

NATIONAL TOXICOLOGY PROGRAM

EXECUTIVE SUMMARY OF SAFETY AND TOXICITY INFORMATION

p, p'-DICHLORODIPHENYL SULFONE

CAS Number 80-07-9

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Submitted to:

NATIONAL TOXICOLOGY PROGRAM

Submitted by:

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Board of Scientific Counselors Draft Report

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OVERVIEW¹

Nomination History: *p,p'*-Dichlorodiphenyl sulfone was nominated for carcinogenicity testing by the National Cancer Institute (NCI) in 1987. The nomination was based on the potential for increasing use and production of this compound, and the absence of subchronic and chronic toxicity data, including mutagenicity and carcinogenicity studies. The NCI also noted that the high temperature use of polysulfone products may increase the potential release of monomer residues.

Chemical and Physical Properties: *p,p'*-Dichlorodiphenyl sulfone is a white powder with a melting point of 145°-149°C (293°-300°F) and a boiling point of 250°C (482°F). This compound is insoluble in water, but is soluble in acetone, olive oil, hot alcohols and aromatics. *p,p'*-Dichlorodiphenyl sulfone is incompatible with oxidizing agents.

Production/Uses/Exposure: *p,p'*-Dichlorodiphenyl sulfone is used as a starting material in the production of polysulfones. Polysulfones are part of the general product group known as engineering plastics which are used in a wide variety of consumer products including electrical equipment, auto components and appliances. The annual production of engineering plastics has increased during the last several years from approximately 7.8 million pounds in 1985 to nearly 1.5 billion pounds in 1988. There are no data available on the annual production of *p,p'*-dichlorodiphenyl sulfone, or on consumer, occupational or environmental exposure to this compound.

Toxicological Effects:

Human: No data were found on the acute, prechronic, chronic/carcinogenic, or reproductive effects of *p,p'*-dichlorodiphenyl sulfone in humans.

Animal: The oral LD₅₀ of *p,p'*-dichlorodiphenyl sulfone in rats and mice has been reported to be 5-20 g/kg and 5-10 g/kg, respectively. Another source

¹The information contained in this Executive Summary of Safety and Toxicity Information (ESSTI) is based on data from current published literature. The summary represents information provided in selected sources and is not claimed to be exhaustive.

reports an oral LD₅₀ of 24 g/kg in mice. In one study, prechronic administration of p,p'-dichlorodiphenyl sulfone to rats induced elevated hepatic enzyme activity and an increase in the lipid content of the liver as well as dystrophic changes and necrotic foci of the liver and heart. In the only study reported in the literature concerning the reproductive effects of p,p'-dichlorodiphenyl sulfone, this compound was found to be embryotoxic in rats. There are no data available on the chronic/carcinogenic effects of p,p'-dichlorodiphenyl sulfone in animals.

Genetic Toxicology: *No data were found on the genotoxic effects of p,p'-dichlorodiphenyl sulfone in prokaryotic or eukaryotic systems.*

Structure Activity Relationships: *No data were found on structure activity relationships for p,p'-dichlorodiphenyl sulfone.*

I. NOMINATION HISTORY AND REVIEW

A: Nomination History

1. Source: National Cancer Institute (NCI)[NCI, 1987a,b]
2. Date: July, 1987
3. Recommendations: Carcinogenicity
4. Priority: Moderate
5. Rationale/Remarks:
 - Potential for increasing use and production
 - Absence of toxicological information, including carcinogenicity, mutagenicity, subchronic and chronic data
 - High temperature use of polysulfone products may increase the potential release of monomer residue
 - Absence of information on monomer residue levels in polymeric products

B. Chemical Evaluation Committee Review

1. Date of Review: September 12, 1990
2. Recommendation:
 - Subchronic studies
 - Mutagenicity
3. Priority: High
4. NTP Chemical Selection Principle(s): 3,8
5. Rationale/Remarks:
 - High production
 - Potential for increased use
 - Lack of toxicological data
 - Lack of information on residues (if any) of chemical in polymeric products and whether the monomer is released from the polymers at high temperatures
 - ITC will recommend chemical to EPA for physical/chemical testing by industry

