irritating to the skin and eyes of rabbits and is a respiratory irritant in mice. Systemic toxicity of CASRNs 95-50-1 and 108-90-7 in oral repeated-dose studies is low in rats and mice; however, the systemic toxicity of CASRN 108-90-7 is moderate in dogs. Systemic toxicity of CASRNs 87-61-6 and 541-73-1 in oral repeated-dose studies is moderate and high, respectively. Systemic toxicity of CASRNs 106-46-7 and 120-82-1 in oral repeated-dose studies is low and moderate, respectively. Systemic toxicity in inhalation repeated-dose studies for CASRN 95-50-1 is low in dogs and for CASRN 108-90-7 is moderate in rats. There were no reproductive toxicity studies for CASRNs 87-61-6 and 541-73-1; however, there was no indication of toxicity to reproductive organs examined in oral repeated-dose studies. The reproductive toxicity of CASRN 120-82-1 via oral exposure is low. The reproductive toxicity of CASRNs 106-46-7 and 108-90-7 via inhalation exposure is low. The prenatal toxicity of CASRN 87-61-6 via oral exposure is low. The prenatal toxicity of CASRN 108-90-7 via inhalation exposure to rats is moderate and to rabbits is low. The pre- and post-natal toxicity via inhalation exposure in rats is low for CASRN 95-50-1 and CASRN 106-46-7. The prenatal toxicity via inhalation exposure in rabbits is low for CASRN 95-50-1 and CASRN 106-46-7. The members of this category did not induce gene mutations or chromosomal

aberrations *in vitro*. However, all members of this category showed increased numbers of micronucleated erythrocytes *in vivo*. There was evidence of carcinogenicity of CASRN 108-90-7 in male rats. However, carcinogenic effects of CASRN 108-90-7 were not observed in female rats or mice of either sex. There was no evidence of carcinogenicity of CASRN 95-50-1.

No data gaps have been identified under the HPV Challenge Program.

Exposure Characterization Summary

EPA identifies a high potential that the general population and the environment might be exposed to these chemicals from environmental releases based on TRI release information, persistence in the environment, presence in monitoring data, and use information.

EPA identifies a high relative ranking for potential worker exposure for CASRNs 108-90-7, 95-50-1, and 541-73-1, and a medium relative ranking for CASRN 87-61-6. These relative rankings are based primarily on the vapor pressures, the aggregated volumes and the uses of the chemicals.

EPA identifies a high potential that consumers might be exposed to these chemicals based on their use in consumer products. While IUR data do not indicate uses in consumer products, other sources, including HSDB, NIH Household Products Database, and Source Ranking Database, indicate uses in consumer products.

EPA identifies a medium potential that children might be exposed to chemicals in this category through household use of some consumer products. While IUR data do not indicate uses in consumer products and products intended for children, other sources, including HSDB, NIH Household Products Database, and Source Ranking Database, indicate uses in consumer products.

Additional Considerations for Prioritization Decision

Regulatory and Related Information Summary

- All members of this category appear on the TSCA Inventory.
- All members of this category were included in test rules under TSCA section 4 during the 1980's. Information submitted under test rules appears in the TSCA Test Submissions (TSCATS) database, which is reviewed during the development of the hazard characterization, and those data are included in this decision. The inclusion of these chemicals in test rules also made them subject to use and exposure information reporting under TSCA section 8(a) and to health and safety data reporting under TSCA section 8(d). Information submitted under TSCA section 8(d) is also included in TSCATS and reviewed during the development of the hazard characterization. EPA maintains information on human health effects resulting from exposure for all members of this category in the Integrated Risk Information System (IRIS), except CASRN 87-61-6.
- All members of this category are on the Toxics Release Inventory, except CASRN 87-61-6.
- EPA regulates all members of this category as air pollutants in new sources under section 111 of the Clean Air Act.

- EPA regulates all members of this category under HON, the Hazardous Organic National Emission Standard for Hazardous Air Pollutants (NESHAP), in section 112(b) of the Clean Air Act.
- EPA regulates CASRNs 106-46-7, 108-90-7, and 120-82-1 as hazardous air pollutants under section 112(b) of the Clean Air Act.
- EPA identifies all members of this category as priority pollutants in the Clean Water Act, except CASRN 87-61-6.
- EPA regulates all members of this category in accordance with the effluent limitations in section 304(b) of the Clean Water Act, except CASRN 87-61-6.
- EPA identifies CASRNs 95-50-1, 106-46-7, and 108-90-7 as hazardous substances under section 311 of the Clean Water Act.
- EPA regulates all members of this category in accordance with the National Primary Drinking Water Regulations of the Safe Water Drinking Act.
- EPA regulates all members of this category under the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA), except CASRN 87-61-6.
- EPA regulates all members of this category under the Resource Conservation and Recovery Act (RCRA), except CASRN 87-61-6.
- EPA lists all members of this category on the CERCLA Priority List of Hazardous Substances in section 110 of the Superfund Amendment Reauthorization Act (SARA).
- All members of this category are candidates for or have published Agency for Toxic Substances and Disease Registry (ASTDR) Toxicological Profiles, except CASRN 87-61-6.
- The Occupational Safety and Health Administration (OSHA) has set Permissible Exposure Limits (PELs) of 50 ppm for CASRN 95-50-1 and 75 ppm (TWA) for CASRNs 106-46-7 and 108-90-7.
- The National Institute of Occupational Safety and Health (NIOSH), an institute of the U.S. Centers for Disease Control and Prevention (CDC), published criteria documents (#93-102) that include criteria for a recommended standard for CASRNs 106-46-7 and 108-90-7.
- NIOSH includes safe handling recommendations for industrial concentrations of CASRNs 87-61-6, 95-50-1, 106-46-7, 108-90-7, and 120-82-1 on International Chemical Safety Cards.
- NIOSH has established Recommended Exposure Limits (RELs) of 50 ppm for CASRN 95-50-1, and 5 ppm for CASRN 102-82-1. NIOSH also limits CASRN 106-46-7 as a potential carcinogen.
- The American Conference of Governmental Industrial Hygienists (ACGIH) has established guideline limits of 25 ppm (TWA) as an ACGIH TLV for CASRN 95-50-1; 5 ppm as an ACGIH TLV (ceiling value) for CASRN 102-82-1; and 10 ppm (TWA) as an ACGIH TLV for CASRNs 106-46-7 and 108-90-7.
- Pesticide Product Codes are found for the following chemicals:
    - CASRN 95-50-1: 059401, 37 canceled products
    - CASRN 106-46-7: 061501, 384 products, 28 active (moth balls)
    - CASRN 108-90-7: 056504, 1 canceled product
    - CASRN 120-82-1: 081101, 1 canceled product

Assumptions and Uncertainties

- EPA has no information on exposures to this chemical and has made assumptions about potential exposures based on all of the information considered including available use information and physical/chemical properties.
- All members of this category are on the Toxics Release Inventory (TRI), except CASRN 87-61-6. Release information was obtained from the 2006 TRI reporting year. No additional data on releases were available from other sources, and EPA assumes potential exposures based on environmental releases reported under TRI.
- There is uncertainty surrounding the potential that consumers might be exposed to a chemical in consumer uses that were identified in other public data sources but were not identified in commercial/consumer uses in IUR submissions. EPA generally assumes a high potential that consumers might be exposed to a chemical in consumer uses that were identified in other public data sources but were not identified in IUR submissions.
- There is uncertainty surrounding the potential that children might be exposed to a chemical with consumer uses that are not specifically intended for children. EPA generally assumes a medium to high potential that children might be exposed to a chemical with consumer uses that are not specifically intended for children.

Appendix A: Screening-Level Hazard Characterization

Chlorobenzenes Category

Sponsored Chemicals

Monochlorobenzene (CASRN 108-90-7)
(CA Index Name: Benzene, chloro-)

1,2-Dichlorobenzene (CASRN 95-50-1)
(CA Index Name: Benzene, 1,2-dichloro-)

1,3-Dichlorobenzene (CASRN 541-73-1)
(CA Index Name: Benzene, 1,3-dichloro-)

1,2,3-Trichlorobenzene (CASRN 87-61-6)
(CA Index Name: Benzene, 1,2,3-trichloro-)

Supporting Chemicals

1,4-Dichlorobenzene (CASRN 106-46-7)
(CA Index Name: Benzene, 1,4-dichloro-)

1,2,4-Trichlorobenzene (CASRN 120-82-1)
(CA Index Name: Benzene, 1,2,4-trichloro-)

Introduction

The sponsor, The Synthetic Organic Chemical Manufacturers Association's (SOCMA) Chlorobenzene Producers Association (CPA), submitted a Test Plan and Robust Summaries to EPA for the chlorobenzenes category on March 14, 2002. EPA posted the submission on the ChemRTK Web site on April 2, 2002 (http://www.epa.gov/chemrtk/pubs/summaries/chlrbnzs/c13650tc.htm). EPA comments on the original submission were posted to the website on November 13, 2002. Public comments were also received and posted to the website. The sponsor submitted revised and final documents on February 6, 2003, which were posted to the ChemRTK website on March 21, 2003. The chlorobenzenes category consists of the following four chemicals and two supporting chemicals:

Sponsored Chemicals

Monochlorobenzene [CA Index Name: benzene, chloro-]	CASRN 108-90-7
1,2-Dichlorobenzene [CA Index Name: benzene, 1,2-dichloro-]	CASRN 95-50-1
1,3-Dichlorobenzene [CA Index Name: benzene, 1,3-dichloro-]	CASRN 541-73-1
1,2,3-Trichlorobenzene [CA Index Name: benzene, 1,2,3-trichloro-]	CASRN 87-61-6

Supporting Chemicals

1,4-Dichlorobenzene [CA Index Name: benzene, 1,4-dichloro-]	CASRN 106-46-7

1,2,4-Trichlorobenzene [CA Index Name: benzene, 1,2,4-trichloro-]CASRN 120-82-1

1. Category and Supporting Chemicals Justification

The category consists of mono-, di- and tri-chlorobenzenes. All four category members and the two supporting chemicals have a benzene ring in which one, two or three hydrogen atoms are replaced by chlorine atoms. The two category members 1,2- and 1,3-dichlorobenzene and supporting chemical 1,4-dichlorobenzene, are isomers – the placement of the chlorines on the benzene ring being in the *ortho*, *meta*, and *para* positions, respectively. Likewise, the supporting chemical, 1,2,4-trichlorobenzene, is an isomer of the category member, 1,2,3-trichlorobenzene with the difference being a chlorine in the *para* position rather than the *meta* position. Based on similarities in structure, physical-chemical properties, environmental fate and toxicity, the chemicals in this category are grouped and evaluated together. Data for the tested category members are extrapolated to provide estimates of similar properties for the untested members.

1,2-Dichlorobenzene (sponsored chemical), 1,4-dichlorobenzene and 1,2,4-trichlorobenzene (both supporting chemicals) have been assessed under the OECD High Production Volume Chemicals Programme and the evaluations published by the United Nations Environmental Programme (UNEP): http://www.chem.unep.ch/irptc/sids/OECDSIDS/95501.pdf and http://ecb.jrc.it/esis/index.php?PGM=hpv.

EPA agrees with the sponsor's category justification and further accepts this category for prioritization in the ChAMP.

2. Physical-Chemical Properties and Environmental Fate

The physical-chemical properties of the chlorobenzenes are summarized in Table 1a, while their environmental fate properties are provided in Table 1b. The structures of the compounds are provided in Table 4 at the end of Appendix A.

Physical-Chemical Properties Characterization

Chlorobenzenes are solids or liquids with moderate water solubility and moderate to high vapor pressure.

Environmental Fate Characterization

The chlorobenzenes are expected to have moderate mobility in soil. The rate of biodegradation decreases with increasing number of chlorine atoms attached to the benzene ring. None of the test substances were readily biodegradable in modified MITI tests (OECD 301C); however some degradation was observed for monochlorobenzene and the dichlorobenzenes using acclimated cultures and closed bottle tests (OECD 301D). The rate of volatilization of the chlorobenzenes from water and moist soil is considered high given their Henry's Law constants. The rate of hydrolysis is considered negligible under environmental conditions. Measured BCF values suggest that bioconcentration is low for monochlorobenzene and the dichlorobenzene isomers; however, measured values greater than 1,000 were observed for trichlorobenzene. Mono- and dichlorobenzenes are judged to have moderate persistence (P2) and low bioaccumulation potential (B1). The trichlorobenzenes are expected to have high persistence (P3) and moderate bioaccumulation potential (B2).

Conclusion: The chlorobenzenes are solids or liquids with moderate water solubility and moderate to high vapor pressure. They are expected to have moderate mobility in soil. Volatilization of the chlorobenzenes is considered high based on their Henry's Law constants. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered negligible to slow. Mono- and dichlorobenzenes are expected to have moderate persistence (P2) and low bioaccumulation potential (B1). The trichlorobenzenes are expected to have high persistence (P3) and moderate bioaccumulation potential (B2).

Table 1a. Physical-Chemical Properties of the Chlorobenzenes Category[1]

Property	Benzene, chloro-	Benzene, 1,2-dichloro-	Benzene, 1,3-dichloro-	Benzene, 1,2,3-trichloro-	Benzene, 1,4-dichloro- (supporting chemical)	Benzene, 1,2,4-trichloro- (supporting chemical)
CASRN	108-90-7	95-50-1	541-73-1	87-61-6	106-46-7	120-82-1
Molecular Weight	112.56	147.00	147.00	181.45	147.00	181.45
Physical State	Liquid	Liquid	Liquid	Solid	Solid	Liquid
Melting Point	-45.2°C (measured)	-17°C (measured)	-25.5°C (measured)	52.6°C (measured)	53.5°C (measured)	17°C (measured)
Boiling Point	132.1°C (measured)	180.5°C (measured)	173°C (measured)	221°C (measured)	174°C (measured)	213°C (measured)
Vapor Pressure	8.8–9.0 mm Hg at 20°C (measured)	0.98 mm Hg at 20°C (measured)	1.35 mm Hg at 20°C (measured)	6.5×10^{-2} mm Hg at 25°C (estimated)[2]; 1.0 mm Hg at 40°C	0.6 mm Hg at 20°C (measured)	0.187 mm Hg at 25°C (estimated)[2]; 0.27 mm Hg at 70°C (measured)
Dissociation Constant (pK_a)	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
Henry's Law Constant	4.55×10^{-3} atm-m^3/mole (estimated)	1.70×10^{-3} atm-m^3/mole at 20°C (measured)	2.63×10^{-3} atm-m^3/mole (estimated)	1.25×10^{-3} atm-m^3/mole (estimated)	2.41×10^{-3} atm-m^3/mole (estimated)	1.42×10^{-3} atm-m^3/mole (estimated)
Water Solubility	210 mg/L at 20°C (measured)	145 mg/L at 20°C (measured)	100 mg/L at 20°C (measured)	17.38 mg/L at 25°C (estimated)	60 mg/L at 20°C (measured)	49 mg/L (measured)
Log K_{ow}	2.84 (measured)	3.39–3.43 (measured)	3.38 (measured)	3.93 (estimated)	3.39 (measured)	3.93 (estimated)

[1]Synthetic Organic Chemical Manufacturers Association (SOCMA) Chlorobenzene Producers Association (CPA). March 31, 2003. Revised Robust Summary and Test Plan for Chlorobenzenes Category. http://www.epa.gov/oppt/chemrtk/pubs/summaries/chlrbnzs/c13650tc.htm.

