Bisphenol A Alternatives in Thermal Paper

Chapter 4

Hazard Evaluation of Bisphenol A (BPA) and Alternatives

FINAL REPORT

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List of Acronyms and Abbreviations

AIM	Analog Identification Methodology
ACR	Acute to Chronic Ratio
ADME	Absorption, Distribution, Metabolism, and Excretion
AIST	Advanced Industrial Science and Technology
ASTM	American Society for Testing and Materials
BAF	Bioaccumulation Factor
BCF	Bioconcentration Factor
BMD	Benchmark Dose
BMDL	Benchmark Dose Lower-confidence Limit
BPA	Bisphenol A
BPS	Bisphenol S
BOD	Biochemical Oxygen Demand
CASRN	Chemical Abstracts Service Registry Number
CDC	Centers for Disease Control and Prevention
CHO	Chinese Hamster Ovary Cells
ChV	Chronic Value
CPSC	Consumer Product Safety Commission
CVL	Crystal Violet Lactone
DfE	Design for the Environment
DOC	Dissolved Organic Carbon
dpi	Dots per inch
EC_{50}	Half Maximal Effective Concentration
ECHA	European Chemicals Agency
ECOSAR	Ecological Structure Activity Relationships
EDSP	Endocrine Disruptor Screening Program
EEC	European Economic Community
Eh	Redox potential
EKG	Electrocardiogram
EPA	U.S. Environmental Protection Agency
EPCRA	Emergency Planning and Community Right-to-Know Act
EPI	Estimations Program Interface
ERMA	Environmental Risk Management Authority
EU	European Union
EWG	Environmental Working Group
FDA	U.S. Food and Drug Administration
GHS	Globally Harmonized System of Classification and Labeling of Chemicals
GLP	Good Laboratory Practice
HGPRT	Hypoxanthine-Guanine Phosphoribosyl-Transferase
HIPAA	Health Insurance Portability and Accountability Act of 1996
HPLC	High Performance Liquid Chromatography
HPV	High Production Volume
HSDB	Hazardous Substances Data Bank
IARC	International Agency for Research on Cancer
IR	Infrared

IRIS	Integrated Risk Information System
IUCLID	International Uniform Chemical Information Database
K_{oc}	Soil adsorption coefficient
K_{ow}	Octanol/water partition coefficient
LC_{50}	Median Lethal Concentration
LCA	Life-cycle Assessment
LD_{50}	Median Lethal Dose
LD	Lactation Day
LFL	Lower Limit of Flammability
LOAEL	Lowest Observed Adverse Effect Level
LOEC	Lowest Observed Effective Concentration
MDI	Mean Daily Intake
MF	Molecular Formula
MITI	Japanese Ministry of International Trade and Industry
MW	Molecular Weight
MSDS	Material Safety Data Sheet
NAICS	North American Industry Classification System
NES	No Effects at Saturation
NGO	Non-Governmental Organization
NHANES	National Health and Nutrition Examination Survey
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NIOSH	National Institute for Occupational Safety and Health
NIR	Near Infrared
NOAEL	No Observed Adverse Effect Level
NOEC	No Observed Effect Concentration
NOEL	No Observed Effect Level
NTP	National Toxicology Program
OECD	Organisation for Economic Cooperation and Development
OPPT	Office of Pollution Prevention and Toxics
P2	Pollution Prevention
PBB	Poly-Brominated Biphenyls
PBDE	Polybrominated Diphenyl Ether
PBT Profiler	Persistent, Bioaccumulative, and Toxic (PBT) Chemical Profiler
PMN	Premanufacture Notice
PNEC	Predicted No Effect Concentration
POS	Point-of-sale
ppb	parts per billion
ppm	parts per million
PVC	Polyvinyl Chloride
REACH	**R**egistration, **E**valuation, **A**uthorisation and Restriction of **Ch**emical substances
RoHS	Restriction of Hazardous Substances
SAR	Structure Activity Relationship
SCAS	Semi-Continuous Activated Sludge
SF	Sustainable Futures
SMILES	Simplified Molecular-Input Line-Entry System
SPARC	Sparc Performs Automated Reasoning in Chemistry

TDI	Total Daily Intake
TOC	Total Organic Carbon
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
QSAR	Quantitative Structure Activity Relationships
UFL	Upper Limit of Flammability
USGS	U.S. Geological Survey
WHO	World Health Organization
WWTP	Wastewater Treatment Plant

4. Hazard Evaluation of Bisphenol A (BPA) and Alternatives

This chapter summarizes the toxicological and environmental hazards of bisphenol A (BPA) and each of the 19 alternative chemicals that were identified as potential functional substitutes for BPA. Evaluations of chemical formulations may also require the consideration of associated substances (e.g., starting materials, byproducts, and impurities) if their presence is specifically required to allow that alternative to fully function in the assigned role. In general, associated substances were assumed to remain unchanged in this assessment, but may need to be considered in the selection of an alternative. Otherwise, pure substances were analyzed in this assessment. Users of the hazard information in this alternatives assessment should be aware of the purity of the trade product they purchase, as the presence of impurities may alter the assessment of the alternative. In general, associated substances were assumed to remain unchanged in this assessment, but may need to be considered in the selection of an alternative. This report is a hazard assessment, not a full risk assessment. Hazard assessment as a risk management tool is discussed in more detail in Section 1.3.

Toxicological and environmental endpoints included in the hazard profiles are discussed in Section 4.1, along with the criteria used to evaluate each hazard endpoint. Data sources and the review methodology are described in Section 4.2. The report then offers a detailed description of the utility of physical/chemical properties in understanding hazard in Section 4.3, and the process of evaluating human health and environmental endpoints in Sections 4.4 and 4.5, respectively. A discussion of the evaluation of endocrine activity is included in Section 4.6. The characteristics of each chemical included in the alternatives assessment are summarized in the comparative hazard summary table in Section 4.7. Lastly, the collected data and hazard profile of each chemical are presented in Section 4.8.

4.1 Toxicological and Environmental Endpoints

The assessment of endpoints with the intent to create hazard profiles for a Design for the Environment (DfE) Alternatives Assessment follows the guidance of the *DfE Alternatives Assessment Criteria for Hazard Evaluation* (U.S. EPA 2011b). The definitions for each endpoint evaluated following these criteria are outlined in Section 4.1.1 and the criteria by which these endpoints are evaluated are outlined in Section 4.1.2. Lastly, there are endpoints that DfE characterizes but does not assign criteria, which are summarized in Section 4.1.3.

4.1.1 Definitions of Each Endpoint Evaluated Against Criteria

Hazard designations for each chemical discussed in this report were made by direct comparison of the experimental or estimated data to the *DfE Alternatives Assessment Criteria for Hazard Evaluation* (U.S EPA 2011b). Table 4-1 provides brief definitions of human health toxicity, environmental toxicity, and environmental fate endpoints.

Table 4-1: Definitions of Toxicological and Environmental Endpoints for Hazard Assessment

Endpoint Category	Endpoint	Definition
Human Health Effects	Acute Mammalian Toxicity	Adverse effects occurring following oral or dermal administration of a single dose of a substance, or multiple doses given within 24 hours, or an inhalation exposure of 4 hours.
	Carcinogenicity	Capability of a substance to increase the incidence of malignant neoplasms, reduce their latency, or increase their severity or multiplicity.
	Mutagenicity/Genotoxicity	Mutagenicity – The ability of an agent to induce permanent, transmissible changes in the amount, chemical properties, or structure of the genetic material. These changes may involve a single gene or gene segment, a block of genes, parts of chromosomes, or whole chromosomes. Mutagenicity differs from genotoxicity in that the change in the former case is transmissible to subsequent cell generations. Genotoxicity – The ability of an agent or process to alter the structure, information content, or segregation of DNA, including those which cause DNA damage by interfering with normal replication process, or which in a non-physiological manner (temporarily) alter its replication.
	Reproductive Toxicity	The occurrence of biologically adverse effects on the reproductive systems of females or males that may result from exposure to environmental agents. The toxicity may be expressed as alterations to the female or male reproductive organs, the related endocrine system, or pregnancy outcomes. The manifestation of such toxicity may include, but is not limited to adverse effects on onset of puberty, gamete production and transport, reproductive cycle normality, sexual behavior, fertility, gestation, parturition, lactation, developmental toxicity, premature reproductive senescence, or modifications in other functions that were dependent on the integrity of the reproductive systems.
	Developmental Toxicity	Adverse effects in the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the lifespan of the organism. The major manifestations of developmental toxicity include: (1) death of the developing organism, (2) structural abnormality, (3) altered growth, and (4) functional deficiency.
	Neurotoxicity	An adverse change in the structure or function of the central and/or peripheral nervous system following exposure to a chemical, physical, or biological agent.

Endpoint Category	Endpoint	Definition
	Repeated Dose Toxicity	Adverse effects (immediate or delayed) that impair normal physiological function (reversible and irreversible) of specific target organs or biological systems following repeated exposure to a chemical substance by any route relevant to humans. Adverse effects include biologically significant changes in body and organ weights, changes that affect the function or morphology of tissues and organs (gross and microscopic), mortality, and changes in biochemistry, urinalysis, and hematology parameters that are relevant for human health; may also include immunological and neurological effects.
	Respiratory Sensitization	Hypersensitivity of the airways following inhalation of a substance.
	Skin Sensitization	A cell-mediated or antibody-mediated allergic response characterized by the presence of inflammation that may result in cell death, following an initial induction exposure to the same chemical substance, i.e., skin allergy.
	Eye Irritation/Corrosivity	Irritation or corrosion to the eye following the application of a test substance.
	Skin Irritation/Corrosion	Skin irritation – Reversible damage to the skin following the application of a test substance for up to 4 hours. Skin corrosion – Irreversible damage to the skin namely, visible necrosis through the epidermis and into the dermis following the application of a test substance for up to 4 hours.
Environmental Toxicity	Environmental toxicity refers to adverse effects observed in living organisms that typically inhabit the wild; this assessment is focused on effects in three groups of surrogate aquatic organisms (freshwater fish, invertebrates, algae).	
	Aquatic Toxicity (Acute)	The property of a substance to be injurious to an organism in a short-term, aquatic exposure to that substance.
	Aquatic Toxicity (Chronic)	The property of a substance to cause adverse effects to aquatic organisms during aquatic exposures which were determined in relation to the life-cycle of the organism.
Environmental Fate	Environmental Persistence	The length of time the chemical exists in the environment, expressed as a half-life, before it is destroyed (i.e., transformed) by natural or chemical processes. For alternatives assessments, the amount of time for complete assimilation (ultimate removal) is preferred over the initial step in the transformation (primary removal).
	Bioaccumulation	The process in which a chemical substance is absorbed in an organism by all routes of exposure as occurs in the natural environment (e.g., dietary and ambient environment sources). Bioaccumulation is the net result of competing processes of chemical uptake into the organism at the respiratory surface and from the diet and chemical elimination from the organism including respiratory exchange, fecal egestion, metabolic biotransformation of the parent compound, and growth dilution.

The hazard profile for each chemical contains endpoint-specific summary statements (see Section 4.8). For each of the endpoints listed in Table 4-1, these summary statements provide the hazard designation, the type of data (experimental or estimated), and the rationale. The endpoint summaries may also include explanatory comments, a discussion of confounding factors, or an indication of the confidence in the data to help put the results in perspective.

4.1.2 Criteria

Table 4-2 summarizes the criteria that were used by the U.S. Environmental Protection Agency (EPA) DfE Program to interpret the data presented in the hazard evaluations. The *DfE Alternatives Assessment Criteria for Hazard Evaluation* underwent internal and public review and comment, and were finalized in 2011 (U.S. EPA 2011b). A hazard designation for each human health endpoint was not given for each route of exposure but rather was based on the exposure route with the highest hazard designation. Data may have been available for some or all relevant routes of exposure.

The details as to how each endpoint was evaluated are described below and in the DfE full criteria document, *DfE Alternatives Assessment Criteria for Hazard Evaluation*, available at: http://www.epa.gov/dfe/alternatives_assessment_criteria_for_hazard_eval.pdf.

Table 4-2: Criteria Used to Assign Hazard Designations

Endpoint	Very High	High	Moderate	Low	Very Low
Human Health Effects					
Acute mammalian toxicity					
Oral median lethal dose (LD_{50}) (mg/kg)	≤50	>50–300	>300–2000	>2000	–
Dermal LD_{50} (mg/kg)	≤200	>200–1000	>1000–2000	>2000	–
Inhalation median lethal concentration (LC_{50}) - vapor/gas (mg/L)	≤2	>2–10	>10–20	>20	–
Inhalation LC_{50} - dust/mist/ fume (mg/L)	≤0.5	>0.5–1.0	>1–5	>5	–
Carcinogenicity					
	Known or presumed human carcinogen (equivalent to Globally Harmonized System of Classification and Labeling of Chemicals (GHS)	Suspected human carcinogen (equivalent to GHS Category 2)	Limited or marginal evidence of carcinogenicity in animals (and inadequate evidence in humans)	Negative studies or robust mechanism-based structure activity relationships (SAR) (as described above)	–

Endpoint	Very High	High	Moderate	Low	Very Low
	Categories 1A and 1B)[1]				
Mutagenicity/Genotoxicity					
Germ cell mutagenicity	GHS Category 1A or 1B: Substances known to induce heritable mutations or to be regarded as if they induce heritable mutations in the germ cells of humans	GHS Category 2: Substances which cause concern for humans owing to the possibility that they may induce heritable mutations in the germ cells of humans OR	Evidence of mutagenicity supported by positive results in *in vitro* OR *in vivo* somatic cells of humans or animals	Negative for chromosomal aberrations and gene mutations, or no structural alerts	–
Mutagenicity and genotoxicity in somatic cells		Evidence of mutagenicity supported by positive results in *in vitro* AND *in vivo* somatic cells and/or germ cells of humans or animals			
Reproductive toxicity					
Oral (mg/kg/day)	–	<50	50–250	>250-1000	>1000
Dermal (mg/kg/day)	–	<100	100–500	>500-2000	>2000
Inhalation - vapor, gas (mg/L/day)	–	<1	1–2.5	>2.5-20	>20
Inhalation - dust/mist/fume (mg/L/day)	–	<0.1	0.1–0.5	>0.5-5	>5
Developmental toxicity					
Oral (mg/kg/day)	–	<50	50–250	>250-1000	>1000
Dermal (mg/kg/day)	–	<100	100–500	>500-2000	>2000
Inhalation - vapor, gas (mg/L/day)	–	<1	1–2.5	>2.5-20	>20
Inhalation - dust/mist/fume (mg/L/day)	–	<0.1	0.1–0.5	>0.5-5	>5
Neurotoxicity					
Oral (mg/kg/day)	–	<10	10–100	>100	–
Dermal (mg/kg/day)	–	<20	20–200	>200	–
Inhalation - vapor, gas (mg/L/day)	–	<0.2	0.2–1.0	>1.0	–

[1] The United Nations' GHS document can be found at http://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs_rev04/English/ST-SG-AC10-30-Rev4e.pdf.

Endpoint	Very High	High	Moderate	Low	Very Low
Inhalation - dust/mist/fume (mg/L/day)	–	<0.02	0.02–0.2	>0.2	–
Repeated-dose toxicity[1]					
Oral (mg/kg/day)	–	<10	10–100	>100	–
Dermal (mg/kg/day)	–	<20	20–200	>200	–
Inhalation - vapor, gas (mg/L/day)	–	<0.2	0.2–1.0	>1.0	–
Inhalation - dust/mist/fume (mg/L/day)	–	<0.02	0.02–0.2	>0.2	–
Sensitization					
Skin sensitization	–	High frequency of sensitization in humans and/or high potency in animals (GHS Category 1A)	Low to moderate frequency of sensitization in human and/or low to moderate potency in animals (GHS Category 1B)	Adequate data available and not GHS Category 1A or 1B	–
Respiratory sensitization	–	Occurrence in humans or evidence of sensitization in humans based on animal or other tests (equivalent to GHS Category 1A and 1B)	Limited evidence including the presence of structural alerts	Adequate data available indicating lack of respiratory sensitization	–
Irritation/corrosivity					
Eye irritation/corrosivity	Irritation persists for >21 days or corrosive	Clearing in 8–21 days, severely irritating	Clearing in ≤7 days, moderately irritating	Clearing in <24 hours, mildly irritating	Not irritating
Skin irritation/corrosivity	Corrosive	Severe irritation at 72 hours	Moderate irritation at 72 hours	Mild or slight irritation at 72 hours	Not irritating
Endocrine activity					
Endocrine activity	For this endpoint, High/Moderate/Low etc. characterizations will not apply. A qualitative assessment of available data will be prepared.				

Endpoint	Very High	High	Moderate	Low	Very Low
Environmental Toxicity and Fate					
Aquatic toxicity					
Acute aquatic toxicity - LC_{50} or Half Maximal Effective Concentration (EC_{50}) (mg/L)	<1.0	1–10	>10–100	>100 or No Effects at Saturation (NES)	–
Chronic aquatic toxicity – Lowest Observed Effect Concentration (LOEC) or Chronic Value (ChV) (mg/L)	<0.1	0.1–1	>1–10	>10 or NES	–
Environmental Persistence					
Persistence in water, soil, or sediment	Half-life >180 days or recalcitrant	Half-life of 60–180 days	Half-life <60 but ≥16 days	Half-life <16 days OR passes Ready Biodegradability test not including the 10-day window. No degradation products of concern	Passes Ready Biodegradability test with 10-day window. No degradation products of concern.
Persistence in air (half-life days)	For this endpoint, High/Moderate/Low etc. characterizations will not apply. A qualitative assessment of available data will be prepared.				
Bioaccumulation					
Bioconcentration Factor (BCF)/Bioaccumulation Factor (BAF)	>5000	5000–1000	<1000–100	<100	–
Log BCF/BAF	>3.7	3.7–3	<3-2	<2	–

[1] Criteria values are to be applied to 90-day repeated dose studies. These values are tripled for chemicals evaluated in 28-day studies or similarly modified for studies of other durations.
Very High or Very Low designations (if an option for a given endpoint in Table 4-2) were assigned only when there were experimental data available for the chemical under evaluation. In addition, the experimental data must have been collected from a well conducted study specifically designed to evaluate the endpoint under review. If the endpoint was estimated using experimental data from a close structural analog, professional judgment, or a computerized model, then the next-level designation was assigned (i.e., High or Low).

4.1.3 Endpoints Characterized but Not Evaluated

Several additional endpoints were characterized, but not evaluated against hazard criteria. This is because the endpoints lacked a clear consensus concerning the evaluation criteria (endocrine activity), data and expert judgment were limited for industrial chemicals (persistence in air, terrestrial ecotoxicology), or the information was valuable for interpretation of other toxicity and fate endpoints (including toxicokinetics and transport in the environment).

Table 4-3: Definitions of Endpoints and Information Characterized but Not Evaluated Against Hazard Criteria

Toxicological Endpoint	Definition
Toxicokinetics	The determination and quantification of the time course of absorption, distribution, metabolism, and excretion (ADME) of chemicals (sometimes referred to as pharmacokinetics).
Biomonitoring Information	The measured concentration of a chemical in biological tissues where the analysis samples were obtained from a natural or non-experimental setting.
Environmental Transport	The potential movement of a chemical, after it is released to the environment, within and between each of the environmental compartments (air, water, soil, and sediment). Presented as a qualitative summary in the alternatives assessment based on physical/chemical properties, environmental fate parameters, and simple volatilization models. Also includes distribution in the environment as estimated from a fugacity model.[2]
Persistence in Air	The half-life for destructive removal of a chemical substance in the atmosphere. The primary chemical reactions considered for atmospheric persistence include hydrolysis, direct photolysis, and the gas phase reaction with hydroxyl radicals, ozone, or nitrate radicals. Results are used as input into the environmental transport models.
Immunotoxicology	Adverse effects on the normal structure or function of the immune system caused by chemical substances (e.g., gross and microscopic changes to immune system organs, suppression of immunological response, autoimmunity, hypersensitivity, inflammation, and disruption of immunological mechanistic pathways).
Terrestrial Ecotoxicology	Reported experimental values from guideline and nonguideline studies on adverse effects on the terrestrial environment. Studies on soil, plants, birds, mammals, invertebrates were also included.
Endocrine Activity	A change in endocrine homeostasis caused by a chemical and/or other stressor.

4.2 Data Sources and Assessment Methodology

This section explains how data were collected (Section 4.2.1), prioritized, and reviewed (Section 4.2.2) for use in the development of hazard profiles. High-quality experimental studies lead to a thorough understanding of behavior and effects of the chemical in the environment and in living organisms. Analog approaches and SAR-based estimation methods are also useful tools and are discussed throughout this section. Information on how the evaluation of polymers differs from the evaluation of discrete chemicals is presented in Section 4.2.3.