C. Board of Scientific Counselors Review

1. Date of Review: October 15, 1990
2. Recommendation: Defer
3. Priority: --
4. Rationale/Remarks:

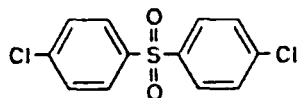
- High production
- Although the chemical is used in a closed system in the manufacture of polymers and other products, there is the possibility for sudden massive release of the chemical
- It is difficult to evaluate the potential for human exposure because there is a lack of information on the amount (if any) of monomeric residues in polymeric products, and whether the chemical is released from these products
- Deferred in order to ascertain whether the Organization for Economic Cooperation and Development has information on chemical properties and toxicity studies

D. Executive Committee Review

1. Date of Review:
2. Decision:

II. CHEMICAL AND PHYSICAL DATA

A. Chemical Identifiers



p,p'-DICHLORODIPHENYL SULFONE

Molecular formula: C₁₂H₈Cl₂O₂S

Molecular weight: 287.16

CAS No. 80-07-9

RTECS No. WR3450000

B. Synonyms and Trade Names

Synonyms: benzene, 1,1'-sulfonylbis (4-chloro-); bis (p-chlorophenyl) sulfone; bis (4-chlorophenyl) sulfone; sulfone, bis (p-chlorophenyl); 1,1'-sulfonylbis(4-chlorobenzene); 4-chloro-1-(4-chlorophenylsulfonyl)benzene; 4-chlorophenyl sulfone; 4,4'-dichlorodiphenyl sulfone

Trade Names: No information available

C. Chemical and Physical Properties

Description: White powder

Melting Point: 145°-148°C (293°-298°F) [Aldrich, 1988-1989]
148°-149°C (298°-300°F) [Budavari, 1989]

Boiling Point: 250°C (482°F) @ 10 mm Hg [Aldrich, 1988-1989]

Specific Gravity: 1.293 [Sloss Industries, 1988]

Refractive Index: No data available

Solubility in Water: Insoluble in water [Sloss Industries, 1988]

Solubility in Other Solvents: Soluble in acetone (9.4 g/100 cc), olive oil (1.3 g/100 cc) [Domenjoz, 1946], hot alcohols, aromatics, slightly soluble in cold alcohols [Sloss Industries, 1988]

Reactive Chemical Hazards:

Incompatible with strong oxidizing agents [Lenga, 1988]. Emits toxic fumes of HCl gas, sulfur oxides [Sax and Lewis, 1989], carbon monoxide and carbon dioxide when heated to decomposition [Lenga, 1988]

Flammability Hazards:

- Combustible
- Flash Point: >100°C (212°F) [Sloss Industries, 1988]
- No other data available

III. PRODUCTION/USE

A. Production

1. Manufacturing Process

p,p'-Dichlorodiphenyl sulfone is prepared via a two step process. First, chlorobenzene, sulfur trioxide and thionyl chloride are reacted to form a mixture of p-chlorobenzenesulfonyl chloride and p,p-dichlorodiphenyl sulfone. Then the p-chlorobenzenesulfonyl chloride is reacted with chlorobenzene in the presence of ferric chloride to yield additional p,p-dichlorodiphenyl sulfone. p,p'-Dichlorodiphenyl sulfone prepared by this procedure is of high purity (>99%) [Garty, et al., 1974; Street, et al., 1971].

2. Producers and importers

U. S. Producers:

- Jim Walter Resources, Inc., (subsidiary of Walter Industries)
Birmingham, Alabama [SRI, 1989]
- Sloss Industries Corporation (subsidiary of Walter Industries)
Birmingham, Alabama [SRI, 1989]
- Union Carbide Corporation
Marietta, Ohio [USEPA, 1990]
- Walter Industries
Tampa, Florida [SRI, 1989]

European Producers:

- Roussel Uclaf
Neuville Sur Saone
Rhone, France [SRI, 1989]
- UCB-Ftal SA
West Vlaanderen, Belgium [SRI, 1989]

Importers:

- D&O Chemicals, Inc.
Englewood, New Jersey [Chemical Week Buyer's Guide, 1989]
- Filo Chemical Corporation
New York, New York [USEPA, 1990]

3. Volume

No production or import data were provided for p,p'-dichlorodiphenyl sulfone in the public file of the EPA TSCA inventory. In addition, no production data were available on p,p'-dichlorodiphenyl sulfone from the United States International Trade Commission's publication Synthetic Organic Chemicals for the years 1985-1988 [USITC, 1986-1989]. However, production information was available from the International Trade Commission on engineering plastics, a product group which includes polysulfones as well as acetal, polycarbonate, polyamide, polyphenylene oxide and polyphenylene sulfide polymers (see Table 1) [USITC, 1986-1989].