[2]U.S. EPA. 2008. Estimation Programs Interface Suite™ for Microsoft® Windows, v3.20. United States Environmental Protection Agency, Washington, DC, USA. http://www.epa.gov/opptintr/exposure/pubs/episuite.htm.

Table 1b. Environmental Fate Characteristics of the Chlorobenzenes Category[1]						
Property	**Benzene, chloro-**	**Benzene, 1,2-dichloro-**	**Benzene, 1,3-dichloro-**	**Benzene, 1,2,3-trichloro-**	**Benzene, 1,4-dichloro- (supporting chemical)**	**Benzene, 1,2,4-trichloro- (supporting chemical)**
CASRN	108-90-7	95-50-1	541-73-1	87-61-6	106-46-7	120-82-1
Photodegradation Half-life	93.6 hours (estimated)	320 hours (estimated)	16 days (measured)	37.7 days (estimated)	26.7 days (estimated)	38.0 days (estimated)
Hydrolysis Half-life	Stable	35.5 days at pH 3; 35.4 days at pH 5; 45.4 days at pH 11 (measured)	Stable	Stable	Stable	Stable
Biodegradation	0–15% in 28 days (measured , not readily biodegradable); 50–60% in 20 days (measured, not readily biodegradable); >90% in 15 days (measured , inherently biodegradable)	0% in 28 days (measured ,not readily biodegradable); 58% in 20 days (measured, not readily biodegradable)	0% in 28 days (measured , not readily biodegradable)	Not readily biodegradable based on results of 1,2,4-trichloro-benzene	20% in 20 days (measured); 0% in 28 days (measured, not readily biodegradable)	56% 5 days (measured); 0% in 14 days (measured, not readily biodegradable)
Bioconcentration	BCF = 3.9–43.6 (measured in carp)[3]	BCF = 90–260 (measured in carp)[3]	BCF = 57–370 (measured in carp)[3]	BCF = 130–1,200 (measured in carp)[3]	BCF = 64–68 (measured in carp)[3]	BCF = 120–1,320 (measured in carp)[3]
Log K_{oc}	2.45 (estimated)	2.46–3.67 (measured)	3.14 (estimated)	3.7 (estimated)	2.6 (estimated)[2]	2.9 (estimated)[2]
Fugacity (Level III Model) Air Water Soil Sediment	 25.5% 31.1% 43.1% 0.264%	 12.4% 19.0% 67.9% 0.72%	 13.1% 20.21% 66.0% 0.75%	 6.45% 11.9% 79.1% 2.55%	 13.1% 19.1% 67.0% 0.801%	 6.27% 12.0% 79.4% 2.4%
Persistence[4]	P2 (moderate)	P2 (moderate)	P2 (moderate)	P3 (high)	P2 (moderate)	P3 (high)
Bioaccumulation[4]	B1 (low)	B1 (low)	B1 (low)	B2 (moderate)	B1 (low)	B2 (moderate)

[1]Synthetic Organic Chemical Manufacturers Association (SOCMA) Chlorobenzene Producers Association (CPA). March 31, 2003. Revised Robust Summary and Test Plan for Chlorobenzenes Category. http://www.epa.gov/oppt/chemrtk/pubs/summaries/chlrbnzs/c13650tc.htm.

[2]U.S. EPA. 2008. Estimation Programs Interface Suite™ for Microsoft® Windows, v3.20. United States Environmental Protection Agency, Washington, DC, USA. http://www.epa.gov/opptintr/exposure/pubs/episuite.htm.

[3]Chemicals Inspection and Testing Institute. 2008. Biodegradation and Bioaccumulation of the Existing Chemical Substances under the Chemical Substances Control Law. Japan Chemical Industry Ecology - Toxicology and Information Center. http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html.

[4]Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

2. Environmental Effects – Aquatic Toxicity

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 2. The table also indicates where data for tested category members are read-across (RA) to untested members of the category. For the chlorobenzene category, data are available for each member for most of the aquatic toxicity endpoints.

Acute Toxicity to Fish

Monochlorobenzene (CASRN 108-90-7)

Rainbow trout (*Salmo gairdneri = Oncorhynchus mykiss*) were exposed to nominal concentrations of monochlorobenzene at 0.03, 1.8, 3.2, 5.8, 10, 18, 32, 58 or 100 mg/L under static conditions 96 hours. Mortality occurred within 20 hours after exposure and was 100% at ≥ 18 mg/L, 40% at 10 mg/L and 0% at ≤ 5.8 mg/L. Due to limitations in the methodology used to test this chemical, at EPA's request the sponsor supported the toxicity value with a 96-hour EC50 value for this endpoint estimated using ECOSAR (13.55 mg/L). The modeled results corroborate the measured results; therefore, the experimental data were accepted for the purpose of characterizing hazard to fish.

96-h LC_{50} = 10.4 mg/L
96-h LC_{50} = 13.5 mg/L (estimated)

1,2-Dichlorobenzene (CASRN 95-50-1)

Fathead minnows (*Pimephales promelas*; 20/concentration) were exposed to nominal concentrations of 1,2-dichlorobenzene at 6.34, 9.75, 15.0, 23.0 or 35.4 mg/L under flow-through conditions for 96 hours. The corresponding measured concentrations were 2.10, 3.34, 5.89, 7.81 and 18.1 mg/L. All fish exposed to 18 mg/L died within 24 hours and those exposed to 2.09, 5.56 and 7.77 showed signs of toxicity including death (1/20, 4/20 and 5/20, respectively).

96-h LC_{50} = 9.47 mg/L

1,3-Dichlorobenzene (CASRN 541-73-1)

Fathead minnows (*P. promelas*; 20/concentration) were exposed to nominal concentrations of 1,3-dichlorobenzene at 5.54, 8.52, 13.1, 20.1 and 30.9 mg/L under flow-through conditions for 96 hours. The corresponding measured concentrations were 1.71, 3.37, 4.62, 5.76 and 14.4 mg/L. The fish showed signs of toxicity including death at ≥ 1.7 mg/L. Mortality was 100% at 14.4 mg/L and occurred within 5 hours of treatment.

96-h LC_{50} = 8.03 mg/L

1,2,3-Trichlorobenzene (CASRN 87-61-6)

Fathead minnows (*P. promelas*) were exposed to nominal concentrations of 1,2,3-trichlorobenzene at 1.1, 1.6, 2.5, 3.9 and 6.0 mg/L for flow-through conditions for 96 hours. The corresponding measured concentrations were 0.69, 0.96, 1.5, 2.2 and 3.5 mg/L. The fish showed signs of toxicity at ≥ 0.96 mg/L. Mortality was 100% at 3.5 mg/L and occurred within 72 hours of treatment. No deaths were seen at ≤ 1.5 mg/L.

96-h LC_{50} = 2.4 mg/L

Acute Toxicity to Aquatic Invertebrates

Monochlorobenzene (CASRN 108-90-7)
Water fleas (*Daphnia magna*) were exposed to measured concentrations (not provided) of monochlorobenzene under static conditions for 24 hours. The submitted study duration deviates from the standard 48-hour daphnid toxicity study duration. The sponsor supported the 24-h toxicity value with a 48-hour EC50 value for this endpoint estimated using ECOSAR (15.38 mg/L). The modeled results indicate lower toxicity than the measured 24-hour results; therefore, the experimental 24-hour data were accepted for the purpose of characterizing hazard to daphnia.
24-h EC_{50} = 4.3 mg/L
48-h EC_{50} = 15.4 mg/L (estimated)

1,2-Dichlorobenzene (CASRN 95-50-1)
D. magna were exposed to measured concentrations (not provided) of 1,2-dichlorobenzene under static conditions for 24 hours. The submitted study duration deviates from the standard 48-hour daphnid toxicity study duration. The sponsor supported the 24-h toxicity value with a 48-hour EC50 value for this endpoint estimated using ECOSAR (6.345 mg/L). The modeled results indicate lower toxicity than the 24-hour results; therefore, the measured 24-hour data were accepted for the purpose of characterizing hazard to daphnia.
24-h EC_{50} = 0.78 mg/L
48-h EC_{50} = 6.5 mg/L (estimated)

1,3-Dichlorobenzene (CASRN 541-73-1)
D. magna were exposed to measured concentrations (not provided) of 1,3-dichlorobenzene under static conditions for 48 hours.
48-h EC_{50} = 4.2 mg/L

1,2,3-Trichlorobenzene (CASRN 87-61-6)
(1) *D. magna* were exposed to measured concentrations (not provided) of 1,2,3-trichlorobenzene under static conditions for 24 hours.
24-h EC_{50} = 0.35 mg/L

(2) *D. magna* were exposed to nominal concentrations (not provided) of 1,2,3-trichlorobenzene under static conditions in a closed system for 48 hours.
48-h EC_{50} = 2.71 mg/L

(3) Mysid shrimp (*Mysidopsis bahia*) were exposed to nominal concentrations of 1,2,3-trichlorobenzene at 0.89, 1.4, 2.1, 3.3 and 5.0 mg/L under flow- through conditions for 96 hours. Corresponding measured concentrations were 0.12, 0.13, 0.21, 0.35 and 0.57 mg/L.
96-h EC_{50} = 0.35 mg/L

Toxicity to Aquatic Plants

Monochlorobenzene (CASRN 108-90-7)

Green algae (*Pseudokirchneriella subcapitata*) were exposed to measured concentrations (taken at equilibrium) of monochlorobenzene at 6.5, 14.3, 23.3, 29.6, 37.8, 45.0 and 63.0 mg/L for 96 hours.
96-h EC_{50} (growth rate) = 12.5 mg/L

1,2-Dichlorobenzene (CASRN 95-50-1)
Green algae (*P. subcapitata*) were exposed to measured concentrations (taken at equilibrium) of 1,2-dichlorobenzene at 0.88, 2.75, 4.99, 6.38, 10.66, 17.55 and 21.19 mg/L for 96 hours.
96-h EC_{50} (growth rate) = 2.2 mg/L

1,2,3-Trichlorobenzene (CASRN 87-61-6)
Green algae (*P. subcapitata*) were exposed to measured concentrations (taken at equilibrium) of 1,2,3-trichlorobenzene at 0.26, 0.45, 1.09, 1.5, 1.79, 1.95 and 2.94 mg/L for 96 hours
96-h EC_{50} (growth rate) = 0.9 mg/L

Conclusion: The evaluation of available toxicity data for aquatic organisms indicates that the potential acute hazard of the chlorobenzenes category members is moderate to fish and high to aquatic invertebrates and plants. A trend of increasing toxicity with increasing chlorine substitution is observed for fish, daphnia and algae.

Table 2. Summary of Environmental Effects – Aquatic Toxicity Data						
Endpoints	**Mono-chlorobenzene (108-90-7)**	**1,2-Di-chlorobenzene (95-50-1)**	**1,3-Di-chlorobenzene (541-73-1)**	**1,4-Di-chlorobenzene (supporting chemical) (106-46-7)**	**1,2,3-Tri-chlorobenzene (87-61-6)**	**1,2,4-Tri-chlorobenzene (supporting chemical) (120-82-1)**
Fish 96-h LC_{50} (mg/L)	**10.4 (m)** 13.5 (e)	**9.47 (m)**	**8.03 (m)**	—**	**2.4 (m)**	—**
Aquatic Invertebrates 48-h EC_{50} (mg/L)	**4.3 (m)[1]** 15.4 (e)	**0.78 (m)[1]** 6.4 (e)	**4.2 (m)**	—**	**0.35 – 2.71 (m)**	—**
Aquatic Plants 96-h EC_{50} (mg/L) (growth)	**12.5 (m)**	**2.2 (m)**	No Data 1.6 – 2.2 (RA)	**1.6 (m)**	**0.9 (m)**	—**

(m) = measured data (i.e. derived from testing); (e) = estimated data (i.e. derived from modeling—ECOSAR); [1]Data available for 24-h duration only; (RA) = Read Across; — indicates endpoint not addressed for this chemical; ** indicates endpoint not necessary for supporting chemical

3. Human Health Effects

A summary of health effects data submitted for SIDS endpoints is provided in Table 3. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

Acute Oral Toxicity

Monochlorobenzene (CASRN 108-90-7)
(1) Sprague-Dawley rats (5/sex/dose) were administered a single oral dose of monochlorobenzene at 250– 4000 mg/kg-bw and observed for 14 days. All deaths occurred within 3 days of dosing.
LD_{50} = 1540 mg/kg-bw

(2) Fischer 344 rats (5/sex/dose) were administered a single oral doses of monochlorobenzene at 250, 500, 1000, 2000 or 4000 mg/kg-bw and observed for 14 days. The mortality was as follows: none at 250 mg/kg-bw, 1 male at 500 mg/kg-bw, 2 females at 1000 mg/kg-bw, 1 male at 2000 mg/kg-bw and 3 males and 4 females at 4000 mg/kg-bw. All deaths occurred within 3 days of dosing. LD_{50} was not calculated.
LD_{50} = 2000 – 4000 mg/kg-bw

(3) B6C3F1 mice (5/sex/dose) were administered a single oral dose of monochlorobenzene at 250, 500, 1000, 2000 or 4000 mg/kg-bw and observed 14 days. The mortality was as follows: 3 males and 2 females at 250mg/kg-bw, 1 male at 500 mg/kg-bw, 5 males and 2 females at 1000 mg/kg-bw and all animals at 2000 and 4000 mg/kg-bw. Most deaths occurred within 4 days of dosing. The LD_{50} was not calculated but appears to be < 250 mg/kg-bw.