4.2.1 Identifying and Reviewing Measured Data

For each chemical assessed, data were collected in a manner consistent with the *High Production Volume (HPV) Chemical Challenge Program Guidance* on searching for existing chemical information (U.S. EPA 1999b). This process resulted in a comprehensive search of the literature for available experimental data. For chemicals well characterized by experimental studies, this usually resulted in the collection of recent high-quality reviews or peer-reviewed risk assessments. In some cases, these reviews and risk assessments were supplemented by primary

[2] A fugacity model predicts partitioning of chemicals among air, soil, sediment, and water under steady state conditions for a default model "environment" (U.S. EPA, 2011e).

searches of scientific literature published after these secondary sources were released, which is explained in greater detail below. For chemicals that are not as well characterized, that is, where these secondary sources were not available or lacked relevant or adequate data, a comprehensive search of the primary scientific literature was done. Subsequently, these searches led to the collection and review of articles from the scientific literature, industrial submissions, encyclopedic sources, and government reports. In addition, data presented in EPA public and confidential databases (e.g., Integrated Risk Information System (IRIS)) were obtained for this project. Generally, foreign language (non-English) reports were not used unless they provided information that was not available from other sources.

Chemical assessments were performed by first searching for experimental data for all endpoints in Table 4-1. For most alternatives assessed, high-quality secondary sources were not available; therefore, a comprehensive search of the primary literature was performed to identify experimental data. In some cases, confidential studies submitted to EPA by chemical manufacturers were also available to support hazard designations. For those chemicals that were expected to form stable metabolites, searches were performed to identify relevant fate and toxicity information for the metabolite or degradation product.

Well-Studied Chemicals – Literature Search Strategy

As mentioned above, for chemicals that have been well characterized (limited to BPA in this DfE Alternatives Assessment), the literature review began with recent, high-quality, authoritative secondary sources, such as in the case of BPA, the 2008 National Toxicology Program (NTP) expert panel review (National Toxicology Program-Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) 2008) and the 2011 Food and Agricultural Organization of the United Nations/World Health Organization expert panel review (FAO/WHO 2011). Using high-quality secondary sources maximized available resources and eliminated potential duplication of effort. However, more than one secondary source was typically used to verify reported values, which also reduced the potential for presenting a value that was transcribed incorrectly from the scientific literature. Although other sources might also contain the same experimental value for an endpoint, effort was not focused on building a comprehensive list of these references, as it would not have enhanced the ability to reach a conclusion in the assessment. In some cases, primary studies were also evaluated to supplement the secondary sources. When data for a selected endpoint could not be located in a secondary source for an otherwise well-studied chemical, the primary literature was searched by endpoint and experimental studies were assessed for relevant information.

Making Predictions in the Absence of Measured Data

In the absence of primary or secondary data, hazard designations were based on (1) Quantitative Structure Activity Relationships (QSAR)-based estimations from the EPA New Chemical Program's predictive methods; (2) analog data; (3) category-based assignments from the EPA Chemical Categories document; and (4) expert judgment by EPA subject matter experts.

For chemicals that lacked experimental information, QSAR assessments were made using either EPA's Estimation Programs Interface (EPISuite™) for physical/chemical property and environmental fate endpoints or EPA's Ecological Structure Activity Relationships (ECOSAR™) QSARs for ecotoxicity. For the cancer endpoint, estimates were also obtained from EPA's OncoLogic expert system. These estimation methods have been automated, and are

available for free (http://www.epa.gov/oppt/sf/tools/methods.htm). Often analog data were used to support predictions from models. These approaches were described in the EPA Pollution Prevention (P2) Framework (U.S. EPA 2005b) and Sustainable Futures (SF) program (U.S. EPA 2011e).

For some physical/chemical properties that could not be estimated using EPISuite™, such as acid/base dissociation constants, other available methods (e.g., the Sparc Performs Automated Reasoning in Chemistry (SPARC) website for dissociation constants) were used. All estimation methods employed were limited to those freely available in the public domain.

The methodology and procedures used to assess polymers are described in Section 4.2.3. In addition, the endpoints for impurities or oligomers with a molecular weight (MW) >1,000 daltons were estimated using professional judgment and the results assessed for inclusion in the overall hazard designation. This process is described, as appropriate, under the corresponding endpoints appearing in Section 4.3.

When QSAR models were not available, professional judgment was used to identify hazards for similar chemicals using the guidance from EPA's New Chemicals Categories (U.S. EPA 2010). This document groups substances that have similar chemical structure and toxicological properties into categories based on EPA's experience evaluating thousands of chemicals under the Toxic Substances Control Act (TSCA) New Chemicals Program. The categories identify substances that share chemical and toxicological properties and possess potential health or environmental concerns. In the absence of an identified category, analogs for which experimental data are available were identified using EPA's Analog Identification Methodology (AIM) or by substructure searches of confidential EPA databases (U.S. EPA 2012a). If a hazard designation was still not available, the expert judgment of scientists from EPA's New Chemical Program would provide an assessment of the physical/chemical properties, environmental fate, aquatic toxicity, and human health endpoints to fill remaining data gaps.

4.2.2 Hierarchy of Data Adequacy

Once the studies were obtained, they were evaluated to establish whether the hazard data were of sufficient quality to meet the needs of the assessment process. The adequacy and quality of the studies identified in the literature review are described in the Data Quality field of the chemical assessments presented in Section 4.8. The tiered approach described below represents a general preferred data hierarchy, but the evaluation of toxicological data also requires flexibility based on expert judgment.

1. One or more studies conducted in a manner consistent with established testing guidelines
2. Experimentally valid but nonguideline studies (i.e., do not follow established testing guidelines)
3. Reported data do not have supporting experimental details
4. Estimated data using SAR methods or professional judgment based on an analog approach
5. Expert judgment based on mechanistic and structural considerations

In general, data were considered adequate to characterize an endpoint if they were obtained using the techniques identified in the HPV data adequacy guidelines (U.S. EPA 1999b). Studies

performed according to Harmonized EPA or Organisation for Economic Cooperation and Development (OECD) guidelines were reviewed to confirm that the studies followed all required steps.

Experimental studies published in the open literature were reviewed for their scientific rigor and were also compared and contrasted to guideline studies to identify potential problems arising from differences in the experimental design. Data from adequate, well-performed, experimental studies were used to assign hazard designations in preference to those lacking in sufficient experimental detail. When multiple adequate studies were available for a given endpoint, any discrepancies that were identified within the set of data were examined further and addressed using a weight-of-evidence approach that was described in the data entry to characterize the endpoint whenever possible.

When available, experimental data from guideline or well-performed experimental studies were generally preferred (Items 1 and 2 in the hierarchy list). Information from secondary sources such as Material Safety Data Sheets (MSDS) or online databases (such as the National Library of Medicine's Hazardous Substances Data Bank (HSDB)) (Item 3 in the hierarchy list) was considered appropriate for some endpoints when it included numerical values for effect levels that could be compared to the evaluation criteria.

4.2.3 Assessment of Oligomeric Mixtures

In this alternatives assessment, there are two chemicals that were mixtures of low molecular weight (MW) oligomers comprised of two or three repeating units. For these materials, all of the oligomers anticipated to be present in the mixture have MW of less than 1,000 daltons. The hazard assessment evaluated all oligomers present. From all the oligomers, the higher concern material was used to assign the hazard designation. This process is essentially identical to the evaluation of the hazards associated with impurities or byproducts present in discrete chemical products. As a result, the alternatives assessment process determined the amount of oligomers and unchanged monomers (starting materials) present and considered their potential hazards in the alternatives designation.

4.3 Importance of Physical and Chemical Properties, Environmental Transport, and Biodegradation

Physical/chemical properties provide basic information on the characteristics of a chemical substance and were used throughout the alternatives assessment process to inform expert judgment and as inputs into predictive models. These endpoints provide information required to assess potential environmental release, exposure, and partitioning as well as insight into the potential for adverse toxicological effects. The physical/chemical properties are provided in the individual chemical hazard profiles presented in Section 4.8. For information on how key physical/chemical properties of alternatives can be used to address the potential for human and environmental exposure, please refer to Section 5.1.6. Descriptions of relevant physical/chemical properties and how they contribute to the hazard assessments are presented below.

Molecular Weight (MW)

MW informs how a chemical behaves in a physical or biological system, including bioavailability and environmental fate. In general, but not strictly, larger compounds tend to be

less mobile in biological and environmental systems. Their large size restricts their transport through biological membranes and lowers their vapor pressure. Oligomers evaluated in this alternatives assessment are mixtures that contain a distribution of components and they may not have a unique MW (see Section 4.2.3). To account for variation in these mixtures, the MW of a representative structure for each oligomer or mixture component was evaluated for this alternatives assessment. Selection of this representative structure is based on expert judgment on how the oligomer is produced.

Melting Point and Boiling Point

These two properties provide an indication of the physical state of the material at ambient temperature. Chemicals with a melting point more than 25°C were assessed as a solid. Those with a melting point less than 25°C and a boiling point more than 25°C were assessed as a liquid and those with a boiling point less than 25°C were assessed as a gas. The physical state was used throughout the assessment, such as in the determination of potential routes of human and environmental exposure, as described in Section 5.1. The melting and boiling points were also useful in determining the potential environmental fate, ecotoxicity, and human health hazards of a chemical. For example, organic compounds with high melting points generally have low water solubility and low rates of dissolution. These properties influence a material's bioavailability and were therefore taken into account in both the assessment process and the evaluation of experimental studies. Similarly, chemicals with a low melting point also have a higher potential to be absorbed through the skin, gastrointestinal tract, and lungs.

In the absence of experimental data, the melting point value was not reported and no estimations were performed. If a chemical decomposes before it melts, this information was included in the assessment. For boiling point, the maximum value reported in the assessment was 300°C for high boiling materials (U.S. EPA 1999b). Melting points for polymers and/or oligomers were not reported as these materials typically reach a softening point and do not undergo the phase change associated with melting (i.e., solid to liquid).

Vapor Pressure

Vapor pressure is useful in determining the potential for a chemical substance to volatilize to the atmosphere from dry surfaces, from storage containers, or during mixing, transfer, or loading/unloading operations (see Section 5.2). In the assessment process, chemicals with a vapor pressure less than $1x10^{-6}$ mm Hg have a low potential for inhalation exposure resulting from gases or vapors. Vapor pressure is also useful for determining the potential environmental fate of a substance. Substances with a vapor pressure more than $1x10^{-4}$ mm Hg generally exist in the gas phase in the atmosphere. Substances with a vapor pressure between $1x10^{-4}$ and $1x10^{-8}$ mm Hg exist as a gas/particulate mixture. Substances with a vapor pressure less than $1x10^{-8}$ mm Hg exist as a particulate. The potential atmospheric degradation processes described below in the Reactivity section generally occur when a chemical exists in the gas phase. Gases in the atmosphere also have the potential to travel long distances from their original point of release. Materials in the liquid or solid (particulate) phases in the atmosphere generally undergo deposition onto the Earth's surface.

A maximum vapor pressure of $1x10^{-8}$ mm Hg was assigned for chemicals without experimental data or for those substances that were anticipated by professional judgment to be nonvolatile (U.S. EPA 1999b).

Water Solubility

The water solubility of a chemical provides an indication of its distribution between environmental media, potential for environmental exposure through release to aquatic compartments, and potential for human exposure through ingestion of drinking water. Water solubility was also used extensively to determine potential human health and ecotoxicity hazards. In general, chemicals with water solubility less than $1x10^{-5}$ g/L indicate a lower concern for both the expression of adverse effects, and potential aquatic and general population exposure due to their low bioavailability. However, chemicals with a low bioavailability also tend to be more environmentally persistent. Low bioavailability is different than no bioavailability, and the two should not be used interchangeably.

Within the context of this alternatives assessment, the following descriptors were used according to ranges of water solubility values: >10,000 mg/L represents very soluble; 1,000–10,000 mg/L represents soluble; 100–1,000 mg/L represents moderately soluble, 1–100 mg/L represents slightly soluble, and <1 mg/L represents insoluble, noting that these guidelines were not followed consistently within the scientific literature (U.S. EPA 2011e). Chemicals with higher water solubility were more likely to be transported into groundwater with runoff during storm events, be absorbed through the gastrointestinal tract or lungs, partition to aquatic compartments, undergo atmospheric removal by rain washout, and possess a greater potential for human exposure through the ingestion of contaminated drinking water. Chemicals with lower water solubility are generally more persistent and have a greater potential to bioconcentrate.

The water solubility of a substance was also used to evaluate the quality of experimental aquatic toxicity and oral exposure human health studies, as well as the reliability of aquatic toxicity estimates. If the water solubility of a substance was lower than the reported exposure level in these experiments, then the study was likely to be regarded as inadequate due to potentially confounding factors arising from the presence of undissolved material. For aquatic toxicity estimates obtained using SARs, when the estimated toxicity was higher than a chemical's water solubility (i.e., the estimated concentration in water at which adverse effects appear cannot be reached because it was above the material's water solubility), the chemical was described as having no effects at saturation (NES). An NES designation is equivalent to a low ecotoxicity hazard designation for that endpoint.

While assessing the water solubility of a chemical substance, its potential to form a dispersion in an aqueous solution was also considered. Ideally, a chemical's potential to disperse would be obtained from the scientific literature. In the absence of experimental data, dispersability can be determined from chemical structure and/or comparison to closely related analogs. There are two general structural characteristics that lead to the formation of dispersions in water: (1) chemicals that have both a hydrophilic (polar) head and a hydrophobic (nonpolar) tail (e.g., surfactants), and (2) molecules that have a large number of repeating polar functional groups (e.g., polyethylene oxide).

The potential for a chemical to form a dispersion influences potential exposure, environmental fate, and toxicity. Dispersible chemicals have greater potential for human and environmental exposure, leachability, and aquatic toxicity than what might be anticipated based on the material's water solubility alone.

Chemicals without experimental data or chemicals that were anticipated by professional judgment to be sufficiently insoluble and thus were not bioavailable were assigned a water solubility maximum value of $1x10^{-6}$ g/L (U.S. EPA 2011e). A water solubility of $1x10^{-3}$ mg/L is the default value used for discrete organics as well as nonionic polymers with a MW >1,000 daltons. According to information contained in the literature concerning polymer assessment and the SF Polymer Assessment guidance assignment this is consistent with an analysis of the chemicals used in the development of the water solubility estimation program in EPA's EPISuite™ software (Boethling and Nabholz 1997; U.S. EPA 2010). The training set for this model included 1,450 chemicals with a MW range 27-628 daltons, and experimental water solubility values ranging from miscible to $4x10^{-7}$ mg/L (Meylan, Howard et al. 1996; U.S. EPA 2011g). Given that water solubility decreases with MW, a default value of $1x10^{-3}$ mg/L is consistent with the limited bioavailability expected for materials with a MW >1,000 daltons. Although no BPA alternatives had a MW >1,000, there are two compounds that may contain small amounts of higher MW oligomeric materials or impurities that were evaluated using a water solubility suggestive of limited bioavailability.

Octanol/Water Partition Coefficient (Kow)

The octanol/water partition coefficient, commonly expressed as its log value (i.e., log K_{ow}) is one of the most useful properties for performing a hazard assessment. The log K_{ow} indicates the partitioning of a chemical between octanol and water, where octanol is used to mimic fat and other hydrophobic components of biological systems. Chemicals with a log K_{ow} less than 1 are highly soluble in water (hydrophilic), while those with a log K_{ow} more than 4 are not very soluble in water (hydrophobic). A log K_{ow} more than 8 indicates that the chemical is not readily bioavailable and is essentially insoluble in water. In addition, a log K_{ow} value greater than approximately 8 may be difficult to obtain experimentally.

The log K_{ow} can be used as a surrogate for the water solubility in a hazard assessment and is frequently used to estimate the water solubility if an experimental value is not available. The log K_{ow} can also be used to estimate other properties important to the assessment, including bioconcentration and soil adsorption, and is a required input for SAR models used to estimate ecotoxicity values.

For chemicals that are not within the domain of EPISuite™ or that were expected to be insoluble in water (WS <$1x10^{-6}$ g/L), a minimum value of 10 was assigned for the log K_{ow} (U.S. EPA 1999b). Insoluble chemicals that could be run through EPISuite™ software were assigned a log K_{ow} >10, if the result appeared to be valid based on expert review. This assignment is consistent with an analysis of the chemicals used in the development of the octanol/water partition coefficient estimation program in the EPISuite™ software. The training set (chemicals used for calibration) for this model included 10,946 chemicals with a MW range of 18-720 daltons and experimental log K_{ow} ranging from -3.89 to 8.70 (Meylan and Howard 1995; U.S. EPA 2011h). Given that log K_{ow} increases with MW, a default value of 10 is consistent with the limited bioavailability expected for materials with a MW >1,000 daltons. Although no BPA alternatives had a MW >1,000, there are two compounds that may contain small amounts of higher MW oligomeric materials or other impurities that were evaluated using a log K_{ow} suggestive of limited bioavailability. A maximum log K_{ow} of -2 was used for water soluble materials. For most polymers and other materials that are anticipated to be insoluble in both water and octanol, the log K_{ow} cannot be measured and was therefore not listed.

Flammability (Flash Point)

The flash point of a substance is defined as the minimum temperature at which the substance emits sufficient vapor to form an ignitable mixture with air. Flash point can be used to identify hazards associated with the handling of volatile chemicals. Substances with a flash point above 37.8°C (100°F) were commonly referred to as nonflammable, as this is the flammability definition used in the shipping industry. There are exceptions to this definition such as chemicals that may form explosive mixtures in the presence of air.

Explosivity

Explosivity refers to the potential for a chemical to form explosive mixtures in air and can be defined using the limits of flammability. The lower limit of flammability (LFL) is defined as the minimum concentration of a combustible substance that is capable of propagating a flame through a homogenous mixture in the presence of an ignition source. The upper limit of flammability (UFL) is similarly defined as the highest concentration that can propagate a flame. LFLs and UFLs are commonly reported as the volume percent or volume fraction of the flammable component in air at 25°C. If the ambient air concentration of the gas (or vapor) is between the upper and lower explosion limit, then the material has the potential to explode if it comes in contact with an ignition source. Knowledge regarding the explosivity of a given material in air is also useful in identifying potential hazards associated with the manufacture and use of that material.

pH

The pH scale measures how acidic or basic a substance is on a range from 0 to 14. A pH of 7 is neutral. A pH less than 7 is acidic, and a pH greater than 7 is basic. This scale is used primarily to identify potential hazards associated with skin or eye contact with a chemical or its aqueous solutions. The corrosive nature of chemicals that form either strongly basic (high pH) or strongly acidic (low pH) solutions are generally likely to result in harm to skin and other biological membranes. For corrosive chemicals, some experimental studies, such as biodegradation tests, require additional analysis to determine if the tests were performed at concentrations that cause harm to microbes in the test (and therefore may result in incorrectly identifying a chemical as persistent in the environment). For chemicals that form moderately basic or acidic solutions in water, the pH of the resulting solution can be used in lieu of a measured dissociation constant.

Dissociation Constant in Water (pKa)

The dissociation constant determines if a chemical will ionize under environmental conditions. The dissociation constant in water provides the amount of the dissociated and undissociated forms of an acid, base, or organic salt in water. Knowledge of the dissociation constant is required to assess the importance of the other physical/chemical properties used in the hazard assessment. As the percentage of ionization increases, the water solubility increases while the vapor pressure, Henry's Law constant, and octanol/water partition coefficient decrease. For acids and bases, the dissociation constant is expressed as the pK_A and $pK_{B,}$ respectively.

Henry's Law Constant

Henry's Law constant is the ratio of a chemical's concentration in the gas phase to that in the liquid phase (at equilibrium). In environmental assessments, the Henry's Law constant is

typically measured in water at 25°C. The Henry's Law constant provides an indication of a chemical's volatility from water, which can be used to derive information about the chemical's tendency to partition within environmental compartments and the amount of material removed by stripping in a sewage treatment plant. Henry's Law constant values less than $1x10^{-7}$ atm-m^3/mole indicate slow volatilization from water to air (the Henry's Law constant for the volatilization of water from water is $1x10^{-7}$ atm-m^3/mole) and values more than $1x10^{-3}$ atm-m^3/mole indicate rapid volatilization from water to air. To aid in determining the importance of volatilization, the assessment uses two models based on the Henry's Law constant. These models determine the half-life for volatilization from a model river and a model lake. A maximum value of $1x10^{-8}$ atm-m^3/mole for the Henry's Law constant was assigned for chemicals without experimental data or for those that were anticipated by professional judgment to be nonvolatile.

Sediment/Soil Adsorption/Desorption Coefficient (Koc)

The soil adsorption coefficient provides a measure of a chemical's ability to adsorb to the organic portion of soil and sediment. This provides an indication of the potential for the chemical to leach through soil and be introduced into groundwater, which may lead to environmental exposures to wildlife or humans through the ingestion of drinking water drawn from underground sources. Chemicals with high soil adsorption coefficients are expected to be strongly adsorbed to soil and are less likely to leach into groundwater. The soil adsorption coefficient also describes the potential for a chemical to partition from environmental waters to suspended solids and sediment. The higher the K_{oc}, the more strongly a chemical is adsorbed to soil. Strong adsorption may impact other fate processes, such as the rate of biodegradation, by making the chemical less bioavailable.