Table 1. U.S. Production of Engineering Plastics

<u>Year</u>	<u>Production (pounds, dry basis)</u>
1985	778,774,000
1986	765,089,000
1987	1,493,630,000
1988	1,491,228,000

4. Technical Product Composition

p,p'-Dichlorodiphenyl sulfone is available from Aldrich Chemical Company at 98% purity [Aldrich, 1988-1989] and from Sloss Industries Corporation at 99.8% purity [Sloss Industries, 1988]. The predominant impurities in p,p'-dichlorodiphenyl sulfone are p,p'-dichlorodiphenyl sulfone isomers (3,4'-dichlorodiphenyl sulfone and 2,4'-dichlorodiphenyl sulfone). The major non-isomeric impurities present in crude p,p'-dichlorodiphenyl sulfone include ortho- and para- dichlorobenzene, dichlorodiphenyl sulfide, trichlorodiphenyl sulfide and tetrachlorodiphenyl sulfide [Garty, et al., 1974].

B. Use

p,p'-Dichlorodiphenyl sulfone is used as a starting material in the production of polysulfones. Polysulfones are a family of thermoplastics which are used in a wide variety of applications because of their mechanical and electrical

properties at high temperatures (300°F-500°F) [Garty, et al., 1974; Walton, 1976]. Examples of applications for polysulfones include the following [Walton, 1976]:

- Appliances - coffee makers, humidifiers, hair dryer components, hot lather dispensers, steam iron components, microwave oven components
- Automotive parts - steering column lock switch, relay insulators, pistons
- Electronics - integrated circuit carriers, television components, capacitor film, printed circuit boards
- Medical equipment - nebulizers, dialysis components, instruments sterilizable packages

Specific polysulfones on the market include Union Carbide's "UDEL" polysulfone, 3 M's polyarylsulfone, "Astrel 360" and ICI's polyether sulfone [Walton, 1976].

IV. EXPOSURE/REGULATORY STATUS

A. Consumer Exposure

Consumers may be exposed to residual levels of p,p'-dichlorodiphenyl sulfone from polysulfone-based products [NCI, 1987b]. No information was found on the levels of p,p'-dichlorodiphenyl sulfone residues in polysulfone containing products.

B. Occupational Exposure

There are no data from the National Occupational Exposure Survey (NOES) on p,p'-dichlorodiphenyl sulfone. Workers involved in the manufacturing and processing of polysulfones are potentially exposed to this compound [NCI, 1987b].

C. Environmental Exposure

No data were found on environmental exposure to p,p'-dichlorodiphenyl sulfone.

D. Regulatory Status

- OSHA has not established a permissible exposure limit (PEL) for p,p'-dichlorodiphenyl sulfone.

E. Exposure Recommendations

- ACGIH has not recommended a threshold limit value (TLV) for p,p'-dichlorodiphenyl sulfone.
- NIOSH has not recommended a recommended exposure limit (REL) for p,p'-dichlorodiphenyl sulfone.

V. TOXICOLOGICAL EFFECTS

A. Chemical Disposition

1. Human Data

No data were found on the chemical disposition of p,p'-dichlorodiphenyl sulfone in humans.

2. Animal Data

No data were found on the chemical disposition of p,p'-dichlorodiphenyl sulfone in animals.

B. Acute

1. Human Data

No data were found on the acute effects of p,p'-dichlorodiphenyl sulfone in humans.

2. Animal Data

The acute toxicity of p,p'-dichlorodiphenyl sulfone has been described in the abstract from a Russian study. The oral LD₅₀ was found to be 5-10 g/kg in mice and 5-20 g/kg in rats (administration vehicle not specified). No other information was reported [Pis'ko, et al., 1982].

The oral LD₅₀ in mice has been reported to be 24 g/kg (administration vehicle not specified). No additional information from this Swiss study was available [Domenjuz, R., 1946].

The dermal LD₅₀ in mice has been determined to be 1000 mg/kg. No other information was available [Sloss Industries, 1988].

C. Prechronic

1. Human Data

No data were found on the prechronic effects of p,p'-dichlorodiphenyl sulfone in humans.

2. Animal Data

The prechronic effects of p,p'-dichlorodiphenyl sulfone have been described in the abstract from a Russian study. Daily administration of 2 mg of p,p'-dichlorodiphenyl sulfone to rats (strain not specified) for 6 months reportedly caused a transient increase in urinary creatine and urea. In addition, an increase in the lipid content of the liver, and an increase in hepatic alanine aminotransferase activity was observed. Blood

vessel wall permeability was found to be elevated in the kidney and the brain. Dystrophic changes, necrotic foci and focal chronic necrosis were observed in the liver and heart muscle. Hypoplasia of the lymphoid tissue in the lungs and liver and an increase in spleen reticular cells were also observed.