LD_{50} < 250 mg/kg-bw

(4) A National Toxicology Program report indicates that the oral gavage LD50 of monochlorobenzene for rats, mice, rabbits and guinea pigs is 2290, 1440, 2250 and 5060 mg/kg-bw, respectively. http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/tr261.pdf

***1,2-Dichlorobenzene* (*CASRN 95-50-1*)**
(1) Guinea pigs (10 mixed sex/dose) were administered a single oral dose of 1,2-dichlorobenzene at 800 or 2000 mg/kg-bw and observed for 14 days. All animals at 800 mg/kg-bw survived and those at 2000 mg/kg-bw died.
800 mg/kg-bw < LD_{50} < 2000 mg/kg-bw
(2) In several studies, rats were administered oral doses of 1,2-dichlorobenzene.
http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html
LD_{50} = 1516-2138 mg/kg-bw

1,3-Dichlorobenzene (CASRN 541-73-1)
Sprague-Dawley rats (5/sex/dose) were administered a single dose of 1,3-dichlorobenzene at 631, 794, 1000, 1260 and 1580 mg/kg-bw and observed for 14 days. At 1580 mg/kg-bw all rats died within 1 day. **LD_{50} = 1100 mg/kg-bw**

1,2,4-Trichlorobenzene (CASRN120-82-1, supporting chemical)
CFE rats (4/sex/dose) and CF No. 1 mice were administered 1,2,4–trichlorobenzene via gavage at various doses (not provided) and observed for10 days. Deaths occurred within 5 days of dosing for rats and within 3 days of dosing for mice.
LD_{50} = 756 mg/kg-bw

Acute Dermal Toxicity

Monochlorobenzene (CASRN 108-90-7)
New Zealand White rabbits (2 males and 1female) were dermally administered monochlorobenzene at 5010 or 7940 mg/kg-bw and observed for 14 days. No mortality was observed.
LD_{50} > 7940 mg/kg-bw

1,4-Dichlorobenzene (CASRN 106-46-7, supporting chemical)
Sherman rats (10/dose, sex distribution not provided) were dermally administered 1,4-dichlorobenzene in xylene up to 6000 mg/kg-bw on shaved backs and observed for 14 days or until all survivors had recovered form signs of toxicity.
LD_{50} = 6000 mg/kg-bw

1,3-Dichlorobenzene (CASRN 541-73-1)
New Zealand White rabbits (4, sex distribution not provided) were dermally administered 1.3-dichlorobenzene at 2000 mg/kg-bw. No signs of toxicity were noted.
LD_{50} > 2000 mg/kg-bw

1,2,4-Trichlorobenzene (CASRN 120-82-1, supporting chemical)
Rats (strain unspecified, 4/sex) were dermally administered undiluted 1,2,4-trichlorobenzene to shorn dorso-lumbar skin under occlusive conditions for 24 hours and observed for 10 days. All deaths occurred within 5 days of exposure. **LD_{50} = 6139 mg/kg-bw**

Acute Inhalation Toxicity

Monochlorobenzene (CASRN 108-90-7)
(1) Sprague-Dawley rats (12 males/concentration) were exposed to monochlorobenzene vapor at concentrations ranging form 2000 – 3500 ppm (approximately 9.2 – 16.1 mg/L) for 6 hours and observed for 14 days.
LC_{50} ~ 13.9 mg/L

(2) Mice (25 females/concentration) were exposed to monochlorobenzene vapor at concentrations ranging form 1400 – 3000 ppm (approximately 6.4 – 13.8 mg/L) for 6 hours and observed for 14 days.
LC_{50} ~ 8.8 mg/L

(3) Sprague-Dawley rats (6 males) were exposed to monochlorobenzene via inhalation at 39.7 mg/L. All animals died within 3.75 hours.
LC_{50} < 39.7 mg/L

***1,2-Dichlorobenzene* (*CASRN 95-50-1*)**
(1) Sprague-Dawley rats (12/concentration) were exposed to 1,2-dichlorobenzene vapor at concentrations ranging from 1000 to 2000 ppm (approximately 6.0 – 12.0 mg/L) for 6 hours and observed for 14 days.
LC_{50} = 9.38 mg/L

(2) Mice (strain not specified, 25/concentration) were exposed to 1,2-dichlorobenzene vapor (concentrations not provided) for 6 hours and observed for 14 days.
LC_{50} = 7.43 mg/L

1,4-Dichlorobenzene (CASRN 106-46-7, supporting chemical)
Sprague-Dawley rats (5/sex) were exposed 1,4-dichlorobenzene vapor at 6 mg/L for 4 hours and observed for 14 days. All animals survived the exposure.
LC_{50} > 6 mg/L

Repeated-Dose Toxicity

Monochlorobenzene (CASRN 108-90-7)
(1) In a 13-week National Toxicology Program (NTP) study, Fisher 344 rats (10/sex/dose) were administered monochlorobenzene via gavage at 0, 62, 125, 250, 500 or 750 mg/kg-bw/day, 5 days/week . Survival was decreased at 500 and 750 mg/ kg-bw/day. Body weight gains were marginally to moderately depressed at 500 and 750 mg/ kg-bw/ day. Dose-dependent hepatocellular necrosis was observed at 250, 500 and 750 mg/ kg/ day. Nephrotoxicity and lymphoid or myeloid depletion of the spleen, bone marrow, and thymus were observed at 500

and 750 mg/ kg/ day. Renal necrosis or degeneration was noted in one male at 250 mg/kg-bw/day. Scattered changes in urinary and clinical chemistry, hematology, organ weight, and porphyrin metabolism parameters were also observed at 500 and 750 mg/ kg/ day.
http://ntp.niehs.nih.gov/?objectid=0706D0A9-EA0B-A103-B5B2CA2F7B2B4B38
LOAEL = 250 mg/kg-bw/day (based on liver and renal effects)
NOAEL = 125 mg/kg-bw/day

(2) In a 13-week NTP study, B6C3F1 mice (10/sex/dose) were administered monochlorobenzene via gavage at 0, 62, 125, 250, 500 or 750 mg/kg-bw/day, 5 days/week. Mortality increased in a dose-dependent manner in both sexes starting at 250 mg/kg-bw/day; all animals dying in the highest dose group. Dose-dependent hepatocellular necrosis was observed at 250, 500 and 750 mg/kg-bw/day. Nephrotoxicity, thymic necrosis, and lymphoid or myeloid depletion of the thymus, spleen and bone marrow were also observed at 250, 500, or 750 mg/kg-bw/day.
http://ntp.niehs.nih.gov/?objectid=0706D0A9-EA0B-A103-B5B2CA2F7B2B4B38
LOAEL = 250 mg/kg-bw/day (based on mortality and multiple organ effects)
NOAEL = 125 mg/kg-bw/day

(3) In a 90-day study, beagle dogs (16/sex/dose) were administered monochlorobenzene orally via capsule at 0, 0.025, 0.050 or 0.250 mL/kg-bw/day (0, 27.25, 54.5 or 272.5 mg/kg-bw/day), 5 days/week. Mortality was seen only at the high dose. Clinical signs before death in these animals included decreased appetite and activity, anorexia, body weight loss, cachexia and coma. Body weight loss; changes in hematology, clinical chemistry and urine analysis; and pathologic changes in liver (bile duct hyperplasia, cytologic changes, leukocytic infiltration, centrolobular degeneration), kidney, gastrointestinal mucosa, and hematopoietic tissue were also observed. There were also gross and/or microscopic changes in the liver to animals in the 54.5 mg/kg-bw/day group.
http://www.epa.gov/ncea/iris/subst/0399.htm
LOAEL ~ 54.5 mg/kg-bw/day (based on slight bile duct proliferation, cytologic alterations and leukocytic infiltration of the stroma; all in liver)
NOAEL ~ 27.3 mg/kg-bw/day

(4) In a six month study, beagle dogs (6/sex/concentration) were exposed to monochlorobenzene via inhalation at 0.79, 1.59 and 2.06 mg/L/day 6 hours/day, 5 days/week. All treated animals had abnormal stool during weeks 7 – 11. This also was evident in controls at week 11. Emesis occurred at the mid and high doses groups during weeks 8 – 10 and 17 – 29. The relative liver weights in the mid- and high-dose females were increased relative to controls and the relative adrenal weights in the mid- and high-dose males were decreased with respect to controls; however, no treatment-related changes were seen during gross and microscopic examinations.
NOAEL = 2.06 mg/L/day

1,2-Dichlorobenzene (CASRN 95-50-1)
(1) In a 90-day study, Sprague-Dawley rats (10/sex/dose) were administered 1,2-dichlorobenzene via gavage at 25, 100 and 400 mg/kg-bw/day. At 400 mg/kg-bw/day, males exhibited decreased mean body weight and absolute and relative spleen weight, and increased absolute and relative kidney and liver weight and relative heart, lung, brain and testes weight. An increase in erythrocytes versus control was noted in high-dose males. Males also had increased

erythrocytes, serum ALT, BUN and serum total bilirubin. In females at this dose, total food consumption was increased during weeks 11 – 13 and increased absolute and relative kidney and liver weight and decreased absolute spleen weight were observed ($p < 0.05$). Serum total bilirubin was also increase in these females. Hepatic degeneration, hypertrophy and necrosis of liver were observed in high-dose males and females. At 100 mg/kg-bw/day, male rats exhibited increased absolute and relative liver weight and increased ALT. Females at this dose had increased absolute and relative liver weight and absolute kidney weight.
LOAEL = 100 mg/kg-bw/day (based on liver and kidney effects)
NOAEL = 25 mg/kg-bw/day

(2) In a 90-day NTP study, Fischer 344 rats (10/sex/dose) were administered 1,2-dichlorobenzene via gavage at 0, 30, 60, 125, 250 or 500 mg/kg-bw/day, 5 days/week. Survival was decreased in males and females at 500 mg/kg-bw/day. Dose-related increases in relative liver weight and liver necrosis were noted in both sexes at 125, 250 and 500 mg/kg-bw/day. Hepatocellular degeneration and depletion of lymphocytes in the thymus and spleen was observed in both sexes at 500 mg/kg-bw/day. The only hematologic changes considered notable were slight decreases in hemoglobin and hematocrit in the 500 mg/kg male and female rats and in red blood cell counts in the 500 mg/kg male rats.
http://ntp.niehs.nih.gov/?objectid=0706B89C-F481-CA0A-7AECAB0C45EE3FCA
LOAEL = 125 mg/kg-bw/day (based on increases in liver weight and liver necrosis in both sexes)
NOAEL = 60 mg/kg-bw/day

(3) In a 13-week NTP study, B6C3F1 mice (10/sex/dose) were administered 1,2-dichlorobenzene via gavage at 0, 30, 60, 125, 250 or 500 mg/kg-bw/day, 5 days/week. At 500 mg/kg-bw/day, morality and decreased body weight and body weight gains were observed in both sexes. Relative liver weight was increased in both sexes. No marked hematological changes were observed in mice. Centrilobular necrosis of the liver, hepatocellular degeneration and depletion of lymphocytes in the thymus and spleen was observed in both sexes at 500 mg/kg-bw/day. At 250 mg/kg-bw/day, necrosis of individual hepatocytes was observed in both sexes. Multifocal mineralization of the myocardial fibers of the heart and skeletal muscle were seen in mice at 500 mg/kg/bw/day. http://ntp.niehs.nih.gov/?objectid=0706B89C-F481-CA0A-7AECAB0C45EE3FCA
LOAEL = 250 mg/kg-bw/day (based on liver effects)
NOAEL = 125 mg/kg-bw/day

(4) In a 6 month study, rats (strain not specified; 20/sex/concentration) were exposed to 1,2-dichlorobenzene via inhalation at nominal concentrations of 65 and 106 ppm (measured concentrations were 49 ppm [~ 0.3 mg/L] and 93 ppm [~ 0.57 mg/L], respectively) 7 hours/day, 5 days/week for 6 – 7 months. At 93 ppm, decreased average body weight was observed in males (statistical significance not stated). There were no effects on mortality, growth, organ weights, gross appearance, behavior or gross and microscopic examination of tissues.
LOAEL ~ 0.57 mg/L (based on decreased body weight in males only)
NOAEL ~ 0.3 mg/L

1,3-Dichlorobenzene (CASRN 541-73-1)
In a 90-day study, Sprague-Dawley rats (10/sex/dose) were administered 1,3-dichlorobenzene via gavage at doses of 0, 9, 37, 147 and 588 mg/kg-bw/day. No mortality or clinical signs were noted in the treated groups. At 588 mg/kg-bw/day, average daily water consumption was increased and body weights were decreased in both sexes. Increased relative kidney and liver weights were seen in both sexes and increased relative brain and testes weights were also seen in males. At 147 mg/kg-bw/day, decreased relative brain and increased relative liver weight were noted in females and increased relative kidney and liver weights were found in males. A variety of blood chemistry changes were observed at ≥ 147 mg/kg-bw/day; consistent effects among sexes and across doses were not clearly apparent. Hepatic inflammation, hepatocellular cytoplasmic alterations, hepatocellular necrosis was observed at all doses. Mild to minimal cytoplasmic vacuolization in the pars distalis of the pituitary was noted in 60, 60, 100 and 100% of males only (vs. 20% in controls) at 9, 37, 147 and 588 mg/kg-bw/day, respectively. Depletion of colloid density in the thyroid was seen in 65, 90, 89 and 94% of treated animals (vs. 15% in controls) at 9, 37, 147 and 588 mg/kg-bw/day, respectively
LOAEL = 9 mg/kg-bw/day (based on effects on liver, thyroid and pituitary)
NOAEL = Not established

1,2,3-Trichlorobenzene (CASRN 87-61-6)
In a 90-day study, Sprague-Dawley rats (10/sex/concentration) were administered 1,2,3-trichlorobenzene via the diet at 1, 10, 100 or 1000 ppm (corresponding to average 0.105, 1.04, 9.8 and 95.5 mg/kg-bw/day) daily. At 1000 ppm, a decrease in body weight gain and an increase in the liver to body weight and kidney to body weight ratios were seen in males. Mild to moderate histopathological changes in the liver and thyroid were observed in males and females, with effects more pronounced in males. Microscopic changes in the liver were mild to moderate increases in cytoplasmic volume and larger than normal nuclei of hepatocytes. Changes in the thyroid included mild to moderate reduction in follicular size and colloid density. Below 1000 ppm the study authors did not consider changes in weight gain and organ-to-body weight ratios to be treatment-related.
LOAEL ~ 95.5 mg/kg-bw/day (based on decreased body weight gain, increased liver- and kidney-to-body weight ratios and microscopic changes in the liver and thyroid)
NOAEL ~ 9.8 mg/kg-bw/day

1,4-Dichlorobenzene (CASRN 106-46-7, supporting chemical)
(1) In a 13-week NTP study, Fischer 344 rats (10/sex/dose) were administered 1,4-dichlorobenzene via gavage, 5 days/week. In the first study, rats were dosed with 300 – 1500 mg/kg-bw/day. Because histological changes were observed in the kidney of male rats at all doses, a second 13-week study was performed at doses of 37.5, 75, 150, 300 and 600 mg/kg-bw/day. Survival was decreased in males at 1200 or 1500 mg/kg-bw/day and in females at 1500 mg/kg-bw/day. Weight gain (significance not stated) was decreased in males at ≥ 300 mg/kg-bw/day and in females at 1200 or 1500 mg/kg-bw/day. Liver weight to brain weight ratios were increased ≥ 900 mg/kg-bw/day for both males and females. The kidney weight to brain weight ratio was increased in males receiving doses of ≥ 600 mg/kg-bw/day. Doses of 1200 or 1500 mg/kg-bw/day produced degeneration and necrosis of hepatocytes, hypoplasia of the bone marrow, lymphoid depletion of the spleen and thymus, and epithelial necrosis of the nasal turbinates in males and females. Renal tubular cell degeneration was observed in males

receiving ≥ 300 mg/kg-bw/day in the first study, but only slight changes were seen at 300 mg/kg-bw/day in the second study. Statistically significant decreases in the hematocrit, red blood cell count and hemoglobin level were seen in all males at 300 – 1200 mg/kg-bw/day. No clear hematologic changes were observed in females. Minimal changes in clinical chemistry parameters were observed, including increased serum cholesterol levels at ≥ 600 mg/kg-bw/day in males and ≥ 900 mg/kg-bw/day in females; reduced serum triglycerides at ≥ 300 mg/kg-bw/day in males. Blood urea nitrogen was increased slightly in males at ≥ 900 mg/kg-bw/day. Urinary porphyrins were increased slightly in males at 1200 or 1500 mg/kg-bw/day and females at 1200 mg/kg-bw/day. However these increases were modest and the study authors considered them indicative of a mild porphyrinuria rather than hepatic porphyria. Liver porphyrins were not increased at any dose. http://ntp.niehs.nih.gov/?objectid=0707D46D-9C42-21DF-D577330353775DE0
LOAEL = 300 mg/kg-bw/day (decreased weight gain, effects on kidneys and hematological changes in males)
NOAEL = 150 mg/kg bw/day