The soil adsorption coefficient, K_{oc}, is normalized with respect to the organic carbon content of the soil to account for geographic differences. The assignments for the degree that a chemical is adsorbed to soil within the context of the assessment were described qualitatively as very strong (above 30,000), strong (above 3,000), moderate (above 300), low (above 30), and negligible (above 3). When determining the potential for a chemical to adsorb to soil and suspended organic matter, the potential for a chemical to form chemical bonds with humic acids and attach to soil also needs to be considered, although this process is generally limited to a small number of chemical classes. A maximum value of 30,000 for the K_{oc} was assigned for chemicals without experimental data or for those that were anticipated by professional judgment to be strongly absorbed to soil (U.S. EPA 2004).

Reactivity

The potential for a substance to undergo irreversible chemical reactions in the environment can be used in the assessment of persistence. The primary chemical reactions considered in an environmental fate assessment are hydrolysis, photolysis, and the gas phase reaction with hydroxyl radicals, ozone, or nitrate radicals. The most important reaction considered in the hazard assessment of organic compounds is hydrolysis, or the reaction of a chemical substance with water. Because the rate of hydrolysis reactions can change substantially as a function of pH, studies performed in the pH range typically found in the environment (pH 5-9) were considered. The second reaction considered in the assessment is photolysis, the reaction of a chemical with sunlight. Both hydrolysis and photolysis occur in air, water, and soil, while only hydrolysis was considered in sediment. The half-lives for reactive processes, if faster than removal via

biodegradation, were used to assign the hazard designation by direct comparison to the DfE persistence criteria.

For the atmospheric compartment, persistence also includes the evaluation of oxidative gas-phase processes. These processes include the reaction with ozone, hydroxyl radicals, and nitrate radicals. Since the average concentration of these oxidative species in the atmosphere has been measured, the experimental or estimated rate constants were converted to, and reported as, a half-life in the assessment using standard pseudo first-order kinetics (U.S. EPA 2011f; U.S. EPA 2011d).

For inorganic compounds, an additional chemical process was considered, the potential to be reduced or oxidized (undergo a redox reaction) under environmental conditions. Redox reactions change the oxidation state of the species through the transfer of electrons to form another compound (such as the reduction of Cr(VI) to Cr(III)). A change in the oxidation state of a metal or inorganic species can result in significant changes in the material's hazard designation. In this example, going from Cr(VI) to Cr(III) makes the compound less toxic.

Environmental Transport

The persistence of a chemical substance is based on determining the importance of removal processes that may occur once a chemical enters the environment. As noted in Section 4.1.2, chemicals with a half-life of less than 60 days are expected to be at most a Moderate hazard designation for persistence. Persistence does not directly address the pathways in which a chemical substance might enter the environment (e.g., volatilization or disposal in a landfill) and focuses instead on the removal processes that are expected to occur once it is released into air, water, soil, or sediment. Similarly, the persistence assessment does not address what might happen to a chemical substance throughout its life-cycle, such as disposal during incineration of consumer or commercial products. Understanding the environmental transport of a chemical substance can help identify processes relevant to environmental assessment. For example, if a chemical is toxic to benthic organisms and partitions primarily to sediment, its potential release to water should be carefully considered in the selection of alternatives.

Biodegradation

In the absence of rapid hydrolysis or other chemical reactions, biodegradation is typically the primary environmental degradation process for organic compounds. Determining biodegradation processes is, therefore, an important component of the assessment. Biodegradation processes are divided into two types. The first is primary biodegradation, in which a chemical substance is converted to another substance. The second is ultimate biodegradation, in which a chemical is completely mineralized to small building-block components (e.g., CO_2 and water). DfE persistence criteria use data that are reported as a percent of theoretical ultimate degradation in the guideline Ready Biodegradability test or as a half-life in other experimental studies; both of these measurements can be compared directly to the DfE criteria in Section 4.1.2. When considering primary degradation, the assessment process includes an evaluation of the potential for the formation of metabolites that were more persistent than the parent materials. Chemical substances that undergo rapid primary degradation but only slow ultimate biodegradation were considered to have stable metabolites. In the absence of measured data on the substance of interest, DfE evaluated the potential for biodegradation for chemicals with a MW <1,000 daltons

using the EPA EPISuite™ models. EPISuite™ estimates the probability for ready biodegradation as well as the potential for primary and ultimate removal, as described in Section 4.5.

4.4 Evaluating Human Health Endpoints

After data collection and analysis of the physical/chemical properties for the chemicals being assessed, the comparison of the data against the hazard criteria can begin. Section 4.4.1 discusses how measured data are used to make hazard designations for human health endpoints, and Section 4.4.2 presents the approach for filling in data gaps to make these hazard designations.

4.4.1 Endpoints Characterized and Evaluated Against Criteria Based on Measured Data

This section provides a short description of how measured data were used to designate the level of hazard for each endpoint. As a reminder, the criteria for the hazard designations are in Section 4.1.2.

For acute mammalian toxicity, the LD_{50}s or LC_{50}s were used to assign the hazard designation. Four levels of hazard designation have been defined ranging from Low to Very High.

For cancer, the hazard designation was contingent on the level of evidence for increased incidence of cancer rather than potency. The definitions applied in DfE criteria are based on International Agency for Research Cancer (IARC) levels of evidence (International Agency for Research on Cancer 2006). For example, a designation of Very High concern requires that the substance be characterized as a "known or presumed human carcinogen," whereas a designation of Low concern requires either negative studies or robust SAR conclusions. A designation of Moderate was applied as a default value when there was an absence of data suggesting High carcinogenicity, and an absence of data supporting Low carcinogenicity (i.e., a lack of negative studies or weak SAR conclusion). Information suggestive of pre-cancerous lesions also merits the designation of Moderate concern.

Similarly, the hazard designation for mutagenicity/genotoxicity was also based on the level of evidence rather than potency. Complete data requirements for this endpoint include both gene mutation and chromosomal aberration assays. For instances of incomplete or inadequate mutagenicity/genotoxicity data, a Low hazard designation cannot be given.

For chronic endpoints, such as reproductive, developmental, neurological and repeated dose toxicity, the hazard designation was based on potency. The evaluation considers both lowest observed adverse effect levels (LOAELs) and identification of no observed adverse effect levels (NOAELs), when available. The LOAEL and the NOAEL are experimental dose levels, and their reliability is dictated by the study design. In studies for which the lowest dose tested resulted in an adverse effect (and therefore a NOAEL was not established), and in studies for which the highest dose tested was a NOAEL, a conservative approach using professional judgment was used to address uncertainty regarding the lowest dose or exposure level that might be expected to cause a particular adverse effect. For example, in the absence of an established a NOAEL, an identified LOAEL might fall within the range of a Moderate hazard; however, it is uncertain if a lower dose, such as one that falls within the range of High hazard exists because no lower doses were tested. In such cases, professional judgment was applied to assign a hazard designation when possible. Some degree of uncertainty was evident in results from studies in which a NOAEL may fall within one hazard range (e.g., Moderate hazard) and the identified LOAEL

falls within a different hazard range (e.g., Low hazard) because the true LOAEL may fall in either category, but there were not enough experimental data points to determine the true LOAEL. Professional judgment was also applied to these cases to assign a hazard descriptor when possible, and the rationale used was described in the assessment.

Developmental neurotoxicity, for which data were only available for BPA, was considered and was evaluated using the developmental toxicity criteria, which are more stringent than the criteria for neurotoxicity, and thus more protective (U.S. EPA 2011b).

The criteria for skin and respiratory sensitization, which are immune-based responses, consider the frequency and potency of the reactions. For skin sensitization, categories were based on the weight of evidence[3] from traditional animal bioassays, but *in vitro* alternative studies were also considered. At this time, there are no standard test methods for respiratory sensitization; as a result there was often no designation for this endpoint.

The evaluation of skin and eye irritation and corrosivity were based on the time to recovery.

4.4.2 SAR – Application of SAR and Expert Judgment to Endpoint Criteria

If measured data pertaining to human health criteria were not available, potential adverse effects were estimated with SAR analysis. To make these estimates, DfE relied on the expertise of scientists in EPA's New Chemicals Program who have reviewed thousands of chemicals and associated data using these methods. SAR uses the molecular structure of a chemical to infer a physicochemical property that can be related to specific effects on human health. These correlations may be qualitative ("simple SAR") or quantitative (QSAR). Information on EPA's use of SAR analysis has been published by EPA (1994). Public access to free validated QSAR models for human health endpoints is far more limited than physical/chemical properties, environmental fate parameters, or ecotoxicology.

Carcinogenicity was assessed using the OncoLogic expert system that provides a qualitative result directly applicable to the DfE criteria. For other endpoints that required SAR approaches, an analog approach using expert judgment was used, as discussed in Section 4.2. All estimates obtained in this project were reviewed by EPA scientists having appropriate expertise. Estimates for the other human health endpoints were based on expert judgment using an analog approach and not through the use of computerized SAR methodologies.

Carcinogenicity

The potential for a chemical to cause cancer in humans was estimated using OncoLogic expert system. This program uses a decision tree based on the known carcinogenicity of chemicals with similar chemical structures, information on mechanisms of action, short-term predictive tests, epidemiological studies, and expert judgment.

Oligomeric Mixtures

Oligomers with MW <1,000 were assessed using a representative structure for all the MW species anticipated to be present in the mixture. The procedures were essentially identical to

[3] Generally, weight of evidence is defined as the process for characterizing the extent to which the available data support a hypothesis that an agent causes a particular effect (U.S. EPA, 1999a).

those employed for the evaluation of impurities or byproducts in discrete chemicals, although in this case, the oligomer with the highest concern was used to drive the hazard designation. Unreacted monomers, if present, were also assessed and considered in the hazard evaluation. In this alternatives assessment, two chemicals are mixtures of low MW oligomers comprised of two or three repeating units.

4.5 Evaluating Environmental Endpoints

As with endpoints previously mentioned, the preferred method for the evaluation of environmental endpoints is the use of experimental data. In their absence, the alternatives assessment uses computerized QSAR models developed by EPA for the evaluation of environmental endpoints that can be directly compared to the DfE criteria. When measured data were not available, the aquatic toxicity was estimated using EPA's ECOSAR™ software, and the persistence designation was estimated using models in EPA's EPISuite™ software. The hazard designation was determined by applying the criteria to these estimates.

As a direct result of the design of these models and their direct application to DfE criteria, the evaluation of environmental endpoints using experimental or estimated data was discussed together in the following subsections.

4.5.1 Ecotoxicity

For ecological toxicity, the alternatives assessment focused on the hazard designations for acute and chronic studies on freshwater species of algae, invertebrates, and fish (often referred to as the "three surrogate species"). Aquatic toxicity values were reported in the assessment as follows:

- Acute (estimated or experimental) - LC_{50} in mg/L or EC_{50} in mg/L
- Chronic (experimental) - No observed effect concentration (NOEC) in mg/L
- Chronic (estimated) - ChV, or the geometric mean between the NOEC and the LOEC, in mg/L

Experimental data and estimates reported in the alternatives assessment includes information on the species tested and typically focus on freshwater aquatic organisms. Test data on other organisms (e.g., worms) were included in the assessment if data or models were readily available. These data would be evaluated using professional judgment in support of the hazard designations assigned using the three surrogate freshwater species; however, they were not used exclusively to assign a hazard designation as DfE criteria are not available. For the estimated results from ECOSAR, the equations are derived from surrogate species of fish, zooplankton, and phytoplankton. While these surrogate species can comprise several genera as well as families, the equations are not intended to be species specific, but rather estimate toxicity to the general trophic levels they represent (Mayo-Bean, Nabholz et al. 2011).

If an experimental or estimated effect level exceeded the known water solubility of a chemical substance, or if the log K_{ow} exceeded the ECOSAR™ cut-off values for acute and chronic endpoints (which are class specific), No Effects at Saturation (NES) were determined for the aquatic toxicity endpoints. NES indicates that at the highest concentration achievable, which is the limit of a chemical's water solubility, no adverse effects were observed (or would be expected). In these cases, a Low hazard designation was assigned. In the cases where both an estimated water solubility and ECOSAR™ estimate were used, then an additional factor of ten

was applied to the water solubility before a NES designation was assigned to account for the combined uncertainty in the model estimates.

In the case where an experimental aquatic toxicity value was significantly higher than the chemical's water solubility, it was likely the result of a poorly conducted study. In this circumstance, which is generally more frequent for formulated products or mixtures, additional details were provided in the data quality section to describe why the reported values could not be used to assign a hazard designation. No effects at saturation are also expected in most cases for insoluble organics, oligomers, or non-ionic polymers with a MW >1,000 daltons resulting in an overall low hazard concern for aquatic toxicity (Nabholz, Clements et al. 1993).

EPA's ECOSAR™ estimation program uses chemical structure to estimate toxicity of a substance using class-specific QSARs. ECOSAR™ automatically determines all classes that a chemical may be related to based on the molecular features of the substance and, therefore, may provide multiple class-specific estimates for some or all of the species and durations estimated (Mayo-Bean, Nabholz et al. 2011). Modeled results are dependent on the functional groups present on the molecule as well as the diversity of chemicals with experimental data used to build the models (the training set). The hazard profiles report estimates for every class identified by ECOSAR™. However, the hazard designation was based on the most conservative ECOSAR™ estimate (highest hazard value). If professional judgement indicate that certain class-specific estimates were not appropriate for a particular substance, the narcosis (baseline toxicity) associated with the neutral organic class will be used. Experimental log K_{ow} values were used preferentially as input into ECOSAR™. In their absence, estimated log K_{ow} values from EPISuite™ were used. ECOSAR™ is maintained and developed as a stand-alone program (http://www.epa.gov/oppt/newchems/tools/21ecosar.htm), but is also accessible through the EPA EPISuite™ program after it is installed; therefore the Estimations Program Interface (EPI) program was may also be used as a citation for the ECOSAR™ values in this report.

There were instances where sufficient experimental data were not available to build a chronic QSAR for some of the three surrogate species. When ECOSAR™ did not provide chronic estimates, the acute value (experimental or estimated) was divided by an acute to chronic ratio (ACR) to arrive at the ChV. ACRs of 10 were used for fish and daphnid, and an ACR of 4 was used for algae (Rand, Wells et al. 1995).

Although no BPA alternatives had a MW >1,000, there are two oligomeric materials that may contain small amounts of higher MW components. The aquatic toxicity hazard potential for these materials was would be assigned a Low designation, as discussed above, and as a direct result, their presence did not influence the hazard designation for this endpoint.

4.5.2 Bioaccumulation

Bioaccumulation is a process in which a chemical substance is absorbed in an organism by all routes of exposure as occurs in the natural environment (e.g., from dietary and ambient environment sources). Bioaccumulation is the net result of the competing processes; this includes uptake, metabolism and elimination of a chemical in an organism. Bioaccumulation can be evaluated using the bioaccumulation factor (BAF), the steady state ratio of a chemical in an organism relative to its concentration in the ambient environment, where the organism is exposed through ingestion and direct contact. Experimental BAFs have not been widely available in the scientific literature and, as a result, experimental bioconcentration factors (BCFs) are more

commonly used to evaluate the bioaccumulation hazard. BCFs are defined as the ratio of the concentration of a dissolved chemical in an aquatic organism to the concentration of the chemical in the exposure medium (surrounding water); BCFs are typically measured for fish (in water) using guideline studies.

Experimental BAF or BCF values can be compared directly to the DfE criteria for this endpoint to assign a hazard designation. The BCF and BAF designations range from <100 for a Low designation to >5,000 for a Very High designation (see Table 4-2). If experimental values were available for both of these endpoints, and the BCF and BAF were >100 (i.e., above the Low designation), the largest factor was used to assign hazard designation. If experimental BCFs <100 were available, the estimated upper trophic BAF from EPISuite™ was used preferentially, if its use resulted in a more conservative hazard designation and the potential for metabolism was accurately accounted for within the model estimates.

In the absence of experimental data, evaluation of bioaccumulation potential can be done using the log K_{ow} and the log octanol/air partition coefficient K_{oa} as estimated by EPISuite™. However, analysis using K_{oa} requires the use of metabolism data for higher trophic, air breathing organisms, which can be difficult to obtain from the scientific literature and cannot be readily estimated. BAFs and BCFs from EPISuite™ were, therefore, typically used for the bioaccumulation hazard designation when experimental data were lacking. These values can be compared directly to DfE criteria, and the most conservative result was used for the hazard designation. For chemicals that had estimated bioaccumulation data, available experimental monitoring data were used to provide insight into the reliability of the model results. For example, an estimated Low bioaccumulation potential may be increased to a Moderate designation if a chemical was routinely identified in samples from higher trophic levels, or a High designation if the chemical was routinely measured in animals at the top of the food chain.

An estimate of Low is the default value used for organics with a MW >1,000 daltons in the assignment of bioaccumulation hazard. This assignment is consistent with an analysis of the chemicals used in the development of the bioconcentration and bioaccumulation estimation programs in the EPISuite™ software (U.S. EPA 2011g). The training sets for these models included 527 and 421 chemicals, respectively, with a MW range 68-992 daltons (959 daltons for BAF). Given that BCF and BAF reach a maximum and then decrease with increasing log K_{ow}, a default value of Low is, in general, consistent with the limited bioavailability expected for materials with a MW >1,000 daltons. DfE used all available well-conducted studies when evaluating bioaccumulation potential for materials with a MW >1,000, including environmental biomonitoring data on higher trophic levels. Although no BPA alternatives had a MW <1,000, there are two compounds that may contain small amounts of higher MW oligomeric impurities; the bioaccumulation hazard potential for these materials was assigned a Low designation as discussed above and, as a result, their presence did not influence the hazard designation for this endpoint.

4.5.3 Environmental Persistence

A chemical's persistence in the environment is evaluated by determining the type and rate of potential removal processes. These removal processes were generally divided into two categories: chemical and biological. Of the chemical degradation processes, an evaluation of environmental persistence includes the reaction of a chemical with water, also known as

hydrolysis, because water is ubiquitous in the environment. Hydrolysis rate constants can be obtained from the literature or can be estimated, and the resulting half-lives can be compared directly to DfE criteria. For chemicals without hydrolyzable groups, biodegradation tends to be the faster degradation process in water, soil, and sediments; however, numerous commercial chemicals possess labile groups, and these may hydrolyze in the environment at significant or even rapid rates. Direct and indirect photolysis also represents other potential chemical degradation processes that are considered in the alternatives assessment, and they are discussed later in this section. Oxidation by hydroxyl radicals and ozone is the dominant degradation process for organic chemicals in air.

Biodegradation, the most prevalent biological removal process, was divided into two types. The first is primary biodegradation, in which a chemical substance is converted to another substance through a single transformation. The second is ultimate biodegradation, in which a chemical is completely degraded to CO_2, water, mineral oxides of certain other elements in the molecule, and low-MW compounds that can directly enter microbial metabolism. DfE criteria utilize ultimate biodegradation preferentially for the persistence hazard designation, although primary removal rates were informative in assigning hazard designations, particularly for materials that were transformed slowly, and to a lesser extent for those that are transformed rapidly.

If ultimate biodegradation data were not available, primary removal data were used in some cases. For primary removal processes, the potential for the formation of degradation products that are more persistent than the parent compounds must be considered in the hazard designation. When present, the persistent degradation products should be evaluated for fate and toxicity. Half-life data on the persistent degradation products, if available, were used to determine the assignment for the persistence designation. In the absence of persistent degradation products, primary biodegradation half-life data were compared directly to the DfE criteria to assign a hazard designation.

Biodegradation processes can be classified as either aerobic or anaerobic. Aerobic biodegradation is an oxidative process that occurs in the presence of oxygen. Anaerobic biodegradation is a reductive process that occurs only in the absence of oxygen. Aerobic biodegradation is typically assessed for soil and water, while anaerobic biodegradation is most relevant for sediments, landfills and sludge digesters in sewage treatment plants; although anoxic conditions can also occur in soil and the water column. For determining the persistence hazard designation, the importance of both aerobic and anaerobic biodegradation, as well as partitioning and transport in the environment, were considered to determine what removal processes were most likely to occur. Anaerobic degradation may use any of several electron acceptors, depending on their availability in a given environment and the prevailing redox potential (Eh). The biodegradative populations that are dominant in a given environment vary with the conditions, and so do their biodegradative capabilities.

One aspect of the assessment is to determine the potential for removal of a chemical substance, and especially removal attributable to biodegradation, within a sewage treatment plant and other environments. In this assessment, the term “ready biodegradability” refers to a chemical’s potential to undergo ultimate degradation in guideline laboratory studies. A positive result in a test for ready biodegradability can be considered indicative of rapid and ultimate degradation in most environments, including biological sewage treatment plants. Ready tests typically include a 10-day window, beginning when the biodegradation parameter (e.g., disappearance of dissolved

organic carbon from test substance, or theoretical oxygen demand) reaches 10%. If the pass level of the test (60% for oxygen demand and CO_2 production; 70% for dissolved organic carbon disappearance) was met in the 10-day window, the chemical received a Very Low hazard designation. Those that did not pass the 10-day window criterion but met the pass level in 28 days received a Low hazard designation. If ready biodegradability test data were available but the chemical did not meet the pass level, the chemical was evaluated based on measured data using the DfE half-life criteria (Table 4-1). These half-life criteria were also used to assign a hazard designation for nonguideline ultimate biodegradation studies reported in the scientific literature.