Daily administration of 0.2 mg/kg to rats for 6 months was found to induce fewer toxic effects. Fluctuations of inorganic phosphorus in the urine and elevated hepatic alanine aminotransferase levels were observed. Following oral administration of p,p'-dichlorodiphenyl sulfone for 6 months at a concentration of 0.02 mg/kg, no toxic effects were observed [Pis'ko, et al., 1982].

D. Chronic/Carcinogenicity

1. Human Data

No data were found on the chronic effects/carcinogenicity of p,p'-dichlorodiphenyl sulfone in humans.

2. Animal Data

No data were found on the chronic effects/carcinogenicity of p,p'-dichlorodiphenyl sulfone in animals.

E. Reproductive Effects and Teratogenicity

1. Human Data

No data were found on the reproductive and teratogenic effects of p,p'-dichlorodiphenyl sulfone on humans.

2. Animal Data

The reproductive effects of p,p'-dichlorodiphenyl sulfone have been described in the abstract from a Russian study. Daily, oral administration of this compound to pregnant rats (strain unspecified), at a concentration of 1 g/kg on days 1 through 15 of gestation was found to be embryotoxic. However, daily oral administration of p,p'-dichlorodiphenyl sulfone at a concentration of 0.5 g/kg was not observed to induce embryotoxic effects. No other data were presented [Pis'ko, et al., 1982].

F. Genetic Toxicology

1. Human Data

No data were found on the genotoxic effects of p,p'-dichlorodiphenyl sulfone in humans.

2. Prokaryotic Data

No data were found on the genotoxic effects of p,p'-dichlorodiphenyl sulfone in prokaryotic systems.

3. Eukaryotic Data

No data were found on the genotoxic effects of p,p'-dichlorodiphenyl sulfone in eukaryotic systems.

G. Other Toxicological Effects

1. Immunotoxicity

No data were found on the immunotoxic effects of p,p'-dichlorodiphenyl sulfone on animals or humans.

2. Neurotoxicity

No data were found concerning the neurotoxic effects of p,p'-dichlorodiphenyl sulfone on animals or humans.

3. Biochemical Toxicology

p,p'-Dichlorodiphenyl sulfone has been tested for its ability to oxidize hemoglobin to methemoglobin in human erythrocytes *in vitro*. This compound did not produce a substantial increase in the percentage of methemoglobin detected, relative to untreated erythrocytes [Kramer, et al., 1972].

VI. STRUCTURE ACTIVITY RELATIONSHIPS

No data were found on structure activity relationships for p,p'-dichlorodiphenyl sulfone.

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APPENDIX I, ON-LINE DATA BASES SEARCHED

	DATE OF SEARCH	TIME PERIOD
DIALOG:		
Agricola	April, 1990	1970-1990
Agris International	April, 1990	1974-1990
Aquatic Science Abstracts	April, 1990	1978-1990
Biosis Previews	April, 1990	1969-1990
Biotechnology Abstracts	April, 1990	1982-1990
CAB Abstracts	April, 1990	1984-1990
Cancerlit	April, 1990	1963-1990
Chemical Engineering Abstracts	April, 1990	1971-1990
Chemical Safety Newsbase	April, 1990	1981-1990
Compendex Plus	April, 1990	1970-1990
Embase	April, 1990	1974-1990
Enviroline	April, 1990	1970-1990
Environmental Bibliography	April, 1990	1974-1990
Federal Register	April, 1990	1977-1990
FSTA	April, 1990	1969-1990
Life Sciences Collection	April, 1990	1978-1990
Medline	April, 1990	1966-1990
Occupational Safety and Health	April, 1990	1973-1990
Pascal	April, 1990	1984-1990
Pollution Abstracts	April, 1990	1970-1990
PTS Prompt	April, 1990	1972-1990
PTS Newsletter	April, 1990	1987-1990
Scisearch	April, 1990	1974-1990
Trade and Industry Index	April, 1990	1981-1990
Trade and Industry ASAP	April, 1990	1983-1990
World Translations Index	April, 1990	1984-1990
MEAD:		
Nexis/Lexis-BNA ENV		
NLM:		
Chemline	April, 1990	
HSDB	April, 1990	
RTECS	April, 1990	
Toxline	April, 1990	1981-1990
Toxline 65	April, 1990	1965-1980
Toxlit	April, 1990	1981-1990
Toxlit 65	April, 1990	1965-1980
STN:		
CA	April, 1990	1967-1990
Chemlist	April, 1990	
Registry	April, 1990	
CSCHEM	April, 1990	

APPENDIX II. SAFETY INFORMATION

- **HANDLING AND STORAGE**

p,p'-Dichlorodiphenyl sulfone is stable under normal laboratory conditions [Sloss Industries, 1988].