(2) In a 13-week NTP study, B6C3F1 mice (10/sex/dose) were administered 1,4-dichlorobenzene via gavage, 5 days/week. The doses for the first study were 600 – 1800 mg/kg-bw/day. Survival was decreased in male and female mice receiving doses of ≥1500 mg/kg-bw/day and body weight gain was decreased at all doses. Hepatocellular degeneration was observed in both sexes at all doses and the liver weight to brain weight ratio was increased at ≥ 900 mg/kg-bw/day. Serum cholesterol levels were increased in males at ≥ 900 mg/kg-bw/day, whereas serum protein and triglycerides were increased at ≥ 1500 mg/kg-bw/day. The study authors concluded that these relatively modest clinical chemistry changes probably reflect the hepatic effects of 1,4-dichlorobenzene. White blood cell count was reduced significantly in males at ≥ 600 mg/kg-bw/day and females at ≥ 1000 mg/kg-bw/day. Hepatic porphyria was not found at any dose. Because hepatic effects were seen at all doses in the first study, a second 13-week study was performed at doses of 0, 84.4, 168.8, 337.5, 675 and 900 mg/kg-bw/day. In this study, hepatocellular cytomegaly was observed in both sexes at ≥ 675 mg/kg-bw/day, but not at 337.5 mg/kg-bw/day. Renal damage was not observed in either 13-week study.
http://ntp.niehs.nih.gov/?objectid=0707D46D-9C42-21DF-D577330353775DE0
LOAEL = 675 mg/kg-bw/day (based on effect on liver)
NOAEL = 337.5 mg/kg-bw/day

1,2,4-Trichlorobenzene (CASRN 120-82-1, supporting chemical)
In a 90-day study, Sprague-Dawley rats (5/sex/concentration) were administered 1,2,4-trichlorobenzene via the diet at 1, 10, 100 and 1000 ppm (corresponding to ~0.07, 0.78, 7.8 and 82 mg/kg-bw/day for males and ~0.11, 1.4, 15 and 101 mg/kg-bw/day for females). There was no effect on body weight. Relative liver and kidney weights of males were significantly increased with respect to control only at the highest dose. Animals treated with 1000 ppm had marked changes in the liver characterized by aggregated basophilia and widespread midzonal vacuolization due to fatty infiltration. Mild to moderate changes in the thyroid included reduction in follicular size and colloid density. Higher activities of hepatic microsomal aniline hydroxylase and aminopyrene demethylase activities were also observed at 1000 ppm.
LOAEL = 82/101 mg/kg-bw/day (males/females; based on effects on liver, kidney and thyroid)
NOAEL = 7.8/15 mg/kg-bw/day (males/females)

Reproductive Toxicity

Monochlorobenzene (CASRN 108-90-7)
In a two-generation reproductive toxicity study, Sprague-Dawley rats (30/sex/dose) were exposed to monochlorobenzene via inhalation at 0, 50, 150 or 450 ppm (~ 0.23, 0.70 or 2.11 mg/L, respectively) for 6 hours/day, 7 days/week. The exposure period for F_0 and F_1 generations was for approximately 10 weeks of premating, during mating (males and females), 0 – 20 days of gestation and 4 – 21 days of lactation (females). No mortalities were observed in the adult generations. Mean food consumption and body weights for adults in both generations were comparable at all doses. Mating and fertility indices for males and females were unaffected by treatment. In the F_1 and F_2 litters, pup and litter survival for all treated groups was comparable to controls. In the F_2 litters, a slight decrease in pup survival index (days 0 – 4) was seen in offspring from high-dose animals. The study authors did not consider this to be treatment-related as it was predominantly due to loss of litters from two dams (one dam lost 12/15 pups and another lost all 10). Increases in absolute and relative liver weight were observed in F_0 and F_1 adults exposed to 150 or 450 ppm. An increase in the incidence of small flaccid testes and dilated renal pelvis was observed in high-dose F_0 and Fl males. There was an increase in the incidence of dilated renal pelvis in F_0 (dose- related) and F_1 males. In the F_1 generation, two females at 150 or 450 ppm had dilated renal pelvis versus none in controls. Microscopically, minimal to mild hepatocellular hypertrophy was noted in the mid- and high-dose F_0 and F_1 males and in one high-dose F_0 female. F_0 and F_1 males in the 150 ppm group and F_1 males in the 450 ppm group exhibited unilateral degeneration and F_0 males of the 450 ppm group exhibited bilateral degeneration of varying degrees in the germinal epithelium of the testes.
LOAEL (systemic toxicity) ~ 0.7 mg/L/day (based on liver, kidney and testicular effects)
NOAEL (systemic toxicity) ~ 0.23 mg/L/day
NOAEL (reproductive toxicity) ~ 2.1 mg/L/day (based on no significant effects at the highest dose tested)

1,2-Dichlorobenzene (CASRN 95-50-1)
In a two-generation reproductive toxicity study, Sprague-Dawley rats (30/sex/dose) were exposed to 1,2-dichlorobenzene via inhalation at 50, 150 and 400 ppm (corresponding to ~0.3, 0.9 and 2.4 mg/L/day) of 6 hours/day, 7 days/week during 10 weeks (premating and mating). Pregnant females were then exposed during gestation (19 days) and lactation (another 23 days). Males were exposed for an additional 3 weeks post-mating. A similar exposure regimen was followed for the F_1 generation. Mean weight gains over the entire pre-mating interval were decreased for males in both generations and for F_0 females. Maternal weight gain during the gestation/lactation interval was comparable to controls at all doses. A slight increase in absolute and relative liver weight in both the F_0 and F_1 adults was observed at 50 ppm. Mean absolute and relative liver weights were increased in F_0 adult males and females at 150 ppm and both generations at 400 ppm; in F_1 adults at 150 ppm, only relative liver weights were increased. Males of both generations had increased relative kidney weights at 150 and 400 ppm. No effects of treatment on reproductive performance, fertility indices, gestation length and litter size were apparent at any dose in either the F_0 or F_1 generation. Pup survival indices were generally comparable to controls for both generations. Mean pup weights were markedly decreased on days 0, 14, 21 and 28 in F_1 litters and on days 14 and 21 in F_2 litters. No adverse effect of

treatment was evident from the gross postmortem evaluations of adults and offspring. Histopathological examination showed treatment-related morphologic abnormalities in the liver and kidneys of the F_0 and F_1 adults. Hypertrophy of the central lobular hepatocytes was seen in almost all F_0 and F_1 adult males and females and numerous males and several females from the mid-exposure group. Kidneys showed dilated tubular lumens with intra-luminal granular casts, predominantly at the cortico-medullary junctions in several F0 and FI adult males from the mid- and high-exposure groups. Intra-cytoplasmic granules/droplets in the proximal convoluted tubular epithelium were seen in almost all F_0 and F_1 adult males for which the kidneys were examined microscopically. Based on mean severity, this kidney effect was dose-dependent. Several F_1 generation animals in all groups had findings suggestive of Sialodacryoadenitis viral (SDAV) infection. All males and females were noted as free of SDAV infection by week 41. The presence of SDAV did not appear to have adversely affected the study.
LOAEL (systemic toxicity) ~ 0.9 mg/L/day (based on liver effects)
NOAEL (systemic toxicity) ~ 0.3
NOAEL (reproductive toxicity) ~ 2.4 mg/L/day (based on no effects at highest dose tested)

1,3-Dichlorobenzene (CASRN 541-73-1)
In the 90-day repeated-dose study in Sprague-Dawley rats described previously, 1,3-dichlorobenzene was administered to both sexes by gavage at 0 (corn oil), 9, 37, 147 or 588 mg/kg-bw/day. High-dose males had markedly increased relative testes weights. However, there were no histopathological lesions observed to correlate the finding. No other effects were observed on the reproductive organs in males or females.

1,2,3-Trichlorobenzene (CASRN 87-61-6)
In the 90-day repeated-dose study in Sprague-Dawley rats described previously, 1,2,3-trichlorobenzene was administered via the diet at 1,10, 100 or 1000 ppm (corresponding to average 0.105, 1.04, 9.8 and 95.5 mg/kg-bw/day) daily. There were no effects observed in the reproductive organs in males or females.

1,4-Dichlorobenzene, (CASRN 106-46-7, supporting chemical)
In a two-generation study, Sprague-Dawley rats (28/sex/dose) were exposed, via inhalation to measured concentrations of 0, 66.3, 211 and 538 ppm (50, 150 and 450 ppm nominal corresponding to ~ 0, 0.3, 0.9 and 2.7 mg/L/day) of 1,4-dichlorobenzene 6 hours/day, 7 days/week, 10 weeks prior to mating, during mating (males and females) through gestation and lactation (females). There was no effect of treatment on reproductive parameters (mating or fertility indices of males or females, gestational index, 7-, 14-, 21- or 28-day survival index, lactation index or number of copora lutea or implantation sites, including resorptions and live conceptuses) in either generation. ***450 ppm***: F_0 and F_1 males and F_1 females exhibited consistently reduced body weights and weight gains throughout the study. F_0 females had reduced body weights for the first week of exposure prior to mating and on gestational day 20. Gestational weight or weight gain of F_0 and F_1 dams was reduced on gestational days 0 – 20. Lactational weights of F_1 females were reduced on postnatal days 0, 4 and 7. Non-exposed male and female F_1 recovery animals exhibited consistently reduced body weights. Food consumption was reduced in F_1 males for 5 of the 11 exposure weeks and was reduced in F_0 and F_1 females and F_0 males during the first week and third week (F_0 females only) of exposure. Food consumption was reduced in recovery animals during the first 2 weeks of the recovery period. Clinical signs

observed in F_0 and F_1 animals included unkempt appearance, tremors, twitches, hypoactivity, ataxia, salivation and periocular and perioral encrustation. F_0 and F_1 females had an increased incidence of urogenital wetness. There were no clinical observations in recovery animals. Liver and kidney weights of F_0 males and females were increased (as well as relative liver, brain, tested and kidney weights of F_0 males and relative liver and kidney weights of F_0 females). An increased incidence of hepatocellular hypertrophy was observed in F_0 males and females and increased incidences of hydronephrosis, hyaline droplet nephropathy[1], tubular proteinosis, granular cast formation, renal tubular cell hyperplasia and interstitial nephritis were observed in F_0 males. Exposure-related histological findings in F_1 adults were similar to those of F_0 adults. ***150 ppm***: Sporadic reductions in body weights and weight gains of F_0 and F_1 animals were observed at this concentration. F_0 and F_1 males had increased absolute and/or relative kidney and liver weights and F_0 females had increased relative liver weights. An increased incidence of nephrosis was observed in F_0 and F_1 males. Histological findings in the liver were similar to those of males treated with 450 ppm (with the exception of no renal cell hyperplasia and the additional finding of renal interstitial fibrosis). No histological alterations were noted in the liver. ***50 ppm***: Absolute and/or relative kidney weights of F_0 and F_1 males and liver weights of F_0 males were increased. There was an increased incidence of nephrosis in F_0 males, with similar histological findings as in the 150 ppm males. F_1 males did not exhibit nephrosis, but had an increased incidence of hyaline droplet formation in the kidneys. No histological alterations were noted in the liver.

LOAEL (systemic toxicity) ~ 0.3 mg/L/day (based on kidney and liver effects)
NOAEL (systemic toxicity) = Not established
NOAEL (reproductive toxicity) ~ 2.7mg/L/day (based on no effects at highest dose tested)

1,2,4-Trichlorobenzene (CASRN 120-82-1, supporting chemical)

In a two-generation study, male and female rats (strain not specified) were exposed to 25, 100 or 400 ppm 1,2,4-trichlorobenzene orally via drinking water during pre-mating (90 days) and then continuously until day 32 of the F_2 generation. The mean doses, calculated based on water intake, for F_0 females were 8.3, 28.0 and 133 mg/kg-bw/day for at 29 days of age and 3.7, 14.8 and 53.6 mg/kg-bw/day at 83 days of age and for F_0 males were 8.5, 27.6 and 133.6 mg/kg-bw/day at 29 days of age and 2.5, 8.9 and 33.0 mg/kg-bw/day at 83 days of age. Food intake was increased in F_0 high-dose males at 29 days and water intake was decreased in high-dose males and females at 83 days of age. At 400 ppm, slight increases in the weight of the left adrenal gland (the only one weighed) of males and females. Fertility, growth, viability, locomotor activity and blood chemical analyses of two generations of rats were not affected at any dose tested.

LOAEL (systemic toxicity) ~ 33/54 mg/kg-bw/day (male/female; based on increased adrenal weight)
NOAEL (systemic toxicity) ~ 9 /15 mg/kg-bw/day (male/female)

[1] The presence of nephropathy in association with the hyaline droplet accumulation in male rats suggests that the nephropathy in the males is occurring by an $alpha_{2u}$-globulin-mediated mechanism which is male rate-specific and not considered relevant to humans. EPA's Risk Assessment Forum has outlined the key events and the data that are necessary to demonstrate this mode of action ($Alpha_{2u}$-Globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Rat, EPA/625/3-91/019F). One of the key events, $alpha_{2u}$-globulin accumulation, has not been demonstrated. Therefore, the nephropathy is assumed to be relevant to human health and it is concluded that a NOAEL for nephropathy in male rats was not established.