In the absence of a reported half-life, experimental data were also used to approximate half-life, as appropriate. For example, a chemical that undergoes <5% removal in 30 days would be expected to have a half-life >60 days and would be assigned a High persistence hazard designation.

When experimental data on the biodegradation of a chemical substance were not available, the potential of that substance to undergo this removal process was assessed from the results of the EPISuite™ models. These models fall into one of four classes: rapid biodegradation models based on linear and non-linear regressions that estimate the probability that a chemical substance will degrade fast; expert survey models that estimate the rate of ultimate and primary biodegradation using semi-quantitative methods; probability of ready biodegradability in the OECD 301C test; and probability of rapid biodegradation under methanogenic anaerobic conditions (specifically under conditions of the OECD 311 test). Each of these is discussed in the following paragraphs.

The first models (Biowin 5 and 6) used in the screening assessment estimated ready biodegradability in the OECD 301C test and are also known as the Japanese Ministry of International Trade and Industry (MITI) models. These models provided the probability that a material passes this standardized test. Those chemicals that were estimated to pass the ready biodegradability test received a Low persistence designation. If a chemical was not estimated to pass the MITI test, the results of the other EPISuite™ biodegradation models were used.

The rapid biodegradation potential models within EPISuite™ (Biowin 1 and 2) were useful for determining if a chemical substance was expected to biodegrade quickly in the environment. If a chemical was likely to biodegrade quickly, it was generally assigned a Low hazard designation for persistence. The results of the estimates from these models may be used in concert with the semi-quantitative output from a second set of models, which include ultimate and primary biodegradation survey models (Biowin 3 and 4) for evaluating persistence. These models provided a numeric result, ranging from 1 to 5, that relates to the amount of time required for complete ultimate degradation (Biowin 3) and removal of the parent substance by primary degradation (Biowin 4) of the test compound. The numeric result from Biowin 3 was converted to an estimated half-life for removal that can be compared directly to DfE criteria. If results from different models (other than the MITI models) led to a different hazard designation, then the ultimate biodegradation model results were used preferentially. If the transport properties indicated the potential for the material to partition to sediment, an anoxic compartment, then the results of the anaerobic probability model (Biowin 7) were also evaluated.

Half-lives for hydrolysis from experimental studies or EPISuite™ estimates were used in preference to biodegradation data when they suggested that hydrolysis is a more rapid removal process. Hydrolysis half-lives were compared directly to DfE criteria to assign the persistence designation. Similar to primary biodegradation, breakdown products resulting from hydrolysis were evaluated for fate and toxicity when they were expected to be more persistent than the parent compound.

Photolysis may also be an important environmental removal process. In general, environmental removal rates from photolysis do not compete with biodegradation or hydrolysis, although there are exceptions such as iodides. Photolysis may be the predominant removal process for chemicals that were not bioavailable because of their limited water solubility. Estimation methods for photolysis rates were not available using computerized SAR tools. If experimental or suitable analog data were available, the rate of photolysis was evaluated relative to other removal processes.

When evaluating the environmental persistence designation, it should be noted that chemicals with a High or Very High designation can degrade over time, although this process may occur at a very slow rate. As a result, a Very High designation may have been assigned if persistent degradates were expected to be produced, even at a very slow rate, in the absence of experimental biodegradation data for the parent substance.

4.6 Endocrine Activity

Chemicals included in this DfE Alternatives Assessment were screened for potential endocrine activity, consistent with the DfE Alternatives Assessment Criteria (U.S. EPA 2011b). Endocrine activity refers to a change in endocrine homeostasis caused by a chemical or other stressor. An endocrine disruptor is an external agent that interferes in some way with the role of natural hormones in the body, in a manner causing adverse effects. Relevant data are summarized in the hazard assessments for each chemical, located in Section 4.8. Data on endocrine activity were available for BPA and 10 of the 19 alternatives included in this report. For chemicals without available data on endocrine activity, this was acknowledged with a "no data available" statement. When endocrine activity data were available, the data were summarized as a narrative. A unique hazard designation of Low, Moderate or High is not provided for this endpoint in Table 4-3, for reasons discussed below.

The document *Special Report on Environmental Endocrine Disruption: An Effects Assessment and Analysis* describes EPA's activities regarding the evaluation of endocrine disruption (U.S. EPA 1997). This report was requested by the Science Policy Council and prepared by EPA's Risk Assessment Forum. This report states that "Based on the current state of the science, the Agency does not consider endocrine disruption to be an adverse endpoint per se, but rather to be a mode or mechanism of action potentially leading to other outcomes, for example, carcinogenic, reproductive or developmental effects, routinely considered in reaching regulatory decisions" (U.S. EPA 1997). The report also states that "Evidence of endocrine disruption alone can influence priority setting for further testing, and the assessment of results of this testing could lead to regulatory action if adverse effects are shown to occur" (U.S. EPA 1997).

The 1996 Food Quality Protection Act (FQPA) directed EPA to develop a scientifically-validated screening program to determine whether certain substances may cause hormonal effects in humans. In response, EPA established the Endocrine Disruptor Screening Program

(EDSP) (U.S. EPA 2012b). The EDSP is developing requirements for the screening and testing of thousands of chemicals for their potential to affect the endocrine system. When complete, EPA will use these screening and testing approaches to set priorities and conduct further testing, when warranted. The science related to measuring and demonstrating endocrine disruption is relatively new, and validated testing methods at EPA are still being developed.

The EDSP proposes a two-tiered approach that includes initial screening, followed by more in-depth testing when warranted (U.S. EPA 2011a). The Tier 1 screening battery is intended to identify chemicals with the potential to interact with the estrogen, androgen, or thyroid hormone systems through any of several recognized modes of action. Positive findings for Tier 1 tests identify the potential for an interaction with endocrine systems, but do not fully characterize the nature of possible effects in whole animals. Tier 2 testing is intended to confirm, characterize, and quantify the effects for chemicals that interact with estrogen, androgen, and thyroid hormone systems. These test methods must undergo a four-stage validation process (protocol development, optimization/prevalidation, validation, and peer-review) prior to regulatory acceptance and implementation. Validation is ongoing for Tier 1 and Tier 2 methods.[4] Once validated test methods have been established for screening and testing of potential endocrine disruptors, guidance must be developed for interpretation of these test results using an overall weight-of-evidence characterization.

To assess the data on endocrine activity, DfE applies the weight-of-evidence approach developed by the EDSP (U.S. EPA 2011c). Generally, weight of evidence is defined as the process for characterizing the extent to which the available data support a hypothesis that an agent causes a particular effect (U.S. EPA 1999a; U.S. EPA 2002; U.S. EPA 2005a). This process integrates and evaluates data, and always relies on professional judgment (U.S. EPA 2011c). To evaluate endocrine activity with this weight-of-evidence approach, DfE examined multiple lines of evidence (when available) and considered the nature of the effects within and across studies, including number, type, and severity/magnitude of effects, conditions under which effects occurred (e.g., dose, route, duration), consistency, pattern, range, and interrelationships of effects observed within and among studies, species, strains, and sexes, strengths and limitations of the in vitro and in vivo information, and biological plausibility of the potential for an interaction with the estrogen, androgen, or thyroid hormonal pathways.

Most test data for chemicals in this report consist of *in vitro* assays, but results of *in vitro* assays alone were not generally expected to provide a sufficient basis to support a hazard designation for endocrine disruption. EPA expects that *in vivo* evidence would typically be given greater overall influence in the weight-of-evidence evaluation than *in vitro* findings because of the inherent limitations of such assays. Although *in vitro* assays can provide insight into the mode of action, they have limited ability to account for normal metabolic activation and clearance of the compound, as well as normal intact physiological conditions (e.g., the ability of an animal to compensate for endocrine alterations).

As described in the DfE Alternatives Assessment Criteria, endocrine activity was summarized in a narrative, rather than by High, Moderate or Low hazard designation. The endocrine activity summaries can be found in the hazard profiles. This is an appropriate approach because there is

[4] Information on the status of assay development and validation efforts for each assay in EPA's EDSP can be found at: http://www.epa.gov/oscpmont/oscpendo/pubs/assayvalidation/status.htm.

no consensus on what constitutes high, moderate or low concern for this endpoint. The summary of endocrine activity largely relies on representative studies and expert review summaries.

Chemical Alternatives and the Toxic Substances Control Act

EPA's Design for the Environment (DfE) program is administered by the Office of Pollution Prevention and Toxics (OPPT), which is charged with the implementation of the Toxic Substances Control Act (TSCA) and the Pollution Prevention Act (PPA).

Central to the administration of TSCA is the management of the TSCA Inventory. Section 8 (b) of TSCA requires EPA to compile, keep current, and publish a list of each chemical substance that is manufactured or processed in the United States. Companies are required to verify the TSCA status of any substance they wish to manufacture or import for a TSCA-related purpose. For more information, please refer to the TSCA Chemical Substance Inventory website: http://www.epa.gov/opptintr/existingchemicals/pubs/tscainventory/basic.html.

TSCA and DfE Alternatives Assessments

Substances selected for evaluation in a DfE Alternatives Assessment generally fall under the TSCA regulations and therefore must be listed on the TSCA inventory, or be exempt or excluded from reporting before being manufactured in or imported to, or otherwise introduced in commerce in, the United States. For more information see http://www.epa.gov/oppt/newchems/pubs/whofiles.htm.

To be as inclusive as possible, DfE Alternatives Assessments may consider substances that may not have been reviewed under TSCA, and therefore may not be listed on the TSCA inventory. DfE has worked with stakeholders to identify and include chemicals that are of interest and likely to be functional alternatives**,** ***regardless of their TSCA status***. Chemical identities are gathered from the scientific literature and from stakeholders and, for non-confidential substances, appropriate TSCA identities are provided.

Persons are advised that substances, including DfE-identified functional alternatives, may not be introduced into US commerce unless they are in compliance with TSCA. Introducing such substances without adhering to the TSCA provisions may be a violation of applicable law. Those who are considering using a substance discussed in this report should check with the manufacturer or importer about the substance's TSCA status. If you have questions about reportability of substances under TSCA, please contact the OPPT Industrial Chemistry Branch at 202-564-8740.

4.7 Hazard Summary Table

Table 4-4: Screening Level Hazard Summary

This table only contains information regarding the inherent hazards of the chemicals evaluated. Evaluation of risk considers both the hazard and exposure. The caveats listed in the legend and footnote sections must be taken into account when interpreting the hazard information in the table below.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard — Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment.

§ Based on analogy to experimental data for a structurally similar compound.

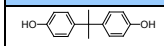
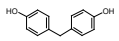
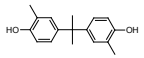
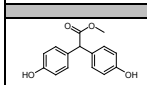
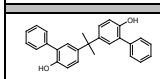
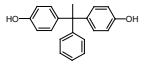
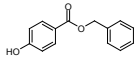
Structure	Chemical (for TSCA inventory name and relevant trade names see the individual profiles in Section 4.8)	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
			Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Bisphenol A and Phenolic Alternatives																	
	Bisphenol A 2,2-bis(p-hydroxyphenyl)propane	80-05-7	L	M	L	M	H	*M*	M	M		M	M	H	H	VL	L
	Bisphenol F Bis(4-hydroxyphenyl)methane	620-92-8	L	*M*	L	*M* §	*H*§	*M*	H	L		VH	*M*§	M	*H*	L	L
	Bisphenol C 2,2'-Bis(4-hydroxy-3-methylphenyl)propane	79-97-0	*L*§	*M*	M	*M* §	*H*§	*M*	*M*§	*M*§		*H*§	*M*§	H	*H*	M	*M*
	MBHA Methyl bis(4-hydroxyphenyl)acetate	5129-00-0	*L*§	*M*	*L*§	*M* §	*H*§	*M*	*M*§	L		*M*§	*M*§	*H*	*H*	*M*	*L*
	BisOPP-A 4,4'-Isopropyllidenebis(2-phenylphenol)	24038-68-4	*L*§	*M*	*L*§	*M* §	*H*§	*M*	*M*§	*M*§		*M*§	*M*§	*L*	*H*	*H*	*M*
	Bisphenol AP 4,4'-(1-Phenylethylidene)bisphenol	1571-75-1	*L*§	*M*	*L*§	*M* §	*H*§	*M*	*M*§	*M*§		*M*§	*M*§	*H*	*H*	*H*	*M*
	Substituted phenolic compound, PROPRIETARY #1		*L*§	*M*	L	*M* §	*H*§	*M*	*M*§	*M*§		*M*§	*M*§	*H*	*M*	*M*	*L*
	Substituted phenolic compound, PROPRIETARY #2		*L*§	*M*	*L*§	*M* §	*H*§	*M*	*M*§	*M*§		*M*§	*M*§	*H*	*H*	*H*	*H*
	PHBB Benzyl 4-hydroxybenzoate	94-18-8	L	*M*	*M*	*L*	*M*	*M*	*L*	*M*§		VL	VL	H	*H*	*L*§	*L*

Table 4-5: Screening Level Hazard Summary (Continued)

This table only contains information regarding the inherent hazards of the chemicals evaluated. Evaluation of risk considers both the hazard and exposure. The caveats listed in the legend and footnote sections must be taken into account when interpreting the hazard information in the table below.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard — Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment.
§ Based on analogy to experimental data for a structurally similar compound.

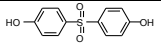
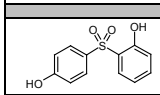
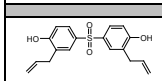
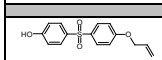
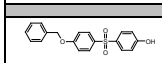
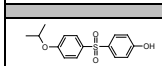
Structure	Chemical (for TSCA inventory name and relevant trade names see the individual profiles in Section 4.8)	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
			Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Hydroxyphenyl Sulfone Alternatives																	
	Bisphenol S 4-Hydroxyphenyl sulfone	80-09-1	L	*M*	M	M	M	*M*	H	L		L	L	M	M	M	L
	2,4-BPS 2,4'-Bis(hydroxyphenyl)sulfone	5397-34-2	*L*§	*M*	M	*M*§	*M*§	*M*	*H*§	*L*§		*L*§	*L*§	*M*	*H*	*M*	*L*
	TGSA Bis-(3-allyl-4-hydroxyphenyl) sulfone	41481-66-7	L	*M*	L	*M*§	*M*§	*M*	H	M	*M*	L	VL	H	M	*H*	*L*
	BPS-MAE Phenol,4-[[4-(2-propen-1-yloxy)phenyl]sulfonyl]-	97042-18-7	L	*M*§	M	*M*§	*M*§	*M*	L	L	*M*	L	VL	H	H	*H*	*L*
	BPS-MPE 4-Hydroxy-4'-benzyloxydiphenylsulfone	63134-33-8	L	*M*	*M*§	*M*§	*M*§	*M*	*H*§	L		L	L	VH	*H*	*H*	*M*
	D-8 4-Hydroxyphenyl 4-isoprooxyphenylsulfone	95235-30-6	L	*M*	L	*M*§	*M*§	*M*	M	*L*§		*L*§	*L*§	H	*H*	M	M

Table 4-6: Screening Level Hazard Summary (Continued)

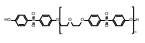
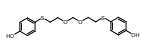
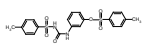
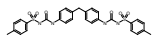
This table only contains information regarding the inherent hazards of the chemicals evaluated. Evaluation of risk considers both the hazard and exposure. The caveats listed in the legend and footnote sections must be taken into account when interpreting the hazard information in the table below.

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard — Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from estimation software and professional judgment.

◊ The highest hazard designation of a representative component of the oligomeric mixture with MWs <1,000.

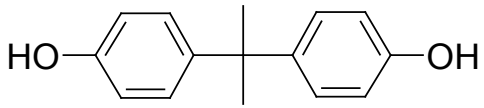
‡ The highest hazard designation of any of the oligomers with MW <1,000

§ Based on analogy to experimental data for a structurally similar compound.

Structure	Chemical (for TSCA inventory name and relevant trade names see the individual profiles in Section 4.8)	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
			Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Oligomeric and Polymeric Alternatives																	
	D-90 Phenol, 4,4'-sulfonylbis-, polymer with 1,1'-oxybis[2-chloroethane]	191680-83-8	L	*M*	L	*L*	*L*	*M*	L	L		M	VL	*L*‡	*L*‡	*VH*‡	*H*‡
	DD-70 1,7-bis(4-Hydroxyphenylthio)-3,5-dioxaheptane	93589-69-6	*L*	*M*	*L*	*M*	*M*§	*M*	*M*§	*M*§		*H*§	*M*§	*H*	*H*	*H*	*L*
	Pergafast 201 N-(p-Toluenesulfonyl)-N'-(3-p-toluenesulfonyloxyphenyl)urea	232938-43-1	L	*M*	L	M	M	*L*	M	L		L	VL	H	H	VH	L
	BTUM 4,4'-bis(*N*-carbamoyl-4-methylbenzenesulfomide)diphenylmethane	151882-81-4	L	*M*	L	*L*	*L*	*L*	M	L		L	L	*H*	*H*	*H*	*L*
	UU Urea Urethane Compound	321860-75-7	L	*M*	L	*L*	*L*	*L*	L	L		L	L	L	*L*◊	VH	L

4.8 Hazard Profiles

Bisphenol A



CASRN: 80-05-7

MW: 228.29

MF: $C_{15}H_{16}O_2$

Physical Forms:
Neat: Solid

Use: Developer for thermal papers

SMILES: Oc1ccc(cc1)C(c1ccc(O)cc1)(C)C

Synonyms: Phenol,4,4'-(1-methylethylidene)bis-; BPA; 2,2-(4,4'-dihydroxydiphenyl)propane; 2,2-bis(4'-hydroxyphenyl)propane; 2,2-bis(4-hydroxyphenyl)propane; 2,2-bis-(4-hydroxy-phenyl)-propane; 2,2-bis(p-hydroxyphenyl)propane; 2,2-bis-4'-hydroxyfenylpropan; 2,2-di(4-hydroxyphenyl)propane; 2,2-di(4-phenylol)propane; 4,4'-(1-Methylethylidene)bisphenol; 4,4'-Dihydroxy-2,2'-diphenylpropane; 4,4'-Dihydroxydiphenyl-2,2'-propane; 4,4'-bisphenol A; 4,4'-dihydroxydiphenyl-2,2-propane; 4,4'-dihydroxydiphenyldimethylmethane; 4,4'-dihydroxydiphenylpropane; 4,4'-dihydroxyphenyl-2,2-propane; 4,4'-isopropylidenebisphenol; 4,4'-isopropylidenediphenol; 4,4-isopropylidenediphenyl; beta, beta'-bis(p-hydroxylphenyl)propane; beta-di-p-hydroxyphenylpropane; bis(4-hydroxyphenyl)dimethylmethane; bis(4-hydroxyphenyl)propane; bis[phenol],4,4'-(1-methylethylidene)-; Bisferol A; bisphenol; Bisphenol,4,4'-(1-methylethylidene)-; Bisphenol-a; Dian; Diano; dimethylbis(p-hydroxyphenyl)methane; dimethylmethylene-p,p'-di-phenol; dimethylmethylene-p,p'-diphenol; Diphenolmethylethylidene; diphenylolpropane; Ipognox88; Isopropylidenebis(4-hydroxybenzene); p,p'-Isopropylidene-bisphenol; p,p'-Isopropylidene-di-phenol; p,p'-bisphenolA; p,p'-dihydroxydiphenyldimethylmethane; p,p'-dihydroxydiphenylpropane; p,p'-isopropylidenebisphenol; p,p'-isopropylidenediphenol; Parabis; ParabisA; Phenol,(1-methylethylidene)bis-; Phenol,4,4'-Isopropylidene-di; Phenol,4,4'-dimethylmethylenedi-; Phenol,4,4'-isopropylidenedi-; Pluracol 245; propane,2,2-bis(p-hydroxyphenyl)-; Rikabanol; ß-Di-p-Hydroxyphenylpropane; Ucarbisphenol A; Ucarbisphenol HP

Polymeric: No **Oligomers:** Not applicable	
Metabolites, Degradates and Transformation Products: BPA glucuronide, BPA sulfate conjugate, BPA diglucuronide, 5-hydroxy BPA and the corresponding sulfate conjugate, isopropyl-hydroxyphenol, BPA glutathione conjugate, glutathionyl-phenol, glutathionyl 4-isopropylphenol, BPA dimmers, monohydroxybisphenol A, beta-glucoside, BPA mono-*O*-ß-D-gentiobioside and the trisaccharide BPA, ß-D -glucopyranoside, mono- and di- *O*-ß-D-glucopyranosides, phenol, 4-isopropenylphenol, 4-isopropylphenol, hexestrol, 5,5'-bis-[1-(4-hydroxy-phenyl)-1-methylethyl]-bisphenyl-2,2'-diol, 4-hydroxyacetephenone, 4-hydroxybenzoic acid, 2,2-bis(4-hydrozyphenyl)-1-propanol, 2, 3- bis(4-hydroxyphenyl)-1, 2-propanediol (Kang, Katayama et al., 2006)	
Analog: None **Endpoint(s) using analog values:** Not applicable	**Analog Structure:** Not applicable
Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)	
Risk Phrases: 37 - Irritating to respiratory system; 41 - Risk of serious damage to eyes; 43 - May cause sensitization by skin contact; 52 - Harmful to aquatic organisms; 62 - Possible risk of impaired fertility (ESIS, 2011).	
Risk Assessments: Risk assessment completed for Bisphenol A by Canada in 2008, the European Union in 2010, and Japan in 2007 (Canada, 2008; EINECS, 2010; Nakanishi and Miyamoto, 2007).	