- **EMERGENCY FIRST AID PROCEDURES**

Eye: First check the victim for contact lenses and remove if present. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center. Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician. If symptoms such as redness or irritation develop, immediately transport the victim to a hospital.

Skin: IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently wash affected skin areas thoroughly with soap and water. If symptoms such as redness or irritation develop, IMMEDIATELY call a physician and be prepared to transport the victim to a hospital for treatment.

Inhalation: IMMEDIATELY leave the contaminated area; take deep breaths of fresh air. If symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop, call a physician and be prepared to transport the victim to a hospital.

Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used.

Ingestion: If the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical and IMMEDIATELY call a hospital or poison control center. Be prepared to transport the victim to a hospital if advised by a physician.

If the victim is convulsing or unconscious, do not give anything by mouth, ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. IMMEDIATELY TRANSPORT THE VICTIM TO A HOSPITAL

- **PROTECTIVE EQUIPMENT**

Eye: Safety glasses

Gloves: Two pairs of dissimilar protective gloves shall be worn when handling the neat chemical, otherwise one pair. When contact with this chemical has been known to occur, change gloves

immediately.

Clothing: Minimally, a disposable laboratory suit (e.g. Tyvek®) shall be worn as specified in the most current NTP Statement of Work or NTP Health and Safety Minimum Requirements.

Respiratory Protection: A chemical cartridge respirator with a combination organic vapor and high-efficiency particulate filter cartridge.

- **EXTINGUISHANT**

Dry chemical, Carbon Dioxide or Halon Extinguisher

- **MONITORING PROCEDURES**

There is no NIOSH analytical method reported in the current literature for p,p'-dichlorodiphenyl sulfone.

- **SPILLS AND LEAKAGE**

Persons not wearing the appropriate protective equipment and clothing shall be restricted from areas of spills until cleanup has been completed. When exposure to unknown concentrations may occur, air-purifying respirators may not be used. Chemical cartridge respirators with organic vapor cartridges may not be used when airborne concentrations exceed 1000 ppm.

If p,p'-dichlorodiphenyl sulfone is spilled the following steps shall be taken:

1. In order to prevent dust formation, use moistened paper towels to clean up a solid spill. Avoid dry sweeping.
2. If a liquid solution is spilled, use vermiculite, sodium bicarbonate, sand, or paper towels to contain and absorb the spill.
3. Clean the spill area with dilute alcohol (approximately 60-70%) followed by a strong soap and warm water washing.
4. Dispose of all absorbed material as hazardous waste.

- **DECONTAMINATION OF LABORATORY EQUIPMENT**

TDMS Terminal: Whenever feasible, a protective covering (e.g., plastic wrap) shall be placed over the keyboard when in use.

General Equipment: Before removing general laboratory equipment (i.e. lab carts, portable hoods and balances) from animal dosing rooms and/or chemical preparation areas, a decontamination process shall be conducted in addition to

routine housekeeping procedures.

• **WASTE MANAGEMENT AND DISPOSAL PROCEDURES**

Waste Management: If an inhalation study is to be conducted, all exhaust air from the inhalation chamber must be cleaned with appropriate air cleaning devices unless the laboratory has informed local and state air pollution regulatory agencies of both the laboratory's operating practices and the potential hazards of the chemicals in use. Compliance with all federal, state and local air pollution laws and regulations is required. A specific air cleaning system design must consider the specific conditions of the laboratory (eg., air flow rates and volumes, mixing of exhaust streams, size of inhalation chamber, etc.) and the dosing regimen selected. Air cleaning systems designs must be described by the laboratory and approved by the NTP Office of Laboratory Health and Safety.

Waste Disposal: Securely package and label, in double bags, all waste material. All potentially contaminated material (i.e., carcasses, bedding, disposable cages, labware) shall be disposed of by incineration in a manner consistent with federal (EPA), state, and local regulations or disposed of in a licensed hazardous waste landfill.