NOAEL (reproductive toxicity) ~ 33/54 mg/kg-bw/day (male/female; based on no effects at the highest dose tested)

Developmental Toxicity

Monochlorobenzene (CASRN 108-90-7)
(1) Pregnant Fischer 344 (30-32/dose) rats were exposed to monochlorobenzene vapor via inhalation at 75, 210 or 590 ppm (~ 0.35, 0.98 or 2.76 mg/L/day) for 6 hours/day during days 6 – 15 of gestation. No maternal deaths or abnormal clinical signs were noted. At 590 ppm, animals lost weight during the first 3 days of exposure. Absolute and relative liver weights of dams at 590 ppm were slightly, but significantly (significance not provided) greater than control at necropsy. No adverse effects were noted in mean litter size or incidence of implantations. With the exception of a cleft palate in one fetus at 75 ppm, the malformations observed were similar to the controls and were within the historical incidences for controls. An increased incidence of some minor skeletal variants in fetuses from treated animals was noted. A higher incidence of delayed ossification of centra of the cervical vertebrae was seen at 75 ppm and 590 ppm, but not 210 ppm. A higher incidence of bilobed centra of the thoracic vertebrae and a lower incidence of cervical spurs were noted at 590 ppm. The study authors concluded the skeletal changes observed at the highest concentration were indicative of a slight delay in skeletal development, but none of the variants were considered to be indicative of a specific teratogenic response.
LOAEL (maternal toxicity) ~ 2.76 mg/L/day (based on decreased body weight and increased liver weight)
NOAEL (maternal toxicity) ~ 0.98 mg/L/day
LOAEL (developmental toxicity) ~ 0.35 mg/L/day (based on delayed ossification, cleft palate)
NOAEL (developmental toxicity) = Not established

(2) Pregnant New Zealand White rabbits (30/dose) were exposed to monochlorobenzene vapor via inhalation at 75, 210 or 590 ppm (~ 0.35, 0.98 or 2.76 mg/L/day) for 6 hours/day during days 6 – 18 of gestation. There was an increase in absolute and relative liver weights at 210 and 590 ppm. Exposure to all concentrations resulted in a variety of malformations in all groups at incidences slightly higher than historical controls, an increased incidence of extra ribs (a variation) in the high dose animals (113 in 26 litters vs. 79 in 24 control litters), head/facial abnormalities in one fetus at 75 ppm and another at 590 ppm and heart defects were seen in one fetus at 210 ppm and two fetuses (in two litters) at 590 ppm. To determine if these malformations were true effects of treatment, the study was repeated at concentrations of 10, 30, 75 and 590 ppm. In the second study, liver weight was increased in dams was seen at 590 ppm. The observed increase in percentage of implantations (61%) at 590 ppm was within the historical control range (19-67%). There were seven fetuses in one litter with ablepharia (missing eyelid) in the 590 ppm group. This anomaly was not observed in the first study. Skeletal examinations revealed an increase in the incidence of extra ribs in the 10 ppm group (94 in 23 litters vs. 72 in 21 control litters). This alteration was considered a skeletal variant.
LOAEL (maternal toxicity) ~ 0.98 mg/L/day (based on effect on liver)
NOAEL (maternal toxicity) ~ 0.35 mg/L/day
NOAEL (developmental toxicity) ~ 2.76 mg/L/day (based on no effects at the highest dose tested)

1,2-Dichlorobenzene (CASRN 95-50-1)

(1) Fischer 344 rats (30-32/dose) were administered 1,2-dichlorobenzene via inhalation at 0, 100, 200 and 400 ppm (~ 0, 0.6, 1.2, 2.4 mg/L, respectively) for 6 hours/day during days 6 – 15 of gestation. Mean body weights of females were reduced during gestation at 400 ppm and mean body weight gains at all concentrations were depressed on days 6 – 8, 12 – 15 and 6 – 20 of gestation. Food consumption was slightly depressed during the first 3 exposure days. An increase in absolute and relative liver weight was seen at 400 ppm and an increase in relative liver weight was noted at 100 ppm. Skeletal evaluation revealed a marked increase in the occurrence of spurs on the first lumbar vertebrae at 200 ppm only. Delayed ossification of cervical vertebral centra was markedly increased at 400 ppm. At 400 ppm, the other malformations included single cases of coarcted and retroesophageal aortic arch, unilateral testicular agenesis, polydactyly, cervical ribs and microphthalmia.
LOAEL (maternal toxicity) ~ 0.6 mg/L/day (based on effects on body weight and liver weights)
NOAEL (maternal toxicity) = Not established
LOAEL (developmental toxicity) ~ 2.4 mg/L (based on delayed ossification and malformations)
NOAEL (developmental toxicity) ~ 1.2 mg/L

(2) Female New Zealand White rabbits were exposed to 1,2-dichlorobenzene vapor via inhalation at 0, 100, 200 and 400 ppm (~ 0, 0.6, 1.2, 2.4 mg/L) for 6 hours/day during gestation days of 6 – 18. Does lost weight during the first 3 days of exposure at all concentrations. Total weight gain over days 6 – 28 was less in treated animals than controls. The ratio of male/female offspring was different in the 200 ppm group. None of the malformations in treated animals were at a higher statistical frequency (p = not provided) than controls.
LOAEL (maternal toxicity) ~ 0.6 mg/L/day (based on effects on body weight)
NOAEL (maternal toxicity) = Not established
NOAEL (developmental toxicity) ~ 2.4 mg/L/day (based on no effects at the highest dose tested)

(3) In the two-generation study previously described, Sprague-Dawley rats (30/sex/dose) were exposed to 1,2-dichlorobenzene via inhalation at 50, 150 and 400 ppm (corresponding to ~0.3, 0.9 and 2.4 mg/L/day) of 6 hours/day, 7 days/week during 10 weeks (premating and mating). Pregnant females were then exposed during gestation (19 days) and lactation (another 23 days). Pup survival indices were generally comparable to controls for both generations. Mean pup weights were markedly decreased on days 0, 14, 21 and 28 in F_1 litters and on days 14 and 21 in F_2 litters. No adverse effect of treatment was evident from the gross postmortem evaluations of adults and offspring.
LOAEL (maternal toxicity) ~ 0.9 mg/L/day (based on kidney and liver effects)
NOAEL (maternal toxicity) ~ 0.3 mg/L/day
LOAEL (developmental toxicity, F_1/F_2) ~ 2.7 mg/L/day (based on effects on pup weight and mortality)
NOAEL (developmental toxicity, F_1/F_2) ~ 0.9 mg/L/day

1,2,3-Trichlorobenzene (CASRN 87-61-6)

Female Sprague-Dawley rats (13/dose, 14/control) were administered 1,2,3-trichlorobenzene via gavage at 0, 150, 300 and 600 mg/kg-bw/day on days 6 – 15 of gestation. The post-exposure period was 7 days. No clinical signs of toxicity were observed. An increase in relative liver weight was observed at 600 mg/kg-bw/day. Aminopyrine N-demethylase (APDM) activity was increased in high-dose animals. Hemoglobin concentrations were slightly decreased at 300 or 600 mg/kg-bw/day. Mild changes in the thyroid were noted at 300 and 600 mg/kg-bw/day. The changes consisted of a reduction of follicle size, which was often accompanied by angular collapse. There was no effect on pregnancy rate, number of resorptions, litter size and fetal weight. No visceral and skeletal abnormalities were seen in pups.

LOAEL (maternal toxicity) = 300 mg/kg-bw/day (based on effect on hemoglobin and changes in thyroid)

NOAEL (maternal toxicity) = 150 mg/kg-bw/day

NOAEL (developmental toxicity) = 600 mg/kg-bw/day (based on no effects at the highest dose tested)

1,4-Dichlorobenzene (CASRN 106-46-7, supporting chemical)

(1) New Zealand White rabbits (28-30/dose) were exposed to 1,4-dichlorobenzene vapor via inhalation at 0, 100, 300 and 800 ppm (~ 0, 0.59, 1.77, 4.72 mg/L/day) for 6 hours/day during days 6 – 16 of gestation. The post-exposure period was 11 days. Does exposed to 800 ppm gained less weight than controls on days 6 – 8 of gestation. There was an increase in the percentage of implantations undergoing resorption and the percentage of litters with resorptions at 300 ppm, but not at 800 ppm. The numbers of litters, corpora lutea/dam, implantation sites/dam, fetuses/litter, resorptions/litter, litters totally resorbed and resorptions/litters with resorptions were not different from control in any of the treated groups. Fetal sex ratio, fetal weight and crown-rump length of treated animals were not different from controls.

LOAEL (maternal toxicity) ~ 4.72 mg/L/day (based on effect on body weight gain)

NOAEL (maternal toxicity) ~ 1.77 mg/L/day

NOAEL (developmental toxicity) ~ 4.72 mg/L/day (based on no effects at the highest dose tested)

(2) In the two-generation study previously described, Sprague-Dawley rats (28/sex/dose) were exposed, via inhalation to measured concentrations of 0, 66.3, 211 and 538 ppm (50, 150 and 450 ppm nominal corresponding to ~ 0, 0.3, 0.9 and 2.7 mg/L/day) of 1,4-dichlorobenzene 6 hours/day, 7 days/week, 10 weeks prior to mating, during mating (males and females) through gestation and lactation (females). At the highest dose, the mean number of F_2 live born pups per litter was reduced. F_1 and F_2 litter size (but not sex ratio) was reduced on lactational day 4. Pups from F_1 and F_2 litters exhibited reduced body weights per litter during lactation. There was an increase in the incidence of stillborn pups (F_2) and postnatal deaths on days 0 – 4 (both F_1 and F_2 pups). There were no effects of treatment on pups at the two lower doses.

LOAEL (maternal toxicity) ~ 0.3 mg/L/day (based on liver effects)

NOAEL (maternal toxicity) = Not established

LOAEL (developmental toxicity, F_1) ~ 0.9 mg/L/day (based on effects on pup weight)

NOAEL (developmental toxicity, F_1) ~ 0.3 mg/L/day

LOAEL (developmental toxicity, F_2) ~ 2.4 mg/L/day (based on effects on pup weight)

NOAEL (developmental toxicity, F_2) ~ 0.9 mg/L/day

Genetic Toxicity – Gene Mutation

In vitro
Monochlorobenzene (CASRN 108-90-7)
Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to monochlorobenzene at 0.02 – 1.28 µL/plate in the presence and absence of metabolic activation. DMSO was the solvent control; other appropriate positive controls were also used. There was no increase in the average number of revertant colonies in any of the tested strains with or without metabolic activation. The controls responded appropriately. Cytotoxicity was apparent at concentration of 1.28 µL/plate in all strains.
Monochlorobenzene was not mutagenic in this assay.

(2) In several other assays, monochlorobenzene was tested up to 3333 µL/plate or 5500 µg/plate and did not induce positive response in tested strains of *S. typhimurium* or *Escherichia coli.*
Monochlorobenzene was not mutagenic in these assays.

1,2-Dichlorobenzene (CASRN 95-50-1)
S. typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to 1,2-dichlorobenzene at 0.02 – 2.56 µL/plate in the presence and absence of metabolic activation. DMSO was the solvent control; other appropriate positive controls were also used and responded appropriately. Cytotoxicity was observed at 1.28 µL/plate in most strains, except 0.32 µL/plate was toxic to strain TA1537 in the absence of metabolic activation and 2.56 µL/plate was required to produce toxicity to strains TA98, TA1537 and TA100 in the presence of metabolic activation. There was no increase in the average number of revertant colonies in any of the tested strains with or without metabolic activation.
1,2-Dichlorobenzene was not mutagenic in this assay.

(2) In several other assays, 1,2-dichlorobenzene was tested up the concentrations of 13,000 µg/plate in *S. typhimurium* strains and *E. coli WP2(trp-, uvRA* in the presence and absence of metabolic activation. None of the assays showed increase in revertant colonies.
1,2-Dichlorobenzene was not mutagenic in these assays.

1,3-Dichlorobenzene (CASRN 541-73-1)
(1) *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to 1,3-dichlorobenzene at 0.02 – 2.56 µL/plate in the presence and absence of metabolic activation. DMSO was the solvent control; other appropriate positive controls were also used and responded appropriately. Cytotoxicity was apparent at a concentration of 1.28 µL/plate in all strains. There was no increase in the average number of revertant colonies in any of the tested strains with or without metabolic activation.
1,3-Dichlorobenzene was not mutagenic in these assays.

(2) In several other assays, 1,3-dichlorobenzene was tested up to 2000 µg/plate and did not induce positive response in the tested strains of *S. typhimurium* or *E. coli.*
1,3-Dichlorobenzene was not mutagenic in these assays.

1,2,3-Trichlorobenzene (CASRN 87-61-6)
S. typhimurium strains TA 98, TA100, TA1535 and TA1537 were exposed to 1,2,3-trichlorobenzene at 3.3, 10, 33.3, 100 and 333.3 µg/plate in the presence and absence of metabolic activation. DMSO was the solvent control; other appropriate positive controls were also used and responded appropriately. Concentrations of 100 and 333.3 µg/plate were toxic to all strains in the absence and presence of metabolic activation, respectively. There was no increase in the average number of revertant colonies in any of the tested strain with or without metabolic activation.
1,2,3-Trichlorobenzene was not mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberrations

In vitro
Monochlorobenzene (CASRN 108-90-7)
Chinese hamster ovary (CHO) cells were exposed to monochlorobenzene at 125, 250 and 500 µg/mL in the presence and absence of metabolic activation for 24 or 48 hours. DMSO was the negative control. Cytotoxicity was seen at 500 µg/mL without metabolic activation and > 500 µg/mL with metabolic activation. There was no increase in the frequency of aberrant cells.
Monochlorobenzene did not induce chromosomal aberrations in this assay.

1,4-Dichlorobenzene (CASRN 106-46-7, supporting chemical)
CHO cells were exposed to 1,4-dichlorobenzene at 50, 100 and 150 µg/mL without metabolic activation and 25, 50 and 100 µg/mL with metabolic activation. Positive and negative controls responses were appropriate. A precipitate was noted at 150 µg/mL. There was an increase in the frequency of aberrant cells at doses of 25 – 150 µg/mL.
1,4-Dichlorobenzene did not induce chromosomal aberrations in this assay.

1,2,3-Trichlorobenzene (CASRN 87-61-6)
CHO cells were exposed to 1,2,3-trichlorobenzene at 15.7 – 125 µg/mL with and without metabolic activation for 24 or 48 hours. The cytotoxic concentration was > 125 µg/mL. There was no increase in the frequency of aberrant cells.
1,2,3-Trichlorobenzene did not induce chromosomal aberrations in this assay.

1,2,4-Trichlorobenzene (CASRN 120-82-1, supporting chemical)
CHO cells were exposed to 1,2,4-trichlorobenzene at 31.3 – 125 µg/mL with and without metabolic activation for 24 or 48 hours. The cytotoxic concentration was 125 µg/mL. There was no increase in the frequency of aberrant cells.
1,2,4-Trichlorobenzene did not induce chromosomal aberrations in this assay.

In vivo
Monochlorobenzene (CASRN 108-90-7)
(1) B6C3F1 male mice (5/dose) were administered monochlorobenzene intraperitoneally for 3 days at doses of 128.8, 257.5 and 515 mg/kg-bw/day. Animals were sacrificed at 24, 48 and 72 hours, bone marrow was aspirated and slides were prepared, stained and evaluated for the presence of micronuclei. There was no increase in micronuclei at any dose level. Positive, negative and solvent controls responded appropriately.