Bisphenol A CASRN 80-05-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	155 (Measured)	EINECS, 2010	Adequate; consistent values reported in secondary sources.
	150-157 (Measured)	EINECS, 2010; Canada, 2008	
	150-155 (Measured)	O'Neil, 2010	
Boiling Point (°C)	360.5 at 760 mm Hg (Measured)	EINECS, 2010; IUCLID, 2000	Adequate.
	250-252 at 13 mm Hg (decomposes) (Measured)	EINECS, 2010	Reduced boiling point consistent with values reported in secondary sources.
	220-398 (Measured)	Canada, 2008	Range of values not entirely consistent with other located sources.
	220 at 4 mm Hg (Measured); decomposes when heated above 220°C	O'Neil, 2010	Data indicate that BPA will decompose at elevated temperatures.
Vapor Pressure (mm Hg)	3.99×10^{-8} (Measured)	EINECS, 2010; Canada, 2008	Adequate; consistent with values reported in other secondary sources.
	3.08×10^{-9} - 3.99×10^{-8} (Measured)	EINECS, 2010	
Water Solubility (mg/L)	300 (Measured)	EINECS, 2010	Adequate; selected value for assessment.
	120-301 (Measured)	Canada, 2008	Adequate; consistent values which span a narrow range have been reported in secondary sources.
	120 (Measured)	Dorn, Chou et al., 1987	Adequate; well conducted nonguideline study.
Log K_{ow}	3.32 (Measured)	Hansch, Leo et al., 1995; Canada, 2008	Adequate; consistent values that span a relatively narrow range have been reported in secondary sources; selected value for assessment.
	2.2 (Measured)	EINECS, 2010	Adequate; reported in a secondary source.
Flammability (Flash Point)	79.4-227°C (Measured)	EINECS, 2010	Lower temperatures in this range are inconsistent with values reported in other secondary sources.

Bisphenol A CASRN 80-05-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	213°C (Measured) Reported as 415°F	CHRIS, 1999	Adequate; reported in a secondary source.
	Auto flammability = approximately 532°C (Measured)	EINECS, 2010	Substantial degradation is anticipated to occur before this temperature is reached.
Explosivity	Minimum explosive concentration (in air) 0.012 g/L with oxygen >5% (Measured)	EINECS, 2010	Adequate; reported in a secondary source.
	Dust is flammable if ignited (Measured)	IUCLID, 2000	Adequate; reported in a secondary source.
pH			No data located.
pK_a	9.59–11.30 (Measured)	Canada, 2008	Adequate; initial value in range is for first ionization. Higher values likely for second ionization step.
HUMAN HEALTH EFFECTS			
Toxicokinetics	**In rats, BPA was rapidly absorbed following oral administration and extensively metabolized, predominantly via first-pass metabolism. BPA and its metabolites did not appear to accumulate. In rats, excretion following oral exposure occurred mainly in the feces (50-83% of the administered dose) and urine (13-42% of the administered dose, mainly as the glucuronide conjugate). Maternal transfer to the rat fetus was demonstrated and excretion may also occur via the mother's milk. In humans, essentially 100% of a relatively small oral dose of BPA was rapidly absorbed, readily metabolized, and excreted in the urine as BPA-glucuronide (essentially 100% of the administered dose). Information was not located regarding the toxicokinetics of BPA following *in vivo* inhalation or dermal exposure.**		
Dermal Absorption *in vitro*	Human skin, 10% of applied millimolar dose was absorbed.	EINECS, 2010	Adequate.
	Pig skin, 10 µg/mL radiolabeled BPA. 2, 5, and 10 hours of exposure; the total BPA skin content was 3%, 6.9%, and 11.4% of the applied dose, respectively. BPA remained in the skin surface and accumulated primarily in the dermis.	NIOSH, 2010	Adequate.

Bisphenol A CASRN 80-05-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Data located for rats, mice, monkeys, and humans indicate that ingested BPA is rapidly and extensively absorbed from the gastrointestinal tract (up to 85-86% in rats and monkeys and essentially 100% of a relatively small dose in humans). Orally-absorbed BPA undergoes extensive first-pass metabolism. In all species studied, the major metabolic pathway involved the conjugation of BPA to BPA-glucuronide. There does not appear to be a selective affinity of yolk sac/placenta or embryo/ fetus for BPA or BPA metabolites. Enterohepatic recirculation of BPA-glucuronide readily occurs in rats, resulting in availability of some free BPA to tissues. Enterohepatic recirculation does not appear to occur in humans. Approximately 13-42% of an administered BPA dose was recovered in the urine of rats as the glucuronide metabolite; 50-83% was eliminated in the feces, mostly as free BPA. Limited excretion in the milk was observed. In monkeys, 82-85% of an orally-administered BPA dose was recovered in the urine; only 2-3% was detected in the feces. In volunteers given relatively low doses of BPA, the dose was completely recovered as BPA-glucuronide in the urine. No animal data were located regarding the toxicokinetics of BPA following *in vivo* exposure via inhalation or dermal routes.	EINECS, 2010	Summary of multiple studies reported in secondary source.

Bisphenol A CASRN 80-05-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Mammalian Toxicity		**LOW: The acute oral and dermal toxicity hazard of BPA is low based on experimental data in animals. Data for exposure via inhalation were inconclusive, as only a single concentration was tested and a LC_{50} was not provided.**		
Acute Lethality	**Oral**	Rat LD_{50} = 3,200 to >5,000 mg/kg bw	EINECS, 2010; European Commission, 2000; NTP, 1982	Adequate; multiple studies, some guideline studies.
		Mouse LD_{50} = 4,000–5,200 mg/kg bw	EINECS, 2010; European Commission, 2000; NTP, 1982	Adequate; multiple studies, some guideline studies.
		Mouse LD_{50} = 1,600 mg/kg bw	EINECS, 2010; European Commission, 2000	Inadequate; insufficient study details, relatively old study, results not supported by other studies.
		Rabbit LD_{50} = 2,230 mg/kg bw	EINECS, 2010; European Commission, 2000	Inadequate; insufficient study details, old study.
	Dermal	Rabbit LD_{50} = 3,000–6,400 mg/kg bw	EINECS, 2010; European Commission, 2000	Adequate; limited study details for multiple studies reported in secondary sources.
	Inhalation	No deaths among male and female F344 rats (10/sex) exposed to BPA dust at 0.17 mg/L (highest attainable concentration) for 6 hours; transient slight nasal tract epithelial damage was evident.	EINECS, 2010; European Commission, 2000	Adequate, although test guidelines were not reported in secondary sources.

Bisphenol A CASRN 80-05-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Carcinogenicity		**MODERATE: Two standard 2-year guideline carcinogenicity studies found no increased incidence of cancer associated with adult exposures. There is concern for carcinogenicity associated with endocrine related mechanisms due to its estrogenic properties. Several nonguideline studies indicate proliferation of mammary ductal epithelium and squamous metaplasia of prostatic epithelium in offspring, conditions thought by many to predispose to neoplasia (FAO/WHO 2011). In response to the uncertainty, NTP and FDA are conducting a new GLP study that is designed to include a wide oral dosing range, to include pre- and perinatal exposures (FAO/WHO 2011). Since data from guideline studies suggest low concern for cancer but there are nonguideline studies that demonstrate evidence of proliferative lesions, carcinogenicity cannot be ruled out at this time. DfE criteria calls for the assignment of a Moderate hazard designation.**		
	OncoLogic Results	Moderate (Estimated) OncoLogic class: phenols and phenolic compounds However, several types of phenolic compounds are of concern based on structural similarities to estrogenic and androgenic compounds known to be potential carcinogens or tumor promoters via endocrine-related mechanisms.	OncoLogic	OncoLogic SAR analysis using the phenols and phenolic compounds class.
	Carcinogenicity	Based on existing carcinogenicity study data, There **is confidence** that exposure to BPA: • Exhibits endocrine activity and has estrogenic properties • Estradiol-17β is classified as carcinogenic (IARC); It **is likely** that exposure to BPA: • May be associated with increased cancers of the hematopoietic system and increased interstitial-cell tumors in the testes • Alters function of microbules	Keri, Ho et al., 2007	2007 consensus statement for NIEHS-funded cancer researchers evaluating evidence of carcinogenicity in human and animal models following exposure to BPA.

Bisphenol A CASRN 80-05-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		• Induces aneuploidy in cells and tissues • Exposure early in life may cause a predisposition for pre-neoplastic lesions in adult mammary gland and prostate gland tissues • Prenatal exposure alters mammary gland development in mice and increases effects relevant to markers of breast cancer risk in humans; It **is possible** that exposure to BPA: • Induces *in vitro* cellular transformation • Promotes tumor progression and reduces time to recurrence in advanced prostate cancers with androgen receptor mutations.		

Bisphenol A CASRN 80-05-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Combined Chronic Toxicity/Carcinogenicity	2-year dietary study in male and female F344 rats (50/sex/group) Dietary concentrations: 0, 1,000, and 2,000 ppm (estimated doses 0, 84, and 167 mg/kg-day for males and females combined). Chronic toxicity: Lower mean body weight of low- and high-dose females and high-dose males likely the result of decreased food consumption. Carcinogenicity: Marginally significant increase in leukemia in male rats, non-significant increase in female rats, significant increase in interstitial-cell tumors of testes (known to occur at high incidence in aging F344 rats) not considered by NTP to be convincing evidence of a carcinogenic effect for BPA.	NTP, 1982	Adequate.
		2-year dietary study in male and female B6C3F1 mice (50/sex/group) Dietary concentrations: 0, 1,000, and 5,000 ppm (males); 0, 5,000, and 10,000 ppm (females) (estimated doses 0, 172, and 858 mg/kg-day for males and 0, 864, and 1,728 mg/kg-day for females). Chronic toxicity: Increased incidence of multinucleated giant hepatocytes in males (incidences of 41/49 and 41/50 versus 1/49 in controls) Carcinogenicity: Non-significant increased incidences of leukemia or lymphomas in low- and high-dose male mice (9/50, 5/50 versus 2/50 in controls) not considered by	NTP, 1982	Adequate.

Bisphenol A CASRN 80-05-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		NTP to be convincing evidence of carcinogenic effect for BPA.		
		Studies that included perinatal (gestational and/or lactational) exposures to BPA (oral doses to the dam from ~10 to 250 µg/kg bw per day) have reported, among other lesions, proliferation of mammary ductal epithelium and squamous metaplasia of prostatic epithelium in offspring, conditions thought by many to predispose to neoplasia (Timms et al., 2005; Moral et al., 2008). Additional treatments with initiating or promoting agents have led to earlier onset of mammary tumors (Jenkins et al., 2009) or prostatic intraepithelial neoplasia (Prins et al., 2011). However, the studies that included exposures to BPA during the appropriate periods all suffered from one or more deficiencies in design or execution that prevent a definitive evaluation of its potential as a carcinogen. These include 1) lack of consideration of litter effects, 2) small numbers of animals, 3) insufficient study duration to determine whether developmental conditions thought to enhance cancer susceptibility actually did so, and 4) additional treatment with a strong initiating or additional promoting agent(s). In the absence of additional studies addressing these deficiencies, there is currently insufficient evidence on which to judge the carcinogenic potential of BPA.	FAO/WHO, 2011	Summary of data, data quality, and conclusions from the expert panel.

Bisphenol A CASRN 80-05-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Genotoxicity		**LOW: Based on determination by FAO/WHO (2011) that: (1) BPA is not a mutagen in *in vitro* test systems, (2) BPA does not induce cell transformation, and (3) *in vivo* evidence for BPA-induced clastogenic effects is inconsistent and inconclusive, although some *in vitro* studies have shown BPA to affect chromosomal structure in dividing cells. The conclusion of FAO/WHO (2011) is that BPA is not likely to pose a genotoxic hazard to humans.**		
		Largely negative results in a variety of *in vitro* test systems, including studies with *Salmonella typhimurium*, Chinese hamster V79 cells, Syrian hamster embryo cells, and mouse lymphoma cells. However, DNA damage was induced in MCF-7 and MDA-MB-231 cells, DNA adduct formation in Syrian hamster ovary cells, and a number of positive findings have been reported for the potential for BPA to inhibit purified microtubule polymerization, affect the spindle apparatus, and produce aneuploidy in *in vitro* studies with Chinese hamster V79 cells or oocytes from Balb/c or MF1 mice. FAO/WHO Expert Panel concludes: BPA is not a mutagen in *in vitro* test systems, nor does it induce cell transformation. BPA has been shown to affect chromosomal structure in dividing cells in *in vitro* studies, but evidence for this effect in *in vivo* studies is inconsistent and inconclusive. BPA is not likely to pose a genotoxic hazard to humans.	FAO/WHO, 2011	Summary of data, data quality, and conclusions from the expert panel.

Bisphenol A CASRN 80-05-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**MODERATE: Key studies identified by NTP indicate there are multiple distinct endpoints with NOAELs in the range of Moderate hazard concern with LOAELs in the range of Low hazard concern. At the target dose of 50 mg/kg-day, the NOAELs are on the margin of High and Moderate hazard, according to DfE criteria. Benchmark Dose (BMD) Modeling conducted by NTP, which interpolates between NOAEL and LOAEL values, yields values that further support a Moderate hazard designation.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

Bisphenol A CASRN 80-05-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction and Fertility Effects	Multigenerational dietary study on fertility and reproductive performance in Sprague-Dawley rats (30/sex/group) BPA concentrations: 0, 0.015, 0.3, 4.5, 75, 750, and 7,500 ppm (Tyl, et al., 2002 estimated target doses of 0, 0.0095, 0.019, 0.285, 5, 50, and 500 mg/kg bw-day) Exposure period: 10 weeks premating, 2 weeks mating, gestation (parental males and females), lactation (parental females); similar exposure regimen for F_1 and F_2 parental males and females; F_3 weanlings exposed for 10 weeks Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for 12% decreased terminal body weight in F_1 parental males Reproductive toxicity: Females: NOAEL = 50 mg/kg bw-day LOAEL = 500 mg/kg bw-day for decreases in number of implantation sites, delayed vaginal opening in F_1, F_2, F_3 offspring BMDLs (change of 1 standard deviation from control) reported for delayed vaginal opening (females)- F_1 = 176 mg/kg-day F_2 = 228 mg/kg-day F_3 = 203 mg/kg-day Males: NOAEL = 50 mg/kg bw-day, LOAEL = 500 mg/kg-day for delayed preputial separation in F_1 males BMDLs (change of 1 standard deviation from control) reported for delayed preputial separation (males)- F_1 = 163 mg/kg-day F_2 = 203 mg/kg-day F_3 = 189 mg/kg-day	Chapin et al. 2008; NTP-CERHR, 2008	Adequate, guideline study as reported in the secondary source. Classified by NTP-CERHR as having as High Utility.

Bisphenol A CASRN 80-05-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Two-generation dietary study of fertility and reproductive performance in CD-1 mice (28/sex/group) Dietary concentrations: 0, 0.018, 0.18, 1.8, 30, 300, and 3,500 ppm (Tyl, et al., 2002 estimated target doses of 0.003, 0.03, 0.3, 5, 50, and 600 mg/kg bw-day) Exposure period: 8 weeks premating, 2 weeks mating, gestation, and lactation for F_0 and F_1 parental mice Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for increased incidences of centrilobular hepatocellular hypertrophy in males and females Reproductive toxicity: NOAEL = 50 mg/kg bw-day LOAEL = 600 mg/kg bw-day for increased gestation length, decreased epididymal sperm concentration in F_1 males, increased incidence of gross ovarian cysts in F_1 and F_2 females BMD_1 (change of 1 standard deviation from control) reported for increased gestation length F_0 = 1144 mg/kg-day (BMDL = 599 mg/kg-day) F_1 = 772 mg/kg-day (BMDL = 531 mg/kg-day) BMD_{10s} (10% extra risk) reported for increased incidence of gross ovarian cysts F_0 = 225 mg/kg-day (BMDL = 141 mg/kg-day) F_1 = 202 mg/kg-day (BMDL = 120 mg/kg-day)	Chapin et al. 2008; NTP-CERHR, 2008	Adequate; guideline study as reported in the secondary source. Classified by NTP-CERHR as having as High Utility.

Bisphenol A CASRN 80-05-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Summary of Reproductive Effects	A large experimental animal literature was reviewed by the NTP-CERHR Expert Panel, assessed for its utility, and weighted based on the criteria established by this expert panel, including an evaluation of experimental design and statistical procedures. These animal data are assumed relevant for the assessment of human hazard. The NTP-CERHR Expert Panel concluded the following: Female effects: There is sufficient evidence in rats and mice that BPA causes female reproductive toxicity with subchronic or chronic oral exposures with a NOAEL of 50 mg/kg bw-day and a LOAEL of 500 mg/kg bw-day. Male effects: There is sufficient evidence in rats and mice that BPA causes male reproductive toxicity with subchronic or chronic oral exposures with a NOAEL of 50 mg/kg bw-day and a LOAEL of 500 mg/kg bw/day.	Chapin et al. 2008; NTP-CERHR, 2008	Classified by NTP-CERHR as having High Utility.
		The joint FAO/WHO Expert Panel reviewed located reproductive and developmental toxicity data for BPA as of November 2010 and noted that most regulatory bodies reviewing the numerous studies on BPA have indicated an oral reproductive and developmental NOAEL of 50 mg/kg bw-day.	FAO/WHO, 2011	Summary of data, data quality, and conclusions from the expert panel.

Bisphenol A CASRN 80-05-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Regarding the potential for low oral doses (<1 mg/kg bw-day) of BPA to alter reproduction and development in rodents, the FAO/WHO noted that: (1) There is sufficient evidence that BPA ***does not:*** * induce gross morphological reproductive abnormalities in F_1 offspring; * reduce F_1 pup survival or body weight; * alter F_1 growth or survival during lactation; * alter F_1 anogenital distance in males or females; or * cause under masculinization of male morphology or masculinization of female morphology. (2) There is evidence (with some uncertainty) that BPA ***does not:*** * reduce P0 implantation, infertility, or fecundity. (3) There is conflicting evidence (with higher uncertainty) that BPA: * alters F_1 pubertal landmarks; * alters P0 male or female reproductive tract organ weights or histopathology; and * alters F_1 male reproductive tract organ weights or histopathology and semen parameters. Furthermore, changes in brain biochemical signaling, morphometric, and cellular endpoints within sexually dimorphic anatomical structures and neuroendocrine endpoints were reported at dietary exposures **below 5 mg/kg bw-day.**		

Bisphenol A CASRN 80-05-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Methodological limitations introduce uncertainty in interpretation of the findings.		
Developmental Effects		**HIGH: The NTP-CERHR (2008) Expert Panel concluded that there is suggestive evidence that BPA causes neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01-0.2 mg/kg bw-day) following developmental exposures. The FAO/WHO (2011) Expert Panel also concluded that while there was broad agreement in a NOAEL of 50 mg/kg bw-day for developmental toxicity based on standard bioassays, specific targeted studies identified neurodevelopmental effects at low doses (<1 mg/kg bw-day), but the human relevance is less certain. There is great variation in results with different types of studies measuring different endpoints; developmental effects at lower doses cannot be ruled out. Taken together these findings support a hazard designation of High concern.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Summary of Developmental Effects	The NTP-CERHR Expert Panel concluded that BPA: * does not cause malformations or birth defects in rats or mice at levels up to the highest doses evaluated: 640 mg/kg/day (rats) and 1,250 mg/kg bw-day (mice). * does not alter male or female fertility after gestational exposure up to doses of 450 mg/kg bw/day in the rat and 600 mg/kg bw-day in the mouse (highest dose levels evaluated). * does not permanently affect prostate weight at doses up to 500 mg/kg bw-day in adult rats or 600 mg/kg bw-day in mice. * does not cause prostate cancer in rats or	Chapin et al., 2008; NTP–CERHR, 2008	Summary of data, data quality, and conclusions from the expert panel.