Monochlorobenzene did not induce chromosomal aberrations in this assay.

(2) NMRI mice were administered intraperitoneal doses of monochlorobenzene (total dose of 225, 450, 675 and 900 mg/kg-bw) in two doses 24 hours apart. Animals were sacrificed 30 hours after the first injection. The femora were removed and the marrow was suspended in serum. Two smears per femur were prepared. One thousand polychromatic erythrocytes (PCEs) per smear were examined for the presence of micronuclei. The number of micronucleated cells/1000 PCEs were significantly (significance was not provided) different from control at all doses. Although the sponsor concluded that inappropriate statistical analysis were used, when compared to the positive control data, EPA concluded that monochlorobenzene was positive in this assay.
Monochlorobenzene induced chromosomal aberrations in this assay.

(3) Male B6C3F1 mice received a single intraperitoneal injection of corn oil or monochlorobenzene in corn oil at 312.5, 625 or 1250 mg/kg-bw following a subcutaneous implantation of a BrdUrd tablet 1 hour before injection. After 17 hours, mice were sacrificed, bone marrow cells from the femur were harvested, fixed and stained and 50 metaphase cells from each animal per treatment group were scored for the presence of chromosomal aberrations. There was no effect of treatment on the percentage of cells with abnormalities although the exposure period (17 hours) was less than the guideline required exposure of 24 hours. In similarly conducted second experiment, male mice were exposed to the doses of 250, 500 or 1000 mg/kg-bw and the cells were harvested from bone marrow at 36 hours. A positive trend was noted with a statistically significant increase in the percent of abnormal cells at 1000 mg/kg-bw ($p < 0.05$).
Monochlorobenzene induced chromosomal aberrations in this assay.

1,2-Dichlorobenzene (CASRN 95-50-1)
(1) Male B6C3F1 mice were administered 1,2-dichlorobenzene via intraperitoneal injection at 150, 300 and 600 mg/kg-bw during 3 days of dosing. Animals were sacrificed at 48 hours after the third treatment, bone marrow was aspirated and slides were prepared, stained and evaluated for the presence of micronuclei. The incidence of micronucleated-PCEs per 1000 PCEs showed barely a positive trend ($p = 0.049$). The test was repeated using the 250 mg/kg-bw dose and was found to be negative by trend analysis ($p = 0.358$). Because of the relatively small increase in micronucleated-PCEs in the initial test and the lack of reproducibility, the overall result of this test was negative.
1,2-Dichlorobenzene did not induce chromosomal aberrations in this assay.

(2) NMRI mice were administered 1,2-dichlorobenzene in corn oil via intraperitoneal injection at 0, 187, 375, 562 and 750 mg/kg-bw in two doses given 24 hours apart. Animals were sacrificed 30 hours after the first injection, bone marrow was aspirated and slides were prepared, stained and evaluated for the presence of micronuclei. One thousand polychromatic erythrocytes (PCEs) per smear were examined for the presence of micronuclei. The number of micronucleated cells/1000 PCEs were markedly (significance was not provided) increased at all doses. Although the sponsor concluded that inappropriate statistical analysis were used, when compared to the positive control data, EPA concluded that monochlorobenzene was positive in this assay.
1,2-Dichlorobenzene induced chromosomal aberrations in this assay.

1,3-Dichlorobenzene (CASRN 541-73-1)
(1) NMRI mice were administered 1,3-dichlorobenzene in corn oil via intraperitoneal injection at 0, 175, 350, 525 and 700 mg/kg-bw in two doses given 24 hours apart. Animals were sacrificed 30 hours after the first injection, bone marrow was aspirated and slides were prepared, stained and evaluated for the presence of micronuclei. There was a dose-related increase in the numbers of micronucleated cells per 1000 PCEs. Although an inappropriate statistical test was used to determine the significance, 1,3-dichlorobenzene was judged to be positive in this test.
1,3-Dichlorobenzene induced chromosomal aberrations in this assay.

1,4-Dichlorobenzene (CASRN 106-46-7, supporting chemical)
NMRI mice were administered 1,4-dichlorobenzene in corn oil via gavage at 2500 mg/kg-bw. Animals were sacrificed 24, 48 or 72 hours after treatment. The incidence of micronucleated PCEs/l000 was not increased markedly and there was no dose response.. The positive control induced 12 micronucleated-PCEs/l000 PCEs. 1,4-dichlorobenzene, in corn oil, was also administered intraperitoneally twice at an interval of 24 hours. There was no difference between treated animals and control in the incidence of MN-PCE/1000.
1,4-Dichlorobenzene did not induce chromosomal aberrations in this assay.
1,2,3-Trichlorobenzene (CASRN 87-61-6) and 1,2,4-Trichlorobenzene
Male NMRI mice were given intraperitoneal doses of 1,2,3-trichlorobenzene at 250, 500, 750 and 1000 mg/kg-bw (in two doses given 24 hours apart). The control group received corn oil only. Animals were killed 30 hours after the first injection. The femora were removed and the marrow was suspended in serum. Two smears per femur were prepared and 1000 PCEs per smear were examined for the presence of micronuclei. The numbers of micronucleated cells/1000 PCEs were increased in a dose-related manner.1,2,3-Trichlorobenzene was positive in the test.
1,2,3-Trichlorobenzene and 1,2,4-trichlorobenzene induced chromosomal aberrations in this assay.

Genetic Toxicity – Other

1,2-Dichlorobenzene (CASRN 95-50-1)
CHO cells were exposed to 1,2-dichlorobenzene at concentrations of 5.9, 19.7 or 59 μg/mL without metabolic activation and 19.7, 59 or 197 μg/mL with metabolic activation in one test and 300, 400 or 500 μg/mL with metabolic activation in another test. The test substance did not induce sister chromatid exchange (SCE) in the absence of metabolic activation. In the first experiment with metabolic activation, concentrations of 19.7, 59.0 and 197.0 μg/mL induced 8.64, 8.98 and 8.90 SCEs per cell (compared to 7.26 in control). In a second experiment with metabolic activation, concentrations of 300, 400 and 500 μg/mL induced 10.68, 10.38 and 10.06 SCEs per cell (compared to 8.46 in control). The positive control induced appropriate responses in both experiments. The test for SCE was positive in the presence of metabolic activation.
1,2-Dichlorobenzene induced sister chromatid exchange in this assay.

1,4-Dichlorobenzene (CASRN 106-46-7, supporting chemical)
CHO cells were exposed to 1,4-dichlorobenzene at 75, 100, 125 and 150 μg/mL without metabolic activation and 75, 100 and 125 μg/mL in one test with metabolic activation and 100,

125 and 150 µg/mL in another with metabolic activation. The solvent control was DMSO. Both positive controls induced approximately a 3-fold increase in SCEs. No treatment-related increase in SCEs was observed at doses of 75 – 150 µg/mL in the absence metabolic activation. A positive result at one concentration (75 µg/mL) was obtained in one test with metabolic activation. The test was repeated and the results at all three concentrations were similar to control. The overall result was negative. No toxicity or cell cycle delay was found. A precipitate was noted at 150 µg/mL.
1,4-Dichlorobenzene did not induce sister chromatid exchange in this assay.

Additional Information

Skin Irritation

1,2-Dichlorobenzene (CASRN 95-50-1)
Rabbits (3/sex) were treated with 0.5 mL undiluted 1,2-dichlorobenzene to the intact skin for 4 hours under semi-occlusive conditions. The test substance caused slight to moderate erythema and oedema up to 72 h post exposure.
http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html
1,2-Dichlorobenzene was slightly irritating to rabbit skin.

Eye Irritation

1,2-Dichlorobenzene (CASRN 95-50-1) – OECD ref.
Rabbits were administered two drops by direct application of undiluted 1,2-dichlorobenzene to the eye. After about 30 s the eye was flushed for two minutes with water and eyes examined after 2, 24, 48 or 168 hours. Pain and slight conjunctival irritation were observed. The inflammatory response resolved within one week.
http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html
1,2-Dichlorobenzene was slightly irritating to rabbit eye.

Respiratory Irritation

1,2-Dichlorobenzene (CASRN 95-50-1) – OECD ref.
Studies with Swiss OF_1 mice indicate that 1,2-dichlorobenzene induces respiratory irritation with a 50% reduction in respiratory rate (RD_{50}) reported at 163 ppm and 182 ppm.
http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html
1,2-Dichlorobenzene was a respiratory irritant in mice.

Carcinogenicity

Monochlorobenzene (CASRN 108-90-7)
(1) In a 103-week NTP study, F344N rats (50/sex/dose) were administered monochlorobenzene in corn oil via gavage at 60 or 120 mg/kg-bw/day, 5 days/week. Survival of high dose male rats was significantly (P=0.033) lower than that of the vehicle controls. No chlorobenzene-induced toxic lesions responsible for this reduction in survival were observed. Mean body weights of dosed rats were essentially the same or greater than those of the controls. Male rats exhibited a

significant (P<0.05) increase in the incidence of neoplastic nodules of the liver. Increased incidences of hepatocellular carcinomas in male rats or of neoplastic nodules or hepatocellular carcinomas in female rats were not observed. No increased tumor incidences were observed in female rats.

Chlorobenzene administration increased the occurrence of neoplastic nodules of the liver in male F344/N rats, providing some but not clear evidence of carcinogenicity of chlorobenzene in male rats. Carcinogenic effects of chlorobenzene were not observed in female F344/N rats.

(2) In a 103-week NTP study, B6C3F1 mice were administered monochlorobenzene in corn oil via gavage at 30 or 60 mg/kg-bw/day (males) and 60 or 120 mg/kg-bw/day (females), 5 days/week. Mean body weights of dosed mice were essentially the same or greater than those of the controls. No increased tumor incidences were observed in female rats or in male or female mice.

Carcinogenic effects of chlorobenzene were not observed in female in male or female $B6C3F_1$ mice.

1,2-Dichlorobenzene (CASRN 95-50-1)

(1) In a 103-week NTP study, F344N rats (50/sex/dose) were administered 1,2-dichlorobenze in corn oil via gavage at 60 or 120 mg/kg-bw/day, 5 days/week. Survival of female rats was comparable to those of the corresponding vehicle controls, but survival of high-dose male rats was (P<0.001) shorter than that of the vehicle controls. In this group there were three accidental deaths and five deaths probably due to the gavage process; in addition aspiration of 1,2-dichlorobenzene in corn oil into the lungs may have been a contributing factor to the deaths of 12 high-dose male rats. Body weight was not affected in either sex or survival of mice or female rats. No compound-related non-neoplastic histological lesions were noted.

There was <u>no evidence</u> of carcinogenicity of 1,2-dichlorobenzene for male or female F344/N rats.

(2) In a 103-week NTP study, B6C3F1 mice were administered 1,2-dichlorobenzene in corn oil via gavage at 60 or 120 mg/kg-bw/day, 5 days/week. Survivals of males and females were comparable to those of the corresponding vehicle. The 120 mg/kg dose level of 1,2-dichlorobenzene did not affect body weight in mice of either sex. An increase in tubular regeneration in the kidney of high dose male mice was observed. No other compound-related non-neoplastic histological lesions were noted.

There was <u>no evidence</u> of carcinogenicity of 1,2-dichlorobenzene for male or female $B6C3F_1$ mice.

1,4-Dichlorobenzene (CASRN 106-46-7)

(1) In a 103-week NTP study, F344N rats (50/sex/dose) were administered 1,4-dichlorobenze in corn oil via gavage at 0, 150 or 300 mg/kg-bw/day (males) and 0, 300, 600 (females), 5 days/week. Survival of females was comparable to that of the vehicle controls; survival of high-dose males was significantly lower than that of the vehicle controls. Mean body weights of high-dose males were 5%-8% lower than those of vehicle controls after week 38, and those of high-dose females were 5%-7% lower than those of vehicle controls after week 55. Males had increased severity of nephropathy and epithelial hyperplasia of the renal pelvis, mineralization of

the collecting tubules in the renal medulla and focal hyperplasia of renal tubular epithelium. There were increased incidences of nephropathy in both low- and high- dose females compared with vehicle controls. The incidence of tubular cell adenocarcinomas of the kidney was increased in males; one tubular cell adenoma was observed in a high-dose male rat. These malignant tumors are uncommon in male F344/N rats. There were no tubular cell tumors in females. There was a marginal increase in the incidence of mononuclear cell leukemia in males compared with that in vehicle controls.
1,4-dichlorobenzene produced clear evidence of carcinogenicity for male F344/N rats. There was no evidence of carcinogenicity for female F344/N rats.

(2) In a 103-week NTP study, B6C3F1 mice were administered 1,4-dichlorobenzene in corn oil via gavage at 0, 300 or 600 mg/kg-bw/day, 5 days/week. Survival of both sexes was comparable to that of the vehicle controls. Mean body weights were comparable to those of vehicle controls throughout the study. Incidences of non-neoplastic liver lesions in male and female mice were increased, including alteration in cell size (cytomegaly and karyomegaly), hepatocellular degeneration and individual cell necrosis. Increases in the incidences of nephropathy in male mice and renal tubular regeneration in female mice were seen. Increased the incidences of hepatocellular carcinomas in high-dose males and females and hepatocellular adenomas in dosed males and high- dose females were also seen. Hepatoblastomas were observed in four high-dose males but not in vehicle controls. This tumor has not occurred in 1,091 male vehicle control mice in NTP studies. An increase in thyroid gland follicular cell hyperplasia was observed in dosed males and there was a marginal positive trend in the incidence of follicular cell adenomas of the thyroid gland in females. Marginal increases were observed in the incidences of pheochromocytomas of the adrenal gland in males.
1,4-dichlorobenzene produced clear evidence of carcinogenicity for both male and female $B6C3F_1$ mice.

Conclusion: The acute oral toxicity of the chlorobenzenes category to rats, mice, rabbits and guinea-pigs is low. Acute dermal toxicity to rats and rabbits is low. Acute inhalation toxicity to rats and mice is moderate. 1,2-Dichlorobenzene is slightly irritating to rabbit skin and eye and is a respiratory irritant in mice. Systemic toxicity of monochlorobenzene and 1,2-dichlorobenzene in oral repeated-dose studies is low in rats and mice and moderate in dogs (monochlorobenzene). Systemic toxicity of 1,3-dichlorobenzene and 1,2,3-trichlorobenzene in oral repeated-dose studies in rats, is high and moderate, respectively. Systemic toxicity of the supporting chemicals 1,4-dichlorobenzene (rats and mice) and 1,2,4-trichlorobenzene (rats) in oral repeated-dose studies is low and moderate, respectively. Systemic toxicity of monochlorobenzene and 1,2-dichlorobenzene in inhalation repeated-dose studies is moderate in rats and low in dogs, respectively. There were no reproductive toxicity studies for 1,3-dichlorobenzene and 1,2,3-trichlorobenzene. However, there was no indication of toxicity to reproductive organs examined in oral repeated-dose studies in rats. The reproductive toxicity of the supporting chemical, 1,2,4-trichlorobenzene via oral exposure to rats is low. The reproductive toxicity of monochlorobenzene and the supporting chemical, 1,4-dichlorobenzene, via inhalation exposure to rats is low. The prenatal toxicity of 1,2,3-trichlorobenzene via oral exposure to rats is low. The prenatal toxicity of monochlorobenzene via inhalation exposure to rats is moderate and to rabbits is low. The pre- and post-natal toxicity of 1,2-dichlorobenzene and the supporting chemical 1,4-dichlorobenzene via inhalation exposure to rats is low and the prenatal toxicity via

inhalation exposure to rabbits is low. The chlorobenzenes category members did not induce gene mutations or chromosomal aberrations *in vitro*. However, all members of the category showed increased numbers of micronucleated erythrocytes in mice *in vivo*. There was evidence of carcinogenicity of monochlorobenzene in male rats. However, carcinogenic effects of monochlorobenzene were not observed in female rats or mice of either sex. There was no evidence of carcinogenicity of 1,2-dichlorobenzene in male or female rats or mice.

Table 3. Summary of Human Health Data

Endpoints	Mono-chlorobenzene (108-90-7)	1,2-Di-chlorobenzene (95-50-1)	1,3-Di-chlorobenzene (541-73-1)	1,4-Di-chlorobenzene (supporting chemical) (106-46-7)	1,2,3-Tri-chlorobenzene (87-61-6)	1,2,4-Tri-chlorobenzene (supporting chemical) (120-82-1)
Acute Oral Toxicity LD_{50} (mg/kg-bw)	**1540 – 4000 (rat)** **< 250 – 1440 (mice)** **2250 (rabbit)** **5060 (guinea-pig)**	**> 800 – < 2000 (guinea-pig)** **1516-2138 (rat)**	**1100**	**—****	No Data 756 (RA)	**756 (mice)**
Acute Dermal Toxicity LD_{50} (mg/kg-bw)	**> 7940**	No Data > 2000 (RA)	**> 2000**	**6000**	No Data 6139 (RA)	**6139**
Acute Inhalation Toxicity LC_{50} (mg/L)	**13.9 – < 39.7 (rat)** **8.8 (mice)**	**9.4 (rat)** **7.4 (mice)**	No Data 7.4 – 9.4 (RA)	**> 6**	No Data 7.4 (RA)	**—****
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	**(rat, mice)** **NOAEL =125** **LOAEL = 250** **(dog)** **NOAEL = 27.3** **LOAEL = 54.5**	**(rat)** **NOAEL = 25** **LOAEL = 100** **(rat)** **NOAEL = 60** **LOAEL = 125** **(mouse)** **NOAEL = 125** **LOAEL = 250**	**(rat)** **NOAEL = NE** **LOAEL = 9**	**(rat)** **NOAEL = 150** **LOAEL = 300** **(mice)** **NOAEL 338** **LOAEL = 675**	**(rat)** **NOAEL = 9.8** **LOAEL = 95.5**	**(rat)** **NOAEL = 8/15 (m/f)** **LOAEL = 82/101 (m/f)**
Repeated-Dose Toxicity NOAEL/LOAEL Inhalation (mg/L/day)	**(dog)** **NOAEL ~ 0.8** **LOAEL ~ 1.6**	**(rat)** **NOAEL ~ 0.3** **LOAEL ~ 0.6**	**—***	**—****	**—***	**—****
Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day) **Systemic Toxicity** **Reproductive Toxicity**	**—***	**—***	Evaluation of repeated-dose studies showed no effects on reproductive organs.	**—****	Evaluation of repeated-dose studies showed no effects on reproductive organs.	**NOAEL = 9/15 (m/f)** **LOAEL = 33/54 (m/f)** **NOAEL = 33/54 (m/f)**

Table 3. Summary of Human Health Data

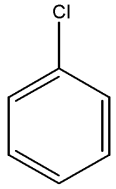
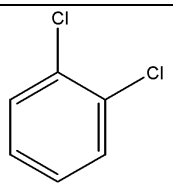
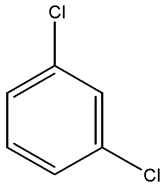
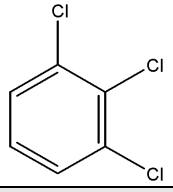
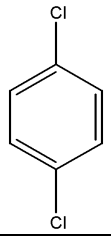
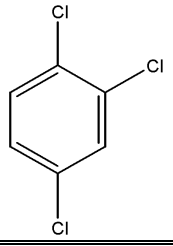
Endpoints	Mono-chlorobenzene (108-90-7)	1,2-Di-chlorobenzene (95-50-1)	1,3-Di-chlorobenzene (541-73-1)	1,4-Di-chlorobenzene (supporting chemical) (106-46-7)	1,2,3-Tri-chlorobenzene (87-61-6)	1,2,4-Tri-chlorobenzene (supporting chemical) (120-82-1)
Reproductive Toxicity NOAEL/LOAEL Inhalation (mg/L/day)			No Data		—*	—**
Systemic Toxicity	**(rat) NOAEL ~ 0.23 LOAEL ~ 0.7**	**(rat) NOAEL ~ 0.3 LOAEL ~ 0.9**	(rat) NOAEL = NE LOAEL ~ 0.3	**(rat) NOAEL = NE LOAEL ~ 0.3**		
Reproductive Toxicity	**NOAEL ~ 2.1**	**NOAEL ~ 2.4**	NOAEL ~ 2.4 (RA)	**NOAEL ~ 2.7**		
Developmental Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	—*	—*	—*	—*		—**
Maternal Toxicity					**(rat) NOAEL = 150 LOAEL = 300**	
Developmental Toxicity					**NOAEL = 600**	
Developmental Toxicity NOAEL/LOAEL Inhalation (mg/L/day)			No Data		—*	—**
Maternal Toxicity	**(rat) NOAEL ~0.98 LOAEL ~ 2.8**	**(rat) NOAEL = NE LOAEL ~ 0.6**	(rat) NOAEL = NE LOAEL = ~ 0.6	**(rabbit) NOAEL~ 1.77 LOAEL ~ 4.72**		
	(rabbit) NOAEL ~0.35 LOAEL ~ 0.98	**(rabbit) NOAEL = NE LOAEL ~ 1.2**	(rabbit) NOAEL = NE LOAEL ~1.2	**(rabbit) NOAEL~ 4.72**		
Developmental Toxicity	**(rat) NOAEL = NE LOAEL ~ 0.35 (rabbit) NOAEL ~2.8**	**(rat) NOAEL ~ 1.3 LOAEL ~ 2.4 (rabbit) NOAEL ~2.4**	(rat) NOAEL ~1.3 LOAEL ~ 2.4 (rabbit) NOAEL ~2.4			
Genetic Toxicity – Gene Mutation *In vitro*	**Negative**	**Negative**	**Negative**	—**	**Negative**	—**
Genetic Toxicity – Chromosomal Aberrations *In vitro*	**Negative**	**Negative**	No Data Negative (RA)	**Negative**	**Negative**	**Negative**

Table 3. Summary of Human Health Data

Endpoints	Mono-chlorobenzene (108-90-7)	1,2-Di-chlorobenzene (95-50-1)	1,3-Di-chlorobenzene (541-73-1)	1,4-Di-chlorobenzene (supporting chemical) (106-46-7)	1,2,3-Tri-chlorobenzene (87-61-6)	1,2,4-Tri-chlorobenzene (supporting chemical) (120-82-1)
Genetic Toxicity – Chromosomal Aberrations *In vivo*	**Positive**	**Positive** (NMRI mice) **Negative** (B6C3F1 mice)	**Positive**	**Negative**	**Positive**	**Positive**
Genetic Toxicity – Other SCE	—*	**Positive**	—*	**Negative**	—*	—**
Other information – Skin irritation	*	**Slight**	*	*	*	—**
Other information – Eye irritation	*	**Slight**	*	*	*	—**
Other information – Respiratory irritation	*	**Irritating**	*	*	*	—**
Additional Information - Carcinogenicity	**Some but not clear evidence**	**No evidence**	—*	**Clear evidence**	—*	—**

Measured Data (bolded); RA = Read Across; NE = Not established; ─ indicates endpoint not addressed for this chemical; * indicates endpoint not included in the base data set for the HPV Challenge Program; ** indicates endpoint not necessary for supporting chemical

Table 4

SPONSORED CHEMICALS		
Chemical Name	**CASRN**	**Chemical Structure**
Benzene, chloro-	108-90-7	
Benzene, 1,2-dichloro-	95-50-1	
Benzene, 1,3-dichloro-	541-73-1	
Benzene, 1,2,3-trichloro-	87-61-6	
SUPPORTING CHEMICALS		
Benzene, 1,4-dichloro-	106-46-7	
Benzene, 1,2,4-trichloro-	120-82-1	

Appendix B: Screening-Level Exposure Characterization

Chlorobenzenes Category

Sponsored Chemicals

Monochlorobenzene (CASRN 108-90-7)
(CA Index Name: Benzene, chloro-)

1,2-Dichlorobenzene (CASRN 95-50-1)
(CA Index Name: Benzene, 1,2-dichloro-)

1,3-Dichlorobenzene (CASRN 541-73-1)
(CA Index Name: Benzene, 1,3-dichloro-)

1,2,3-Trichlorobenzene (CASRN 87-61-6)
(CA Index Name: Benzene, 1,2,3-trichloro-)

This exposure characterization was completed using both public, non-confidential sources, and one or more IUR submissions that were available as of this writing.

Volume and Use Information

The four chlorobenzenes category chemicals had aggregated production and/or import volumes in the United States between 20 and 101 million pounds. Non-confidential information in the Inventory Update Rule (IUR) submissions indicates that these chemicals were manufactured and/or imported at the following companies and sites:

CASRN 108-90-7:
- BASF Corporation / Florham Park, NJ
- PPG Industries, Inc. / New Martinsville, WV
- Solvay Advanced Polymers, LLC / Augusta, GA

CASRN 95-50-1
- PPG Industries, Inc. / New Martinsville, WV

CASRN 541-73-1
- Clariant Corporation / Elgin, SC

CASRN 87-61-6
- Ashland Inc. / Dublin, OH
- BASF Corporation / Florham Park, NJ

There may be other companies and sites that are claimed confidential. Persons submitting IUR information for 2005 asserted that some or all of the information was confidential. Only non-confidential versions of reported IUR data are included in this summary.

Table 1 for each chemical at the end of this summary lists the non-confidential industrial processing and uses from IUR submissions. No commercial/consumer uses are reported in IUR submissions.

The Organization for Economic Cooperation and Development (OECD) Screening Information Data Set (SIDS) dossier was found for one of the chlorobenzenes category chemicals: CASRN 95-50-1. The dossier for this chemical states that the chemical is used primarily used in chemical synthesis and as a solvent. The chemical is also used as a degreaser, in paint strippers, industrial deodorants, and a slight amount in pharmaceutical preparation.[5]

The HSDB indicates that the chlorobenzene category chemicals are used as follows:[6]

CASRN 108-90-7:	Manufacture of phenol, aniline, DDT; as a solvent for paints; heat transfer medium; and many other uses.
CASRN 95-50-1:	The active ingredient is no longer contained in any registered pesticide products ... "cancelled."; solvent for waxes, gums, resins, tars, rubbers, oils, asphalts, insecticide for termites and locust borers; removing sulfur from illuminating gas; as intermediate in manufacture of dyes; as heat transfer medium; as degreasing agent for metals, leather, wool; as ingredient of metal polishes; herbicide, insecticide, and soil fumigant; and other uses, including potential consumer uses, e.g., ingredient in paint.
CASRN 541-73-1:	Fumigant and insecticide; intermediate.
CASRN 87-61-6:	Chemical intermediate; dye carrier and solvent; solvent for high melting products; coolant in electrical installations & glass tempering; polyester dyeing; lubricants; heat transfer medium, insecticides.

Environmental Releases

Environmental releases may impact general population and environmental exposures. Factors affecting releases include volumes produced, processed and used; numbers of sites; and processes of manufacture, processing, and use.

[5] OECD 2007. Organization for Economic Cooperation and Development. Accessed 8/8/08. http://www.chem.unep.ch/irptc/sids/OECDSIDS/95501.pdf

[6] HSDB, 2008. Hazardous Substances Data Bank. Accessed, 8/8/08. CASRN 108-90-7, 95-50-1, 541-73-1, 87-61-6. http://toxnet.nlm.nih.gov/.

Based on IUR data, the maximum total number of industrial sites manufacturing, processing, or using this chemical is confidential.

The following release statements are made based on inferences regarding the non-confidential use information found in public sources or reported in IUR and summarized in Table 1 below for each chemical.

Many chemicals designated as "reactant" (CASRN 108-90-7, 95-50-1) or "intermediates" (CASRN 108-90-7) have industrial releases that are a relatively low percentage of the volume. Lower percentage releases occur when a high percentage of the chemical reacts without excess loss during its use as a reactant/ intermediate. The actual percentages and quantities of release of the reported chemicals associated with these processing or uses are not known.

Many chemicals designated as "product component" (CASRN 108-90-7) have industrial releases that are a relatively low percentage of the volume. Lower percentage releases occur when a high percentage of the volume is incorporated at without significant process losses during its incorporation into formulation, mixture, or product. The actual percentages and quantities of release of the reported chemical associated with this processing or use are not known.

Many chemicals processed by "repackaging" (CASRN 108-90-7) have industrial releases that are a relatively low percentage of the volume. Lower percentage releases occur when a high percentage of the chemical is repackaged without significant process losses during its repackaging. The actual percentages and quantities of release of the reported chemical associated with this processing or use are not known.

Chemicals designated to be "used in non-incorporative activities" (CASRN 95-50-1) or to have industrial use function "other" (CASRN 108-90-7) can have variable release percentages during industrial processing and use. The actual percentages and quantities of release of the reported chemicals associated with these processing or uses are not known.

Many chemicals designated to have industrial use as agricultural chemicals (CASRN 108-90-7, 95-50-1) have releases during end use that are a relatively high percentage of the volume. Higher percentage releases occur when the product containing the chemical is used in a dispersive pattern on land. The actual percentages and quantities of release of the reported chemicals associated with this category are not known but could be high.

Many chemicals designated to have industrial use as solvents for chemical manufacture and processing (CASRN 108-90-7, 95-50-1) have industrial and/or end use releases that are a relatively high percentage of the volume. Higher percentage releases occur when the chemical's intended use is as a solvent that may evaporate into the atmosphere or may be collected and disposed to aqueous media. In some cases, some engineering controls or capture for recycle or reclamation may reduce these losses. The actual percentages and quantities of release of the reported chemicals associated with this category are not known but could be high.