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		mice after adult exposure at up to 148 or 600 mg/kg bw-day, respectively. * does change the age of puberty in male or female rats at high doses (ca. 500 mg/kg bw-day). And that rodent studies ***suggest*** that BPA: * causes neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01-0.2 mg/kg bw-day).		
		The joint FAO/WHO Expert Panel reviewed reproductive and developmental toxicity data for BPA located as of November 2010 and noted that most regulatory bodies reviewing the numerous studies on BPA have indicated an oral reproductive and developmental NOAEL of 50 mg/kg bw-day. Regarding the potential for low oral doses (<1 mg/kg bw-day) of BPA to alter reproduction and development in rodents, the FAO/WHO noted that: (1) There is sufficient evidence that BPA ***does not:*** *induce gross morphological reproductive abnormalities in F_1 offspring; *reduce F_1 pup survival or body weight; *alter F_1 growth or survival during lactation; *alter F_1 anogenital distance in males or females; or	FAO/WHO, 2011	Summary of data, data quality, and conclusions from the expert panel.

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		*cause under masculinization of male morphology or masculinization of female morphology. (2) There is evidence (with some uncertainty) that BPA ***does not:*** *reduce P0 implantation, infertility or fecundity. (3) There is conflicting evidence (with higher uncertainty) that BPA: *alters F_1 pubertal landmarks; *alters P0 male or female reproductive tract organ weights or histopathology; and *alters F_1 male reproductive tract organ weights or histopathology and semen parameters. Furthermore, changes in brain biochemical signaling, morphometric and cellular end-points within sexually dimorphic anatomical structures and neuroendocrine end-points were reported at dietary exposures **below 5 mg/kg bw-day.** Methodological limitations introduce uncertainty in interpretation of the findings.		
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on structural alert.

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Repeated Dose Effects	**MODERATE: BPA produced histopathologic changes in the liver (centrilobular hepatocyte hypertrophy) from oral dosing at 50 mg/kg bw-day (NOAEL = 5 mg/kg bw-day) and there is uncertainty regarding the potential for BPA doses between the NOAEL of 5 mg/kg bw-day and the LOAEL of 50 mg/kg-day to cause adverse systemic effects. Furthermore, lesions in the nasal cavity of rats were reported following repeated inhalation exposure to BPA dust at 0.05 mg/L. These findings indicate a Moderate hazard concern for the oral and inhalation exposure routes.**		
	The FAO/WHO Expert Panel reviewed the located information regarding repeated-dose oral toxicity of BPA and concluded that results demonstrated effects on the liver, kidney, and body weight at doses of 50 mg/kg bw-day and higher and that the lowest NOAEL was 5 mg/kg-day, as identified in several studies.	FAO/WHO, 2011	Summary of data, data quality, and conclusions from the expert panel.
	Multigenerational dietary study on fertility and reproductive performance in Sprague-Dawley rats (30/sex/group) BPA concentrations: 0, 0.015, 0.3, 4.5, 75, 750, and 7,500 ppm (Tyl, et al., 2002 estimated target doses of 0, 0.0095, 0.019, 0.285, 5, 50, and 500 mg/kg bw-day) Exposure period: 10 weeks premating, 2 weeks mating, gestation (parental males and females), lactation (parental females); similar exposure regimen for F_1 and F_2 parental males and females; F_3 weanlings exposed for 10 weeks Parental systemic toxicity: NOAEL = 4.75 mg/kg bw-day LOAEL = 47.5 mg/kg bw-day for 12% decreased terminal body weight in F_1 parental males	Chapin et al. 2008; NTP-CERHR, 2008	Adequate; guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Two-generation dietary study of fertility and reproductive performance in CD-1 mice (28/sex/group) Dietary concentrations: 0, 0.018, 0.18, 1.8, 30, 300, and 3,500 ppm (Tyl, et al., 2002 estimated target doses of 0.003, 0.03, 0.3, 5, 50, and 600 mg/kg bw-day) Exposure period: 8 weeks premating, 2 weeks mating, gestation, lactation for F_0 and F_1 parental mice Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for increased incidences of centrilobular hepatocellular hypertrophy in males and females	Chapin et al. 2008; NTP-CERHR, 2008	Adequate; guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.
	Inhalation study (whole body, dust) in Fischer 344 rats Exposure concentrations: 0, 10, 50, 150 mg/m^3 (0, 0.01, 0.05, 0.15 mg/L) Exposure period: 6 hours/day, 5 days/week for 13 weeks NOAEL = 0.01 mg/L LOAEL = 0.05 mg/L based on microscopic changes in the anterior portion of the nasal cavity Nasal epithelium changes were reversible (not apparent after 4-week recovery period)	EINECS, 2010; European Commission, 2000	Adequate.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Inhalation study in rats (species not defined) Exposure concentrations: 0, 15-86 mg/m^3; Mean = 47 mg/m^3 (0.047 mg/L) Exposure period: 4 hours/day for 4 months. NOAEL = None established LOAEL = 0.047 mg/L for decreased body weight gain, increased liver and kidney weight, unspecified "morphological changes" in liver, kidney, and lungs	European Commission, 2000; EINECS, 2010	Inadequate; single exposure level, insufficient study details in secondary sources.
		Inhalation study in male Alderley Park rats Exposure concentrations: Saturated atmosphere Exposure period: 6 hours/day for five exposures Results: No signs of toxicity, no gross macroscopic changes	EINECS, 2010	Inadequate; single exposure level, insufficient study duration, lack of study details in secondary sources.
Skin Sensitization		**MODERATE: Recent data from three BPA manufacturing facilities indicate that BPA does not elicit skin sensitization. However, results of some human studies suggest the possibility of a dermal sensitization response, although cross-sensitization was not ruled out. Most animal studies were negative for dermal sensitization, although assays may not have been maximized. There is evidence of ear swelling in a photoallergy test in mice and moderate redness and swelling following repeated dermal exposure in rabbits. Based on suggestive evidence of skin sensitization in humans and mice, a Moderate hazard designation is warranted.**		
	Skin Sensitization	Negative in a modified local lymph node assay of mice administered BPA epicutaneously on the ears at concentrations up to 30% on 3 consecutive days.	EINECS, 2010	Adequate, although the assay did not include concentrations >30%.
		Negative in a local lymph node assay modified to test for photoreactivity in mice administered BPA epicutaneously on the ears at concentrations up to 30% on 3 consecutive days and irradiated with UV light immediately following application.	EINECS, 2010	Adequate, although the assay did not include concentrations >30%.

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		Negative in several sensitization tests using guinea pigs.	European Commission, 2000; EINECS, 2010	Inadequate; study details lacking and induction and challenge concentrations may not have been maximized.
		Negative, mouse; BPA applied as 1% solution in acetone and corn oil for 2 days; induced UV-photosensitization on flank and ears.	European Commission, 2000	Inadequate; insufficient experimental details.
		Positive in 2/16 guinea pigs receiving BPA (50% in dimethyl phthalate) for 4 hours (occluded) once per week for 3 weeks and single challenge (4 hours occluded) 2 weeks later.	European Commission, 2000; EINECS, 2010	Inadequate; insufficient experimental details.
		Positive, mouse ear swelling photoallergy test.	European Commission, 2000	Inadequate; no data on concentrations, methods, or GLP.
		Negative in comprehensive medical surveillance data obtained from three BPA manufacturing plants for 875 employees examined for several years where workers were potentially exposed to other chemicals (phenol, acetone) that are not considered to be skin sensitizers.	EINECS, 2010	Adequate.
		Positive, rabbits; repeated dermal application (30 times over 37 days) of BPA (pure powder) produced moderate swelling and redness; skin turned yellow followed by dark pigmentation after day 15.	NIOSH, 2010	Adequate.
		Limited human data provide suggestive evidence that BPA may potentially act as a dermal sensitizer, although concomitant exposure to other potential dermal sensitizers may reflect a cross-sensitization	EINECS, 2010	Inadequate; possible cross-sensitization responses.

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		response.		
		The Joint FAO/WHO Expert Meeting review of the toxicological aspects of BPA concludes that BPA is capable of producing a skin sensitization response in humans.	FAO/WHO, 2011	Summary of data, data quality, and conclusions from the expert panel.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**MODERATE: BPA was slightly to highly irritating to rabbit eyes.**		
	Eye Irritation	Rabbit, slightly to highly irritating	EINECS, 2010; European Commission, 2000	Adequate; study details provided for multiple studies indicate potential for BPA to cause eye irritation.
Dermal Irritation		**MODERATE: BPA was slightly irritating to moderately irritating to rabbit skin. NIOSH has assigned BPA as a skin irritant.**		
	Dermal Irritation	Rabbit, nonirritating to slightly irritating when applied as undiluted or 10% aqueous suspension to intact or abraded skin.	European Commission, 2000; EINECS, 2010; NIOSH, 2010	Adequate; study details provided for multiple studies indicate potential for BPA to cause dermal irritation.
		Rabbit, moderately irritating when applied as 40% solution in dimethyl sulfoxide under non-occlusive conditions.	European Commission, 2000	Adequate.
		Guinea pig, not irritating when applied as 5% solution in acetone for 24 hours under occlusive conditions.	European Commission, 2000	Adequate.
		Although a limited number of studies were identified that contained data on the direct hazard of skin exposures to BPA, located evidence indicates that mild skin irritation following prolonged dermal exposure may occur. Therefore, on the basis of the data for this assessment, BPA is assigned the SK: DIR (IRR) notation; (potential to be a skin irritant following exposure to the skin).	NIOSH, 2010	Adequate; summary of conclusions provided by NIOSH.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Endocrine Activity	**BPA displays endocrine activity in *in vitro* assays, but yields mixed results in *in vivo* studies. *In vitro* assays demonstrate that BPA can bind to estrogen receptors, elicit estrogen-induced gene transcription, induce progesterone receptors, and induce cell proliferation in MCF7 cancer cells. The data located indicate that the *in vitro* endocrine activity of BPA is approximately 3-5 orders of magnitude less than that of 17β-estradiol, although the results are influenced by cell-type. *In vitro* assays suggest that BPA did not elicit an androgenic response but there is some evidence of anti-androgenic activity. Limited comparative *in vitro* data suggest that the estrogenicity of BPA is similar in magnitude to that of bisphenol AP, bisphenol C, and bisphenol F and somewhat more potent than bisphenol S. Based on *in vitro* data, there is also evidence of biological interactions involving rapid signaling networks. Data from *in vivo* studies exhibit a more complex picture; oral BPA does not consistently produce robust estrogenic responses. EINECS provides summary data to suggest that BPA has been shown to act as an estrogen or xenoestrogen in ecological systems.**		
	Reviews		
	The estrogenicity of BPA has since been evaluated using several different kinds of *in vitro* assays, including binding assays, recombinant reporter systems, MCF-7 cells, rat pituitary cells, rat uterine adenocarcinoma cells, human adenocarcinoma cells, fish hepatocytes (vitellogenin production), and frog hepatocytes (vitellogenin production). According to the NTP-CERHR Expert Panel, there is considerable variability in the results of these studies with the estrogenic potency of BPA ranging over about 8 orders of magnitude.	NTP-CERHR, 2008	Summary of data, data quality, and conclusions from NTP-CERHR.
	A number of *in vivo* tests have been conducted with most of the focus on effects on uterine weight in immature or ovariectomized animals. These studies indicate that the potency of BPA in increasing uterine weight varies over ~4 orders of magnitude. According to the NTP-	NTP-CERHR, 2008	Summary of data, data quality, and conclusions from NTP-CERHR.

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	CERHR Expert Panel, oral BPA does not consistently produce robust estrogenic responses and, when seen, estrogenic effects after oral treatment occur at high-dose levels.		
	A limited number of studies have evaluated androgen activity of BPA. These studies provide little evidence of androgenic effects, but there is limited evidence of antiandrogenicity.	NTP-CERHR, 2008	Summary of data, data quality, and conclusions from NTP-CERHR.
	Positive estrous response; subcutaneous injections of BPA to ovariectomized rats (strain not specified) (positive response measured by cornification in vaginal smears).	European Commission, 2000	Adequate.
	Numerous studies were located regarding the behavior of BPA as an estrogen or xenoestrogen in ecological organisms. Important results include findings that BPA increases plasma vitellogenin concentration in freshwater and saltwater fish at a potency in the range of 10^{-4} that of 17β-estradiol and that BPA can bind to the estrogen receptor of fish, albeit at a lower affinity than that of 17β-estradiol.	EINECS, 2010	Adequate.
	BPA can interact with non-classic estrogen receptor systems at similar or lower concentrations than interactions with ERα and ERβ. BPA has a high binding affinity to estrogen-related receptor-γ (ERRγ), an orphan receptor that shares a sequence homology with ERα and ERβ but is not activated by estradiol.	NTP, 2010	Adequate.

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	BPA also impacts cellular physiology through rapid signaling mechanisms, independent of nuclear hormone receptor activity, to modify the activities of various intracellular signaling networks. Maximal rapid signaling effects for BPA and 17β-estradiol are often observed at similar concentrations.	NTP, 2010	Adequate.
	Representative *in vitro* studies **Receptor Binding Assays**		
	In a human ER binding assay, the relative binding affinity (RBA) of BPA was 0.195% compared to 126% for 17β-estradiol. RBAs for other bisphenol compounds included 0.129% for bisphenol C, 0.0803% for bisphenol AP, 0.0719% for bisphenol F, and 0.0055% for bisphenol S. An RBA of 0.00473% was reported for PHBB.	METI, 2002	Adequate.
	In a competitive ER binding assay using human ERα, the RBA for BPA was 0.32% that of 17β-estradiol. RBAs for other bisphenol compounds included 1.68% for bisphenol C, 1.66% for bisphenol AP, and 0.09% for bisphenol F.	Coleman, Toscano et al., 2003	Adequate.
	In a rat uterine cytosol assay that evaluated ER binding affinity, ER binding affinities for BPA and bisphenol F were approximately 3 orders of magnitude less than that for 17β-estradiol.	Perez, Pulgar et al., 1998	Adequate.
	In a rat uterine cytosolic ER-competitive binding assay, results for BPA, bisphenol S, and PHBB indicated a weak affinity for ER.	Laws, Yavanhxay et al., 2006	Adequate.

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	BPA exhibited weak ER binding activity in preparations from uteri of ovariectomized Sprague-Dawley rats as evidenced by a relative binding affinity (RBA) that was 0.008% of the binding affinity of 17β-estradiol. RBAs for other tested chemicals included 0.003% for PHBB, 0.0009% for bisphenol F, and 0.0007% for the proprietary substituted phenolic compound.	Blair, Branham et al., 2000	Adequate.
	Representative *in vitro* studies **Gene Transcription Assays**		
	BPA exhibited evidence of estrogenic activity in a yeast (*Saccharomyces cerevisiae*) two-hybrid assay using ERα and the coactivator TIF2. Based on estrogenic activity that was 5 orders of magnitude lower than that of 17β-estradiol, BPA was considered weakly estrogenic. Assessment of other bisphenols resulted in a ranking of relative potency as follows: bisphenol C ≥ BPA > bisphenol F > bisphenol S.	Chen, Michihiko et al., 2002	Adequate.
	BPA exhibited estrogenic activity approximately 10,000-fold less than that of 17β-estradiol) in an *in vitro* recombinant yeast estrogen assay; the estrogenic activities of bisphenol F and PHBB were 9,000-fold and 4,000-fold less than that of 17β-estradiol.	Miller, Wheals et al., 2001	Adequate.
	BPA exhibited evidence of estrogenic activity in a yeast (*Saccharomyces cerevisiae*) two-hybrid assay using ERα and the coactivator TIF2.	Nishihara, Nishikawa et al., 2000	Adequate.

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	In a yeast two-hybrid system (reporter gene assay) using β-galactosidase activity as a measure of estrogenic activity, an estrogenic response was elicited by BPA and bisphenol F but not by bisphenol S.	Hashimoto and Nakamura, 2000	Adequate.
	In a yeast two-hybrid assay (reporter gene assay) using β-galactosidase activity as a measure of estrogenic activity, an estrogenic response was elicited by BPA and bisphenol F.	Ogawa, Kawamura et al. 2006	Adequate.
	In a reporter gene assay of estrogen-induced transcriptional activity, relative activity (RA) for BPA was 0.00278% compared to 81.7% for 17β-estradiol. RAs for other bisphenol compounds included 0.00189% for bisphenol C, 0.000639% for bisphenol F, 0.000254% for bisphenol S, and 0.000184% for bisphenol AP. An RA of 0.000592% was reported for PHBB.	METI, 2002	Adequate.
	In an ER-mediated reporter gene expression assay, BPA induced reporter gene expression at a relative activity (RA) of $2.75x10^{-3}$ that of 17β-estradiol. RAs for other bisphenol compounds included $5.3x10^{-4}$ for bisphenol F, $4.9x10^{-4}$ for bisphenol C, and $9.0x10^{-5}$ for bisphenol AP.	Coleman, Toscano et al., 2003	Adequate.
	In an ERE-luciferase reporter assay using MCF-7 cells, an EC_{50} was 0.63 µM for BPA compared to an EC_{50} of $8.6x10^{-6}$ for 17β-estradiol (i.e., BPA was approximately 5 orders of magnitude less potent than 17β-estradiol at inducing estrogenic activity). EC_{50} values for other bisphenol compounds	Kitamura, Suzuki et al., 2005	Adequate.

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	included 0.42 µM for bisphenol C, 1.0 µM for bisphenol F, and 1.1 µM for bisphenol S.		
	In an ERE-luciferase reporter assay using MCF-7 cells in the presence of 17β-estradiol, neither BPA, bisphenol C, bisphenol F, bisphenol S, nor bisphenol M appeared to exert an anti-estrogenic effect.	Kitamura, Suzuki et al., 2005	Adequate.
	Representative *in vitro* studies **Progesterone Receptor Induction**		
	BPA induced progesterone receptors in cultured human mammary cancer cells (MCF-7) cells, but the magnitude of the induction was not specified.	EINECS, 2010; European Commission, 2000	Adequate.
	In an assay designed to evaluate estrogenic effects on the number of progesterone receptors (PgR) in MCF7 cells, 17β-estradiol, BPA, and bisphenol F each increased the concentration of PgR by approximately 10- to 15-fold.	Perez, Pulgar et al., 1998	Adequate.
	Representative *in vitro* studies **Cell Proliferation Assays**		
	In an E-SCREEN test of MCF7 cell proliferation (an indicator of estrogenic activity), the proliferative potency of BPA was approximately 10^{-5} that of 17β-estradiol, suggestive of a weakly estrogenic effect for BPA. The potency of bisphenol F was somewhat less than that of BPA.	Perez, Pulgar et al., 1998	Adequate.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In a proliferation assay of MCF-7 human breast cancer cells that contain ERα and ERβ and are known to proliferate in response to estrogens, BPA induced a proliferative response that was $2.0x10^{-3}$ that of 17β-estradiol. Proliferative values for other bisphenol compounds included $1.6x10^{-3}$ for bisphenol C, $1.0x10^{-3}$ for bisphenol F, and $6.0x10^{-4}$ for bisphenol AP.	Coleman, Toscano et al., 2003	Adequate.
	In an E-screen test for estrogenicity, BPA and bisphenol F increased proliferation of MCF-7 cells with EC_{50} values of 410 nM and 84.8 nM, respectively, compared to an EC_{50} of 0.0045 nM for 17β-estradiol. The results indicate a weak estrogenic effect with bisphenol F exerting a more potent effect than BPA.	Stroheker, Picard et al., 2004	Adequate.
	In an E-screen test for estrogenicity, BPA, bisphenol F, and bisphenol S increased proliferation of MCF-7 cells at concentrations in the range of 10^{-4} to 10^{-7} M. BPA appeared to be more effective than bisphenol S or bisphenol F.	Hashimoto, Moriguchi et al., 2001	Adequate.
	BPA increased the rate of proliferation of MCF-7 cells at 3-5 orders of magnitude less than that of 17β-estradiol.	EINECS, 2010; European Commission, 2000	Adequate.
	In an assay that measured induction and secretion of pS2 in cultured MCF7 cells (ELSA-pS2 immunoradiometric assay), induction of pS2 by BPA and bisphenol F was approximately 1,000-fold less than that of 17β-estradiol.	Perez, Pulgar et al., 1998	Adequate.

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	Representative *in vivo* studies		
	Exposure of immature female rats to BPA (gavage dosing once daily for 4 days) resulted in no apparent effects on uterine weight. Bisphenol F-treated rats exhibited significantly increased uterine weight. There were no effects on uterine weight of bisphenol F- or BPA-treated ovariectromized rats.	Stroheker, Picard et al., 2004	Adequate.
	In uterotrophic assays using ovariectomized mice, BPA treatment at doses in the range of 20 to 500 mg/kg/day for 3 days resulted in dose-related increased relative uterus weights of 147-185% that of controls compared to nearly 500% increased uterus weight in mice administered 17β-estradiol at 50 µg/kg/day. This result is indicative of an estrogenic effect *in vivo*.	Kitamura, Suzuki et al., 2005	Adequate.
	In an uterotrophic assay in which immature female rats were injected with bisphenol F, bisphenol S, or bisphenol M subcutaneously for three consecutive days, observed changes in uterine weight indicated that bisphenol F, bisphenol S, and bisphenol M exerted both estrogenic and anti-estrogenic responses.	Akahori, Makai et al., 2008	Adequate.
	Representative Androgen Assays		
	In an ARE-luciferase reporter assay using a mouse fibroblast cell line (NIH3T3 cells), neither BPA, bisphenol C, bisphenol F, nor bisphenol S exerted an androgenic effect	Kitamura, Suzuki et al., 2005	Adequate.