All of the chlorobenzenes category chemicals are on the Toxics Release Inventory except CASRN 87-61-6.[7]

For chlorobenzene (CASRN 108-90-7), the total releases reported in 2006 from all reporting sites is 706,124 pounds. This total includes air releases of 468,409 pounds from on-site fugitive and point sources, in addition to on-site water releases of 667 pounds. Most of the remaining volume of release was deep-well injected or sent to off-site landfills. No additional data on releases were available from other sources.

For 1,2-dichlorobenzene (CASRN 95-50-1), the total releases reported in 2006 from all reporting sites is 106,925 pounds. This total includes air releases of 42,580 pounds from on-site fugitive and point sources, in addition to on-site water releases of 892 pounds. Most of the remaining volume of release was deep-well injected. No additional data on releases were available from other sources.

For 1,3-dichlorobenzene (CASRN 541-73-1), the total releases reported in 2006 from all reporting sites is 267,540 pounds. This total includes air releases of 1,040 pounds from on-site fugitive and point sources, in addition to on-site water releases of 293 pounds. Most of the remaining volume of release was deep-well injected or disposed to on-site landfills. No additional data on releases were available from other sources.

The chemicals in this category have vapor pressures ranging from about 0.065 to 9 mm Hg at ambient conditions. Experience has shown that air releases due to volatilization have not been an issue for chemicals with vapor pressures below 0.01 mm Hg. These chemicals' vapor pressures could result in air releases.

Exposures to the General Population and the Environment

Based on the information under the release section above, it is likely that there would be some releases to water, land, or air during manufacturing, processing, and use. Therefore, potential exposure to the general population and the environment is likely. A search of additional relevant databases did provide further information on releases of this chemical.

According to the Current National Recommended Water Quality Criteria, potential exposures to these chemicals that may exceed recommended water quality criteria for general population and the environment are likely.[8] (CASRN 108-90-7, 95-50-1, 541-73-1).

According to selected Indoor Air Articles, potential exposure to the general population and children from this chemical in indoor air is likely.[9] (CASRN 108-90-7, 95-50-1, 541-73-1, 87-61-6).

[7] USEPA, 2008. Toxic Release Inventory. Accessed, 10/24/08 http://www.epa.gov/triexplorer/
[8] USEPA, 2006. National Recommended Water Quality Criteria. Accessed, 08/08/08. http://www.epa.gov/waterscience/criteria/wqcriteria.html
[9] Indoor Air Articles published by Brown et al. (1994), Daisey et al. (1994), Immerman and Schaum (1990), Samfield (1992), Shah et al. (1988), Sheldon et al. (1992), and Shields et al. (1996)

According to the National Contaminant Occurrence Database (NCOD), potential exposure to the general population, environment, and children is likely for this contaminant found in drinking water.[10] (CASRN 108-90-7, 95-50-1, 541-73-1, 87-61-6).

According to the National Emission Inventory (NEI) Database, potential exposure to the general population, environment, and children is likely from this chemical found in the air as a point, non-point or mobile source.[11] (CASRN 108-90-7).

According to the National Health and Nutrition Examination Survey (NHANES), potential exposure to the general population, environment, and children is likely for this chemical included in a study that evaluates how environmental exposures function as risk factors for disease.[12] (CASRN 108-90-7, 541-73-1).

According to the National Water Quality Assessment (NAWQA) Program, potential exposure to the general population, environment, and children is likely from this chemical found in ground water.[13] (CASRN 108-90-7, 95-50-1, 541-73-1, 87-61-6).

According to the Total Exposure Assessment Methodology (TEAM) studies, potential exposure to the general population, environment, and children is likely from this chemical measured in humans.[14] (CASRN 108-90-7, 95-50-1).

According to the National Fish Tissue Study, potential exposure for the general population and children is likely to this chemical in fish tissue from lakes and reservoirs of the continental US.[15] (CASRN 95-50-1, 541-73-1, 87-61-6).

According to the National Human Adipose Tissue Survey (NHATS), potential exposure to the general population and children is likely from this chemical that was found in a study of human adipose tissue.[16] (CASRN 95-50-1).

According to the National Sediment Inventory (NSI) Tissue Data, potential exposure to the general population and the environment is likely from this chemical found in sediments.[17] (CASRN 95-50-1, 87-61-6).

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[10] USEPA, 2006. National Contaminant Occurrence Database (NCOD). Accessed, 08/08/08. http://www.epa.gov/safewater/data/ncod/index.html
[11] USEPA, 2002. National Emission Inventory (NEI) Database. Accessed, 08/08/08. http://www.epa.gov/ttn/chief/net/
[12] CDC, 2008. National Health and Nutrition Examination Survey. Accessed, 08/08/08. http://www.cdc.gov/nchs/nhanes.htm
[13] USGS, 2007. the National Water Quality Assessment (NAWQA) Program. Accessed, 08/08/08. http://infotrek.er.usgs.gov/servlet/page?_pageid=543&_dad=portal30&_schema=PORTAL30
[14] USEPA, 2008. Total Exposure Assessment Methodology (TEAM) Studies.
[15] USEPA, 2006. National Fish Tissue Study. Accessed, 08/08/08. http://www.epa.gov/waterscience/fishstudy/overview.htm
[16] USEPA, 1986. National Human Adipose Tissue Survey (NHATS). Accessed, 08/08/08. http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=55204
[17] USEPA, 2008. National Sediment Inventory (NSI) Tissue Data. Accessed 08/08/08. http://www.epa.gov/waterscience/cs/nsidbase.html

Persistence and bioaccumulation ratings for these chemicals are P2 and B1 for the mono- (CASRN 108-90-7) and dichlorobenzenes (CASRN 95-50-1 and 541-73-1). These ratings suggest that these chemicals are persistent in the environment; and are not bioaccumulative. The trichlorobenzene (CASRN 87-61-6) is rated as very persistent (P3) and bioaccumulative (B2).

Based on the information considered including environmental fate, known uses, and the Agency's expert judgment, EPA identifies, for purposes of risk-based prioritization, a high potential for exposure to the general population and the environment.

Exposures to Workers

Worker exposures may be impacted by many factors, including but not limited to volumes produced, processed and used; physical forms and concentrations; processes of manufacture, processing, and use; chemical volatility, and exposure controls, such as engineering controls and personal protective equipment.

Based on IUR data, the maximum total number of workers reasonably likely to be exposed to this chemical category during manufacturing and industrial processing and use may be 1,000 or greater. (>1000 workers: CASRN 108-90-7; 100-999 workers: CASRN 95-50-1, 87-61-6; <100 workers: CASRN 541-73-1).

The National Occupational Exposure Survey (NOES), conducted from 1981 to 1983, estimated the following number of workers potentially exposed to these chemicals[18]:

CASRN 108-90-7:	18,055 workers
CASRN 95-50-1:	92,250 workers
CASRN 541-73-1:	418 workers
CASRN 87-61-6:	691 workers

Differences between numbers of workers estimated by IUR submitters and by the NOES are attributable to many factors, including time, scope, and method of the estimates. For example, NOES estimates are for all workplaces while IUR are for industrial workplaces only, and NOES used a survey and extrapolation method while IUR submitters simply provide their best estimates based on available information for the specific reporting year.

Based on IUR data, all of the chlorobenzenes category chemicals are manufactured in liquid forms. Worker exposures are possible for this chemical in these forms. There may be other physical forms that are claimed confidential. Also, the non-confidential maximum concentration is greater than 90% for all chemicals except CASRN 87-61-6, which has a maximum concentration up to 30%. There may be other concentrations that are claimed confidential.

The chemicals in this category have vapor pressures ranging from 0.065 to 9 mm Hg at ambient conditions. Experience has shown that worker exposures to vapors have not been an issue for

[18] NIOSH, 1983. National Occupational Exposure Survey (NOES, 1981-1983). Accessed, 8/8/08. http://www.cdc.gov/noes/

chemicals with vapor pressures below 0.001 mm Hg. These chemicals' vapor pressures could result in worker exposures to vapors if workers are proximal to the liquids.

Additional information on worker exposure is available in the HSDB.[19]

Two of the chlorobenzenes category chemicals have OSHA Permissible Exposure Limits (PELs)[20]:

CASRN 108-90-7: PEL 8-hr Time Weighted Avg: 75 ppm (350 mg/ m^3);
CASRN 95-50-1: PEL Ceiling value: 50 ppm (300 mg/ m^3).

Based on the information considered, including IUR data and HSDB information, and in combination with the Agency's professional judgment, EPA identifies, for the purposes of risk-based prioritization, high relative rankings for potential worker exposure for the mono- and di-chlorobenzenes in the category (CASRN 108-90-7, 95-50-1, and 541-73-1) and a medium relative ranking for potential worker exposure for the trichlorobenzene in the category (CASRN 87-61-6). These relative rankings are based primarily on the vapor pressures, the aggregated volumes, and the uses of the chemicals.

Exposures to Consumers

IUR submissions did not include consumer uses.

EPA identifies, for the purposes of risk-based prioritization, a low potential for exposures to consumers from products containing these chemicals based on the IUR data.

There is also potential for exposure to consumers based on information from public data sources. The HSDB results reported in the Volume and Use Information section above indicated potential consumer uses for all the chemicals.
The National Institutes of Health (NIH) Household Product Database [21] and Source Ranking Database (SRD)[22] indicated these additional consumer uses:

CASRN 108-90-7: NIH: herbicides
SRD: rubber molding, herbicide, insulation

CASRN 95-50-1: NIH: overglaze, lubricants
SRD: polish and cleaners; deodorants, rubber molding

EPA identifies, for the purposes of risk-based prioritization, a high potential for exposures to consumers from products containing these chemicals based on information from public data

[19] HSDB, 2008. Hazardous Substances Data Bank. Accessed, 8/8/08, CAS# 108-90-7, 95-50-1, 541-73-1, 87-61-6. http://toxnet.nlm.nih.gov
[20] OSHA, 2008. Table Z-1 Limits for Air Contaminants. Accessed, 10/24/08 through http://www.osha.gov.
[21] National Institutes of Health (NIH) Household Product Database. CAS# 109-90-7; 95-50-1; Accessed 8/8/08. http://hpd.nlm.nih.gov/products.htm
[22] Source Ranking Database. CAS# 109-90-7; 95-50-1. Accessed 8/8/08. http://www.epa.gov/opptintr/exposure/pubs/srd.htm

sources. The only consumer products identified for CASRN 541-73-1 are pesticides, which are not TSCA uses.

Exposures to Children

No uses in products specifically intended to be used by children were reported in the IUR, nor were any found in other data sources. Exposures to children, however, may be expected to occur through the household use of some consumer products. Therefore, EPA identifies, for the purposes of risk-based prioritization, a medium potential that children might be exposed to the chlorobenzenes category chemicals.

Non Confidential IUR Data Summary **Benzene, chloro- (CASRN 108-90-7)**

Manufacturing/Import Information

Production and import volume:	10 million to 50 million pounds
List of non-CBI companies/ sites*:	PPG Industries, Inc. / New Martinsville, WV Solvay Advanced Polymers, LLC / Augusta, GA BASF Corporation / Florham Park, NJ
Maximum number of exposed workers**:	1,000 or greater
Highest non-CBI maximum concentration*:	greater than 90%
Non-CBI physical forms*:	liquid

* There may be other companies/ sites, concentrations and physical forms that are claimed confidential.
** Includes all manufacturing and industrial processing and use workers. There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information

Processing Activity	Industrial Sector	Function in Industrial Sector
Processing as a reactant	Other Plastics Product Manufacturing	Other
Processing as a reactant	Other Basic Organic Chemical Manufacturing	Other
Processing as a reactant	Pesticide and Other Agricultural Chemical Manufacturing	Agricultural chemicals (nonpesticidal)
Processing--incorporation into formulation, mixture, or reaction product	Pesticide and Other Agricultural Chemical Manufacturing	Intermediates
Processing--repackaging	Other Basic Organic Chemical Manufacturing	Solvents (for chemical manufacture and processing and are not part of product at greater than 1% by weight)
One or more items may have been claimed as confidential.		

Table 2
Commercial/ Consumer Uses Information

Commercial/ Consumer Product Category Description	Highest Maximum Concentration Range	Use in Children's Products
None reported		

Non Confidential IUR Data Summary **Benzene, 1,2-dichloro- (CASRN 95-50-1)**

Manufacturing/Import Information

Production and import volume: 10 million to 50 million pounds

List of non-CBI companies/ sites*: PPG Industries, Inc. / New Martinsville, WV

Maximum number of exposed workers**: between 100 and 999

Highest non-CBI maximum concentration*: greater than 90%

Non-CBI physical forms*: liquid

* There may be other companies/ sites, concentrations and physical forms that are claimed confidential.
** Includes all manufacturing and industrial processing and use workers. There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information

Processing Activity	Industrial Sector	Function in Industrial Sector
Processing as a reactant	Pesticide and Other Agricultural Chemical Manufacturing	Agricultural chemicals (nonpesticidal)
Use--nonincorporative activities	Other Plastics Product Manufacturing	Solvents (for chemical manufacture and processing and are not part of product at greater than 1% by weight)
One or more items may have been claimed as confidential.		

Table 2
Commercial/ Consumer Uses Information

Commercial/ Consumer Product Category Description	Highest Maximum Concentration Range	Use in Children's Products
None reported		

Non Confidential IUR Data Summary **Benzene, 1,3-dichloro- (CASRN 541-73-1)**

Manufacturing/Import Information

Production and import volume: 10,000 to 500,000 pounds

List of non-CBI companies/ sites*: Clariant Corporation / Elgin, SC

Maximum number of exposed workers**: less than 100

Highest non-CBI maximum concentration*: greater than 90%

Non-CBI physical forms*: liquid

* There may be other companies/ sites, concentrations and physical forms that are claimed confidential.
** Includes all manufacturing and industrial processing and use workers. There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information

Processing Activity	Industrial Sector	Function in Industrial Sector
None reported		

Table 2
Commercial/ Consumer Uses

Commercial/ Consumer Product Category Description	Highest Maximum Concentration Range	Use in Children's Products
None reported		

Non Confidential IUR Data Summary **Benzene, 1,2,3-trichloro- (CASRN 87-61-6)**

Manufacturing/Import Information

Production and import volume: 10,000 to 500,000 pounds

List of non-CBI companies/ sites*: Ashland Inc. / Dublin, OH
BASF Corporation / Florham Park, NJ

Maximum number of exposed workers**: between 100 and 999

Highest non-CBI maximum concentration*: up to 30%

Non-CBI physical forms*: liquid

* There may be other companies/ sites, concentrations and physical forms that are claimed confidential.
** Includes all manufacturing and industrial processing and use workers. There may be additional potentially exposed industrial workers that are not included in this estimate since not all submitters were required to report on industrial processing and use and/or there may be at least one use that contains a "Not Readily Obtainable" (NRO) response among the submissions.

Table 1
Industrial Processing and Use Information

Processing Activity	Industrial Sector	Function in Industrial Sector
None reported		

Table 2
Commercial/ Consumer Uses

Commercial/ Consumer Product Category Description	Highest Maximum Concentration Range	Use in Children's Products
None reported		