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		In an ARE-luciferase reporter assay using a mouse fibroblast cell line (NIH3T3 cells), BPA inhibited the androgenic activity of dihydrotestosterone. Anti-androgenic responses were elicited by bisphenol C, bisphenol F, and bisphenol S as well.	Kitamura, Suzuki et al., 2005	Adequate.
		BPA and bisphenol F induced androgenic effects in MDA-MB453 cells transfected with an AR responsive luciferase reporter gene; anti-androgenic effects were elicited in the presence of dihydrotestosterone. Relative potency of the androgenic and anti-androgenic effects elicited by BPA was similar to that of bisphenol F.	Stroheker, Picard et al., 2004	Adequate.
		Representative Thyroid Assays		
		In an assay of thyroid hormonal activity whereby induction of growth hormone production is assessed in GH3 cells, neither BPA nor bisphenol C inhibited growth hormone production.	Kitamura, Suzuki et al., 2005	Adequate.
		BPA did not exhibit thyroid hormone receptor binding in a yeast two-hybrid assay system with TRα and coactivator TIF-2.	Kitagawa, Takatori et al., 2003	Adequate.
Immunotoxicity		**Sufficient data was not located to determine a hazard designation for the immunotoxicity endpoint.**		
	Immune System Effects (Included under Repeated Dose)	Rodent studies (direct or *in utero* exposure) suggest that BPA may modulate immune homeostasis, but due to study variations and deficiencies, there is no clear evidence that BPA interferes with immune function.	Willhite, Ball et al., 2008; FAO/WHO, 2011	Inadequate; few of the studies followed regulatory protocols (U.S. EPA, 1999) or GLP requirements.
ECOTOXICITY				
ECOSAR Class		Phenols		

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Toxicity	**HIGH: Based on experimental data indicating a High hazard concern for fish, Daphnid, and green algae.**		
Fish LC_{50} **Freshwater**	*Oryzias latipes* (Medaka fish) 96-hour LC_{50} = 13 mg/L (Experimental)	EINECS, 2010; Wright-Walters et al., 2011	Adequate; guideline study (OECD 204).
	Oryzias latipes (Medaka fish, early life stage) 96-hour LC_{50} = 13.9 mg/L (Experimental)	Wright-Walters et al., 2011	Adequate; secondary source considered the study valid. Test concentrations were not analytically measured.
	Oryzias latipes (Medaka fish) 72-hour LC_{50} = 5.1 mg/L (embryo) 72-hour LC_{50} = 6.8 mg/L (adult male) 72-hour LC_{50} = 8.3 mg/L (adult female) (Nominal, daily renewal)	EINECS, 2010; Wright-Walters, et al., 2011	Adequate; secondary sources considered the study valid. Measured test concentrations.
	Pimephales promelas (fathead minnow) 96-hour LC_{50} = 4.7 mg/L (static) 96-hour LC_{50} = 4.6 mg/L (flow-through) (Experimental) No toxicity at levels ≤2.29 mg/L	Alexander, Dill et al., 1988; EINECS, 2010; European Commission, 2000	Adequate; ASTM guideline study. Similar LC_{50} values for static and flow-through measurements indicated stability of BPA in water during the 96-hour test period.
	Multiple additional studies of freshwater fish species reported 48-96-hour LC_{50} values in the range of 3-15 mg/L	European Commission, 2000; Wright-Walters et al., 2011	Although individual studies were inadequate based on lack of provided study details or insufficient exposure duration, the LC_{50} range supports the results of studies considered adequate.
	Fish 96-hour LC_{50} = 12 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Fish 96-hour LC_{50} = 2 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.11	

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Fish LC_{50} Saltwater	*Menidia menidia* (silverside fish) 96-hour LC_{50} = 9.4 mg/L (flow-through) (Experimental) No discernible effect concentration >4.8 mg/L	EINECS, 2010; Wright-Walters et al., 2011; European Commission, 2000	Adequate; U.S. EPA guideline study.
	Cyprinodon variegates (sheepshead minnow) 96-hour LC_{50} = 7.5 mg/L (Experimental)	EINECS, 2010	Adequate; EINECS considered the study "apparently valid", but noted missing data such as pH, temperature, dissolved oxygen.
Daphnid LC_{50}	*Daphnia magna* (water flea) 48-hour EC_{50} = 10.2 mg/L (Experimental)	EINECS, 2010; European Commission, 2000; Alexander, Dill et al., 1988	Adequate; ASTM guideline study.
	Daphnia magna (water flea) 48-hour EC_{50} = 3.9 mg/L (Nominal)	EINECS, 2010; European Commission, 2000	Adequate; European Commission, 2000 indicates that analytical monitoring was used.
	Daphnid 48-hour LC_{50} = 7.9 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid 48-hour LC_{50} = 9.3 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.11	
Saltwater Invertebrate LC_{50}	*Mysidopsis bahia* (mysid shrimp) 96-hour LC_{50} (flow-through) = 1.1 mg/L (Experimental)	EINECS, 2010; European Commission, 2000; Alexander, Dill et al., 1988	Adequate; OPPT 830.1035 guideline study.
	Acartia tonsa (copepod) 48-hour LC_{50} (static) = 3.4-5.0 mg/L (Nominal)	EINECS, 2010	Inadequate; nominal concentrations only, organisms 10-12 days old at start of test.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae EC_{50} Freshwater	*Pseudokirchneriella subcapitata* 96-hour EC_{50} = 2.7 mg/L (biomass) 96-hour EC_{50} = 3.1 mg/L (cell volume) (Experimental)	EINECS, 2010; European Commission, 2000; Alexander, Dill et al., 1988	Adequate; ASTM guideline study.
	Pseudokirchneriella subcapitata 96-hour EC_{50} (biomass) = 2.5 mg/L (Experimental)	European Commission, 2000	Inadequate; test conditions not specified in secondary source.
	Green algae 96-hour EC_{50} = 9.7 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Green algae 96-hour EC_{50} = 1.7 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.11	
Green Algae EC_{50} Saltwater	*Skeletonema costatum* 96-hour EC_{50} = 1.0 mg/L (biomass) 96-hour EC_{50} = 1.8 mg/L (chlorophyll a content) (Experimental)	European Commission, 2000; Wright-Walters, Volz et al., 2011; Alexander, Dill et al., 1988	Adequate; ASTM guideline study. Cell count and chlorophyll a content are both measures of biomass.
Chronic Aquatic Toxicity	**HIGH: Based on experimental data from multiple studies indicating a High hazard concern for fish.**		
Fish ChV	*Branchydanio rerio* (Zebrafish) 14-day survival NOEC = 3.2 mg/L LOEC = 10.15 mg/L (Experimental)	EINECS, 2010; Wright-Walters, Volz et al., 2011	Adequate; guideline study (OECD 204).
	Branchydanio rerio (Zebrafish) growth and reproduction NOEC = 0.75 mg/L LOEC = 1.5 mg/L	EINECS, 2010; Wright-Walters, Volz et al., 2011	Inadequate; lack of experimental design details.

Bisphenol A CASRN 80-05-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	(Experimental)		
	Oryzias latipes (Medaka fish) 60-day survival: NOEC = 1.82 mg/L Growth: NOEC = 0.355 mg/L LOEC = 1.82 mg/L (Experimental)	EINECS, 2010; Wright-Walters, Volz et al., 2011	Adequate; modified OECD 210 early life stage study.
	Oryzias latipes (Medaka fish) 14-day hatchability NOEC = 6.25 mg/L LOEC = 12.5 mg/L (Nominal)	EINECS, 2010; Wright-Walters, Volz et al., 2011	Adequate; early life stage toxicity study, although test concentrations apparently not measured analytically.
	Oryzias latipes (Medaka fish) 21-day reproductive capacity test NOEC = 3.1 mg/L (Experimental)	EINECS, 2010	Adequate; reproductive toxicity study of adult fish. Test methods subsequently recommended by OECD for elucidation of effects on survival, growth, and reproduction of potential endocrine disrupting compounds.
	Oryzias latipes (Medaka fish) 14-day hatchability NOEC = 0.68 mg/L LOEC = 2.3 mg/L (Experimental)	EINECS, 2010; Wright-Walters, Volz et al., 2011	Inadequate; early life stage toxicity study, insufficient study details in secondary sources. Test concentrations not measured analytically.
	Pimephales promelas (Fathead minnow) multigenerational toxicity study Survival, growth: NOEC = 0.16 mg/L LOEC: = 0.64 mg/L Hatchability: NOEC = 0.016 mg LOEC = 0.16 mg/L	EINECS, 2010; Wright-Walters, Volz et al., 2011	Adequate, although secondary sources did not mention guidelines followed. Test concentrations were analytically measured.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	(Experimental)		
	Pimephales promelas (Fathead minnow) 32-day post-hatch survival and growth NOEC = 0.64 mg/L (Experimental)	Wright-Walters, Volz et al., 2011	Adequate; considered valid GLP study by secondary source. Chemical exposures measured analytically.
	Pimephales promelas (Fathead minnow) 29-30 day survival, growth, and development study Survival, growth: NOEC = 1.0 mg/L Development: NOEC = 0.1 mg/L (Experimental)	Wright-Walters, Volz et al., 2011	Adequate; considered valid GLP study by secondary source. Chemical exposures measured analytically.
	Oncorhynchus mykiss (Rainbow trout) 28-day growth NOEC = 3.64 mg/L LOEC = 11 mg/L (Experimental)	EINECS, 2010; Wright-Walters, Volz et al., 2011	Adequate; guideline study (OECD 215) of juvenile growth rate.
	Cyrinus carpio (carp) 28- and 49-day growth 28-day NOEC = 0.6 mg/L 49-day NOEC = 0.1 mg/L (Experimental)	EINECS, 2010	Adequate; guideline study (not specified).
	Cyrinus carpio (carp) 28-day survival/ growth NOEC = 0.74 mg/L (Experimental)	Wright-Walters, Volz et al., 2011	Inadequate; non-GLP and abstract only.
	Poecilia reticulata (guppy) 21-day sperm count LOEC = 0.274 mg/L (Experimental)	Wright-Walters, Volz et al., 2011	Inadequate; insufficient study details in secondary source.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Poecilia reticulata (guppy) 30-day survival NOEC = 0.5 mg/L LOEC = 5.0 mg/L (Experimental)	EINECS, 2010; Wright-Walters, Volz et al., 2011	Inadequate; insufficient study details in secondary source.
	Fish ChV = 1.4 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Fish ChV = 0.9 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.11	
Daphnid ChV	*Daphnia magna* 21-day survival, molting success, growth, reproduction NOEC = 3.16 mg/L (Experimental)	Caspers, 1998; EINECS, 2010; European Commission, 2000	Adequate; guideline study (OECD 202).
	Daphnid ChV = 1.1 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid ChV = 3.2 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.11	
Green Algae ChV	Green algae ChV = 3.3 mg/L (ECOSAR: Neutral organics)	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use

Bisphenol A CASRN 80-05-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
		Green algae ChV = 0.278 mg/L (ECOSAR: polyphenols)	ECOSAR version 1.11	
Teratogenicity in Frog Embryos		*Rana temporaria* (common frog) 20-day embryo survival NOEC = 0.1 mg/L LOEC = 1 mg/L (Experimental)	EINECS, 2010; Wright-Walters, Volz et al., 2011	Inadequate; embryos used, no chemical analysis of exposure concentrations.
		Xenopus laevis (African clawed frog) 90-day survival, growth, development NOEC = 0.5 mg/L (Experimental)	EINECS, 2010; Wright-Walters, Volz et al., 2011	Adequate GLP study, although study guidelines were not mentioned in the secondary source. Test concentrations were analytically measured.
		Xenopus laevis (African clawed frog) 12-week survival, growth NOEC = 0.23 mg/L (Experimental)	EINECS, 2010; Wright-Walters, Volz et al., 2011	Inadequate; study report lacks information regarding test conditions (e.g., temperature, water quality). Test concentrations were not analytically measured. Non-GLP study.
ENVIRONMENTAL FATE				
Transport		**Based on the Level III fugacity models incorporating the located experimental property data, BPA is expected to partition primarily to soil. BPA is expected to be moderately mobile in soil based on experimental K_{oc} studies. Leaching of BPA through soil to groundwater is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that it will be nonvolatile from surface water. Volatilization from dry surfaces is also not expected based on its measured vapor pressure. In the atmosphere, BPA is expected to exist in the particulate phase based on its measured vapor pressure. Particulates will be removed from air by wet or dry deposition.**		
	Henry's Law Constant(atm-m^3/mole)	$<1x10^{-8}$ (Estimated)	EPI	Cutoff value for nonvolatile compounds based on professional judgment.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	890 ± 30 L/kg OECD Test Guideline 106 (Measured)	Höllrigl-Rosta, Vinken et al., 2003; EINECS, 2010	Adequate, data from guideline study as reported in secondary source.
		795.9 OECD Test Guideline 106 (Measured)	Fent, Hein et al., 2003; EINECS, 2010	Adequate, data from guideline study as reported in secondary source.
		251-1507, mean value of 962 (Measured)	Ying and Kookana, 2005; EINECS, 2010	Adequate, data from guideline study as reported in secondary source.
		335-703, mean value of 375 (Measured)	Loffredo and Senesi, 2006; EINECS, 2010	Adequate, data from guideline study as reported in secondary source.
		778 (Measured)	Ying and Kookana, 2003; EINECS, 2010	Adequate, valid nonguideline study as reported in secondary source.
		115 (Measured)	Zeng, Zhang et al., 2006; EINECS, 2010	Adequate, valid nonguideline study as reported in secondary source.
		335-703; reported as Log K_{oc} = 2.53-2.85 at pH 4.5-5.9 (Measured)	Canada, 2008	Adequate, data from guideline study as reported in secondary source.
		The levels of BPA measured in water and bed sediments were used to calculate K_{oc} values. The range of results was 11,220-17,000 (log K_{oc} 4.04-4.23). (Measured)	Patrolecco, Capri et al., 2006; EINECS, 2010	Adequate, data are from a valid nonguideline study; K_{oc} values are likely for the unionized species.
	Level III Fugacity Model	Air = <1% (Estimated) Water = 8.4% Soil = 74% Sediment = 18%	EPI	Experimental water solubility (0.12 g/L) and vapor pressure ($3.99x10^{-8}$ mm Hg) used in model calculations.
Persistence		**VERY LOW: BPA has passed Ready Biodegradability tests, OECD 301 F and OECD 301C, within the 10-day window. Experimental data using a wide variety of innocula have demonstrated that rapid primary and ultimate biodegradation of BPA occurs under aerobic condition in water and soil. The biodegradation of BPA does not result in the formation of stable metabolites. Aerobic biodegradation processes are anticipated to be the predominant environmental removal process. Experimental data indicate that BPA does not biodegrade under anaerobic conditions. Although models suggest that BPA may display limited partitioning to sediment, it has been detected in sediment samples. BPA may also undergo removal by both direct and indirect photolysis in environmental waters, although this process is anticipated to be far slower than aerobic biodegradation processes.**		

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Water	**Aerobic Biodegradation**	OECD 301B: No biodegradation of BPA was observed with modified Sturm test (Measured)	EINECS, 2010	Adequate, data from a guideline study as reported in secondary source.
		OECD 301C: Reported biodegradation half-lives of <3.5 days in river surface water samples (Measured)	MITI, 1992; Canada, 2008	Adequate, data from a guideline study as reported in secondary source.
		OECD 301D: No biodegradation of BPA was observed with OECD 301D closed bottle test (Measured)	EINECS, 2010	Adequate, data from a guideline study as reported in secondary source.
		OECD 301F: Average percent removal by biochemical oxygen demand (BOD) was 89%; 10-day window met and no BPA detected by HPLC after 28 days (Measured)	CERI, 2004; EINECS, 2010	Adequate, data from a guideline study.
		OECD 301F: Rapid biodegradation by standard aerobic 28-day ready biodegradability test (Measured)	West and Goodwin, 1997; Canada, 2008; EINECS, 2010	Adequate, data from a guideline study.
		BPA met the criteria for inherently biodegradable substances; using a modified semi-continuous activated sludge (SCAS) procedure (Measured)	Turner and Watkinson, 1986; EINECS, 2010	Adequate, data from a valid nonguideline study.
		Degradation was noted in 40 of 44 river water systems; 6 river water systems were able to mineralize the substance completely and 34 showed total organic carbon (TOC) removal of 40-90% (Measured)	Ike, Chen et al., 2006; EINECS, 2010	Adequate, data from a valid nonguideline study.
		BPA biodegradation half-life of <4 days was measured in natural waters following a 1- to 4-day adaptation period – acclimation (Measured)	Dorn, Chou et al., 1987; Canada, 2008	Adequate, data from a valid nonguideline study.
		Biodegradation half-lives of 0.5-3.5 days in river surface water samples after a lag phase of 2-8 days (Measured)	Klečka, Gonsior et al., 2001; Canada, 2008	Adequate, data from a valid nonguideline study.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		River water samples had BPA biodegradation half-lives of 2, 3 and 6 days; BPA was completely degraded after 10-15 days (Measured)	Kang and Kondo, 2002; Canada, 2008; EINECS, 2010	Adequate, data from a valid nonguideline study.
		River water degradation of BPA half-life of 3-4 days; some seawater degradation of BPA after lag period of 30-40 days (Measured)	Kang and Kondo, 2005; EINECS, 2010	Adequate, data from a valid nonguideline study.
		>90% degradation after 56 days in seawater; or BPA degradation half-life of 14.4 after lag period of 35 days (Measured)	Ying and Kookana, 2003; EINECS, 2010	Adequate, data from a valid nonguideline study.
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**	Biodegradation half-life of 7 days (Measured)	EINECS, 2010; Canada, 2008; Ying and Kookana, 2005	Adequate, data from a valid nonguideline study.
		Biodegradation half-life of 3 days ^{14}C-BPA was transiently converted to up to five metabolites. The parent ^{14}C-BPA and ^{14}C-BPA metabolites were not detected after 3 days (Measured)	Fent, Hein et al., 2003; Canada, 2008	Adequate, data from a valid nonguideline study.
	Anaerobic Biodegradation	No biodegradation after 70 days (Measured)	Ying and Kookana, 2005; EINECS, 2010	Adequate, data from a valid nonguideline study.
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation	No biodegradation after 70 days; anaerobic conditions with aquifer water and sediment (Measured)	Ying and Kookana, 2003; Canada, 2008; EINECS, 2010	Adequate, data from a valid nonguideline study.
		50% dissipation times in days Aerobic conditions:	Canada, 2008	Invalid; losses of up to 40% of the initial amount applied occurred in the

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		river water-sediment test system: 0.57 groundwater-aquifer test system: 1.212 Anaerobic conditions: river water-sediment test system: 1.38 groundwater-aquifer test system: 2.75 (Measured)		sterile (control) treatments.
		BPA was not biodegraded under anaerobic conditions using estuarine sediments (Measured)	Voordeckers, Fennell et al., 2002	Adequate, data from a valid nonguideline study.
Air	**Atmospheric Half-life**	1.6 hours (Estimated)	EPI	
Reactivity	**Photolysis**	Direct and indirect photochemical transformation of BPA in aquatic media has been described (Measured)	Chin, Miller et al., 2004; Canada, 2008; EINECS, 2010	Adequate; the located secondary sources do not quantify the importance of this process, although it is not anticipated to compete with biodegradation in natural waters.
	Hydrolysis	Not a significant fate process (Estimated)	Wolfe and Jeffers, 2000; Professional judgment	Substance does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.
	Pyrolysis			No data located.
Environmental Half-life		75 days (Estimated)	EPI; PBT Profiler	Half-life estimated for the predominant compartment as determined by EPI and the PBT Profiler methodology.
Bioconcentration		**LOW: The measured fish BCF values reported for a number of experimental studies are <100.**		
	Fish BCF	3.5–68 (Measured)	Canada, 2008	As reported in secondary source.
		67 (Measured)	EINECS, 2010	As reported in secondary source.
		38 ± 21 L/kg in halibut (*Varaspar variegates*) (Measured)	EINECS, 2010; Lee, Soyano et al., 2004	As reported in secondary source.
		73.4 Killifish (*Oryzias latipes*) (Measured)	Takino, Tsuda et al., 1999; EINECS, 2010	Adequate.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		5.1-13.8 (Measured) <20-67.7 (Measured)	Canada, 2008; MITI, 1992	Adequate.
		3.5-5.5 (Measured)	Lindholst, Pedersen et al., 2001; Canada, 2008;	Adequate.
	Green Algae BCF	From the Tama River, Japan Periphytons: 18-650 Benthos: 8-170 (Measured)		Adequate.
	Earthworms BCF	7.9 kg/kg (Estimated)	EINECS, 2010	Adequate.
	Metabolism in fish	Metabolites identified 7 days after exposure in fish (*Danio rerio)* (Measured)	Kang, Katayama et al., 2006; Canada, 2008,	Adequate.
		Fish plasma half-life of BPA was calculated to be 3.75 hours following injection of the compound (Measured)	Lindholst, Pedersen et al., 2001; Canada, 2008	Adequate.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		BPA was detected in environmental samples, including those from groundwater, wastewater treatment plume water, landfill lagoon water, drinking water, streams and rivers, and sediments.		
Ecological Biomonitoring		BPA was found in ecological samples; detectable levels were found in snails, mussels, fish, clams, and zooplankton.		
Human Biomonitoring		BPA was detected in a variety of human biological samples including serum, breast milk, urine, fetal blood, and umbilical cord blood. This chemical was included in the NHANES biomonitoring report (CDC, 2011).		

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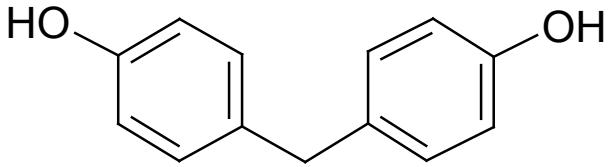
Bisphenol F



CASRN: 620-92-8

MW: 200.24

MF: $C_{13}H_{12}O_2$

Physical Forms:
Neat: Solid

Use: Developer for thermal paper

SMILES: OC(CCC(C1)CC(CCC(O)C2)C2)C1

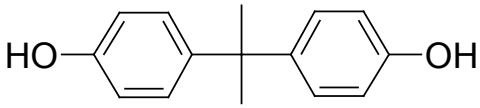
Synonyms: Phenol, 4,4'-methylenebis-; Bis(4-hydroxyphenyl)methane; 4,4'-Methylenebis(phenol); 4,4'-Dihydroxydiphenylmethane; 4,4'-Methylene diphenol; Bis(4-hydroxyphenyl)methane; Bis(p-hydroxyphenyl)methane; Phenol, 4,4'-methylenedi-; p,p'-Bis(hydroxyphenyl)methane; p-(p-Hydroxybenzyl)phenol

Polymeric: No
Oligomers: Not applicable

Metabolites, Degradates and Transformation Products: 4,4'-dihydroxybenzophenone, bis(4-hydroxyphenyl)methanol, 4-hydroxyphenyl-4-hydroxybenzoate, 4-hydroxybenzoate and 1,4-hydroquinine, sulfate conjugate of bisphenol F

Analog: Bisphenol A (80-05-7)
Endpoint(s) using analog values: Reproductive and developmental toxicity, dermal irritation

Analog Structure:



Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)

Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2011).

Risk Assessments: None identified

Bisphenol F CASRN 620-92-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	162.5 (Measured)	Lide, 2008	Adequate.
Boiling Point (°C)	Sublimes	Lide, 2008	Adequate.
Vapor Pressure (mm Hg)	$3.7x10^{-7}$ (Estimated)	EPI	
Water Solubility (mg/L)	190 (Estimated)	EPI	
Log K_{ow}	2.91 (Measured)	Hansch, Leo et al., 1995	Adequate.
Flammability (Flash Point)			No data located.
Explosivity			No data located.
pH			No data located.
pK_a	7.55 (Measured)	Serjeant and Dempsey, 1979	Adequate.

Bisphenol F CASRN 620-92-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Bisphenol F is readily absorbed following oral exposure and is widely distributed, metabolized to multiple metabolites, and excreted primarily in the urine and to a lesser extent in the feces.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Single gavage doses of 7 or 100 mg/kg [^{3}H]bisphenol F were administered to pregnant or nonpregnant Sprague-Dawley rats. Approximately 15-20% of the administered radioactivity was recovered in the urine during the first 24 hours postdosing, indicating that bisphenol F was readily absorbed. By 96 hours postdosing, nearly 50% of the dose had been recovered in the urine; fecal excretion accounted for <20% of the dose. Parent compound accounted for <25% of the radioactivity in the urine and at least six urinary metabolites were detected; the major urinary metabolite (>50%) appeared to be a sulfate conjugate of bisphenol F. At 96 hours postdosing, <1% of the administered radioactivity was detected in selected organs and tissues; the highest levels were found in the liver (0.5% of dose). Radioactivity was detected in placenta, amniotic fluid, and fetuses of pregnant rats. In bile-cannulated rats, nearly 50% of an administered dose of [^{3}H]bisphenol F was collected in the bile between 2 and 8 hours postdosing, indicating the involvement of enterohepatic cycling of bisphenol F and/or its metabolites.	Cabaton, Chagnon et al., 2006	Adequate.

Bisphenol F CASRN 620-92-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Mammalian Toxicity		**LOW: Based on an experimental rat LD_{50} of 4,950 mg/kg. No data were located to assess acute inhalation or dermal toxicity.**		
Acute Lethality	**Oral**	Rat oral LD_{50} = 4,950 mg/kg	Smyth, Carpenter et al., 1962	Adequate.
	Dermal			No data located.
	Inhalation			No data located.
Carcinogenicity		**MODERATE: Estimated using OncoLogic expert system which describes a concern for this compound as a potential carcinogen or tumorigenesis promoter arising from its structural similarity to estrogenic/androgenic compounds, using the "phenols and phenolic compounds" structural alert.**		
	OncoLogic Results	Moderate (Estimated) OncoLogic class: phenols and phenolic compounds	OncoLogic	OncoLogic SAR analysis using the phenols and phenolic compounds class.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
Genotoxicity		**LOW: Bisphenol F did not cause gene mutations or chromosomal aberrations in located *in vitro* assays in multiple test strains and cell types. Bisphenol F did cause DNA damage in a Comet assay. However, assessment guidance indicates a low concern given the negative results for gene mutations and chromosomal aberrations assays.**		
	Gene Mutation *in vitro*	Negative; Ames assay in *Salmonella Typhimurium* strains TA98, TA100, TA1535, TA1537, and *Escherichia coli* W2 *uvrA* pKM101 with and without metabolic activation	Cabaton, Dumont et al., 2009	Adequate.
		Negative; umu test in *S. typhimurium* strain TA1335 with and without metabolic activation	Chen, Michihiko et al., 2002	Adequate.
		Negative; gene mutation tests at the Na+/K+ ATPase locus and hprt locus of Syrian hamster embryo cells	Tsutsui, Tamura et al., 2000	Adequate.

Bisphenol F CASRN 620-92-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Negative; chromosomal aberrations in Syrian hamster embryo cells	Tsutsui, Tamura et al., 2000	Adequate.
		Negative; micronucleus test in HepG2 cells	Cabaton, Dumont et al., 2009	Adequate.
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair	Positive; DNA damage (single and double strand breaks); Comet assay HepG2 cells	Cabaton, Dumont et al., 2009	Adequate.
	Other			No data located.
Reproductive Effects		**MODERATE: Estimated based on analogy to BPA. Key studies identified by NTP for the analog BPA indicate there are multiple distinct endpoints with NOAELs in the range of Moderate hazard concern with LOAELs in the range of Low hazard concern. At the target dose of 50 mg/kg-day (BPA), the NOAELs are on the margin of High and Moderate hazard, according to DfE criteria. Benchmark Dose (BMD) Modeling conducted by NTP, which interpolates between NOAEL and LOAEL values, yields values that further support a Moderate hazard designation. The limited test data on bisphenol F were inadequate for the evaluation of hazard using DfE criteria. Changes in uterine weight were reported following *in vivo* exposure in rats. However, a 28-day gavage study reported no effects on reproductive organ weights, estrous cycles, or spermatocytes at doses up to 500 mg/kg-day.**		
	Reproduction/ Developmental Toxicity Screen	Bisphenol F increased absolute and relative uterine weight in a rat uterotrophic assay.	Yamasaki, Noda et al., 2004	Adequate.
		28-Day study with Crj:CD Sprague-Dawley rats (10/sex/dose), gavaged with 0, 20, 100, or 500 mg/kg-day: **NOAEL = 500 mg/kg-day** (endocrine/reproductive parameters). No changes in spermatological findings, estrous cycles, reproductive organ weight, or thyroid weight.	Higashihara, Shiraishi et al., 2007	Adequate.

Bisphenol F CASRN 620-92-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Exposure to bisphenol F in immature rats resulted in a dose-dependent increase in relative wet and dry uterine weight and increased vaginal cornification in immature female Wistar rats. LOAEL = 100 mg/kg-day (based on increased relative wet uterine weight **NOAEL = 50 mg/kg-day**	Stroheker, Chagnon et al., 2003	Adequate.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

Bisphenol F CASRN 620-92-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction and Fertility Effects	Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for 12% decreased terminal body weight in F_1 parental males Reproductive toxicity: Females: NOAEL = 50 mg/kg bw-day LOAEL = 500 mg/kg bw-day for decreases in number of implantation sites, delayed vaginal opening in F_1, F_2, F_3 offspring BMDLs (change of 1 standard deviation from control) reported for delayed vaginal opening (females)- F_1 = 176 mg/kg-day F_2 = 228 mg/kg-day F_3 = 203 mg/kg-day Males: NOAEL = 50 mg/kg bw-day, LOAEL = 500 mg/kg-day for delayed preputial separation in F_1 males BMDLs (change of 1 standard deviation from control) reported for delayed preputial separation (males)- F_1 = 163 mg/kg-day F_2 = 203 mg/kg-day (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; adequate, guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.

Bisphenol F CASRN 620-92-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for increased incidences of centrilobular hepatocellular hypertrophy in males and females Reproductive toxicity: NOAEL = 50 mg/kg bw-day LOAEL = 600 mg/kg bw-day for increased gestation length, decreased epididymal sperm concentration in F_1 males, increased incidence of gross ovarian cysts in F_1 and F_2 females BMD_1 (change of 1 standard deviation from control) reported for increased gestation length F_0 = 1144 mg/kg-day (BMDL = 599 mg/kg-day) F_1 = 772 mg/kg-day (BMDL = 531 mg/kg-day) BMD_{10s} (10% extra risk) reported for increased incidence of gross ovarian cysts F_0 = 225 mg/kg-day (BMDL = 141 mg/kg-day) F_1 = 202 mg/kg-day (BMDL = 120 mg/kg-day) (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; adequate, guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.

Bisphenol F CASRN 620-92-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Female effects: There is sufficient evidence in rats and mice that BPA caused female reproductive toxicity with subchronic or chronic oral exposures with a NOAEL of 50 mg/kg bw-day and a LOAEL of 500 mg/kg bw-day. Male effects: There is sufficient evidence in rats and mice that BPA causes male reproductive toxicity with subchronic or chronic oral exposures with a NOAEL of 50 mg/kg bw-day and a LOAEL of 500 mg/kg bw/day. (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; Classified by NTP-CERHR as having High Utility.
		The joint FAO/WHO Expert Panel reviewed reproductive and developmental toxicity data for BPA located as of November 2010 and noted that most regulatory bodies reviewing the numerous studies on BPA have indicated an oral reproductive and developmental NOAEL of 50 mg/kg bw-day. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.

Bisphenol F CASRN 620-92-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Developmental Effects		**HIGH: Estimated based on analogy to BPA. The NTP-CERHR (2008) Expert Panel concluded that there is suggestive evidence that BPA causes neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01-0.2 mg/kg bw-day) following developmental exposures. The FAO/WHO (2011) Expert Panel also concluded that while there was broad agreement in a NOAEL of 50 mg/kg bw-day for developmental toxicity based on standard bioassays, specific targeted studies identified neurodevelopmental effects at low doses (<1 mg/kg bw-day), but the human relevance is less certain. There is great variation in results with different types of studies measuring different endpoints; developmental effects at lower doses cannot be ruled out. Taken together these findings support a hazard designation of High concern.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

Bisphenol F CASRN 620-92-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Summary of Developmental effects	The NTP-CERHR Expert Panel concluded that BPA: *does not cause malformations or birth defects in rats or mice at levels up to the highest doses evaluated: 640 mg/kg/day (rats) and 1,250 mg/kg bw-day (mice). *does not alter male or female fertility after gestational exposure up to doses of 450 mg/kg bw-day in the rat and 600 mg/kg bw-day in the mouse (highest dose levels evaluated). *does not permanently affect prostate weight at doses up to 475 mg/kg bw-day in adult rats or 600 mg/kg bw-day in mice. *does not cause prostate cancer in rats or mice after adult exposure at up to 148 or 600 mg/kg bw-day, respectively. *does change the age of puberty in male or female rats at high doses (ca. 475 mg/kg/day). And that rodent studies ***suggest*** that BPA: *causes neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01–0.2 mg/kg/day). (Estimated by analogy)	NTP–CERHR, 2008; Professional judgment	Based on the analog BPA.

Bisphenol F CASRN 620-92-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		The joint FAO/WHO Expert Panel reviewed reproductive and developmental toxicity data for BPA located as of November 2010 and noted that most regulatory bodies reviewing the numerous studies on BPA have indicated an oral reproductive and developmental NOAEL of 50 mg/kg bw-day.	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert. (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on structural alert.
Repeated Dose Effects		**HIGH: Based on adverse effects (12% lower body weight than controls; decreased total cholesterol, glucose, and albumin in the serum) in female rats administered bisphenol F by gavage for 28 days at 20 mg/kg-day (the lowest dose tested). Because the standard criteria thresholds are for 90-day studies, this study was evaluated using modified criteria at 3 times the threshold values.**		
		28-day oral study of Crj:CD Sprague-Dawley rats (10/sex/dose), gavaged with 0, 20, 100, or 500 mg/kg-day. **LOAEL = 20 mg/kg-day** (based on significant decreases in final mean body weight [12% less than controls], serum total cholesterol, glucose, and albumin in female rats).	Higashihara, Shiraishi et al., 2007	Adequate 28-day repeated dose toxicity study; this study will be evaluated using modified criteria at 3 times the thresholds because the standard thresholds are based on 90-day studies.
Skin Sensitization		**LOW: One study in guinea pigs suggested bisphenol F is not a skin sensitizer.**		
	Skin Sensitization	Negative for skin sensitizing capacity in guinea pig maximization test	Bruze, 1986	Adequate.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.

Bisphenol F CASRN 620-92-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Eye Irritation		**VERY HIGH: One study of rabbits indicated that bisphenol F caused severe eye injury.**		
	Eye Irritation	Severe corneal injury in rabbits	Smyth, Carpenter et al., 1962	Adequate.
Dermal Irritation		**MODERATE: Bisphenol F is estimated to be slightly irritating to moderately irritating to rabbit skin based on test data for the analog BPA. NIOSH has assigned the analog BPA as a skin irritant.**		
	Dermal Irritation	Rabbit, nonirritating to slightly irritating when applied as undiluted or 10% aqueous suspension to intact or abraded skin. (Estimated by analogy)	EINECS, 2010; European Commission, 2000; NIOSH, 2010; Professional judgment	Based on the analog BPA; the details provided for multiple studies indicate potential for BPA to cause dermal irritation.
		Rabbit, moderately irritating when applied as 40% solution in dimethyl sulfoxide under non-occlusive conditions. (Estimated by analogy)	European Commission, 2000; Professional judgment	Based on the analog BPA; adequate.
		Guinea pig, not irritating when applied as 5% solution in acetone for 24 hours under occlusive conditions. (Estimated by analogy)	European Commission, 2000; Professional judgment	Based on the analog BPA; adequate.
Endocrine Activity		**Based on *in vitro* and *in vivo* data. Bisphenol F exhibited estrogenic and anti-estrogenic activity in some *in vivo* studies of female rats. *In vitro* assays indicate that BPA can bind to estrogen receptors (ERs), elicit estrogen-induced gene transcription, induce progesterone receptors (PgR), and induce cell proliferation in MCF7 cancer cells. Bisphenol F has been shown to exhibit androgenic and anti-androgenic properties *in vitro*. Bisphenol F appears to exhibit estrogenic potency similar to or somewhat less than the potency of BPA.**		

Bisphenol F CASRN 620-92-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Receptor Binding Assays		
	Bisphenol F exhibited weak ER binding activity in preparations from uteri of ovariectomized Sprague-Dawley rats as evidenced by a relative binding affinity (RBA) that was 0.0009% of the binding affinity of 17β-estradiol. RBAs for other tested chemicals included 0.008% for BPA, 0.003% for PHBB, and 0.0007% for the proprietary substituted phenolic compound.	Blair, Branham et al., 2000	Adequate.
	In a human ER binding assay, the RBA of bisphenol F was 0.0719% compared to 126% for 17β-estradiol. RBAs for other bisphenol compounds included 0.195% for BPA, 0.129% for bisphenol C, 0.0803% for bisphenol AP, and 0.0055% for bisphenol S. An RBA of 0.00473% was reported for PHBB.	METI, 2002	Adequate.
	In a competitive ER binding assay using human ERα, the RBA for BPA was 0.32% that of 17β-estradiol. RBAs for other bisphenol compounds included 1.68% for bisphenol C, 1.66% for bisphenol AP, and 0.09% for bisphenol F.	Coleman, Toscano et al., 2003	Adequate.
	In a human ER binding assay, the RBA of bisphenol F was 0.0719% relative to 17β-estradiol (set at 100%). RBAs for other bisphenol compounds included 0.175% for bisphenol M and 0.0055% for BPA.	Yamasaki, Noda et al., 2004	Adequate.

Bisphenol F CASRN 620-92-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In a rat uterine cytosol assay that evaluated ER binding affinity, ER binding affinities for BPA and bisphenol F were approximately 3 orders of magnitude less than that for 17β-estradiol.	Perez, Pulgar et al., 1998	Adequate.
	Gene Transcription and Reporter Gene Assays		
	Bisphenol F exhibited evidence of estrogenic activity in a yeast (*Saccharomyces cerevisiae*) two-hybrid assay using ERα and the coactivator TIF2. Based on estrogenic activity that was 5 orders of magnitude lower than that of 17β-estradiol, BPA was considered weakly estrogenic. Assessment of other bisphenols resulted in a ranking of relative potency as follows: bisphenol C ≥ BPA > bisphenol F > bisphenol S.	Chen, Michihiko et al., 2002	Adequate.
	Bisphenol F exhibited estrogenic activity approximately 9,000-fold less than that of 17β-estradiol) in an *in vitro* recombinant yeast estrogen assay. The estrogenic activities of BPA and PHBB were 10,000-fold and 4,000-fold less than that of 17β-estradiol.	Miller, Wheals et al., 2001	Adequate.
	In a yeast two-hybrid system (reporter gene assay) using β-galactosidase activity as a measure of estrogenic activity, an estrogenic response was elicited by bisphenol F and BPA but not by bisphenol S.	Hashimoto and Nakamura, 2000	Adequate.

Bisphenol F CASRN 620-92-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In yeast two-hybrid systems (reporter gene assay) using β-galactosidase activity as a measure of estrogenic activity, an estrogenic response was elicited by bisphenol F and BPA both in the absence and presence of exogenous metabolic activation. Bisphenol S elicited a similar response only in the presence of exogenous metabolic activation.	Hashimoto and Nakamura, 2000; Hashimoto, Moriguchi et al. 2001	Adequate.
	In a yeast two-hybrid assay (reporter gene assay) using β-galactosidase activity as a measure of estrogenic activity, an estrogenic response was elicited by bisphenol F and BPA.	Ogawa, Kawamura et al. 2006	Adequate.
	In a reporter gene assay of estrogen-induced transcriptional activity, relative activity (RA) for bisphenol F was 0.000639% compared to 81.7% for 17β-estradiol. RAs for other bisphenol compounds included 0.00278% for BPA, 0.00189% for bisphenol C, 0.000254% for bisphenol S, and 0.000184% for bisphenol AP. An RA of 0.000592% was reported for PHBB.	METI, 2002	Adequate.
	In an ER-mediated reporter gene expression assay, bisphenol F induced reporter gene expression at a RA of $5.3x10^{-4}$ that of 17β-estradiol. RAs for other bisphenol compounds included $2.75x10^{-3}$ for BPA, $4.9x10^{-4}$ for bisphenol C, and $9.0x10^{-5}$ for bisphenol AP.	Coleman, Toscano et al., 2003	Adequate.

Bisphenol F CASRN 620-92-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In an ERE-luciferase reporter assay using MCF-7 cells, an EC_{50} was 1.0 µM for bisphenol F compared to an EC_{50} of $8.6x10^{-6}$ for 17β-estradiol (i.e., BPA was approximately 5 orders of magnitude less potent than 17β-estradiol at inducing estrogenic activity). EC_{50} values for other bisphenol compounds included 0.63% for BPA, 0.42 µM for bisphenol C, and 1.1 µM for bisphenol S.	Kitamura, Suzuki et al., 2005	Adequate.
	In an ERE-luciferase reporter assay using MCF-7 cells in the presence of 17β-estradiol, neither bisphenol F, BPA, bisphenol C, nor bisphenol S appeared to exert an anti-estrogenic effect	Kitamura, Suzuki et al., 2005	Adequate.
	Weakly estrogenic in a transcriptional activation assay using human ER and HepG2 cells.	Cabaton, Dumont et al., 2009	Adequate.
	Progesterone Receptor Induction		
	In an ERE-luciferase reporter assay using MCF-7 cells, an EC_{50} was 1.0 µM for bisphenol F compared to an EC_{50} of $8.6x10^{-6}$ for 17β-estradiol (i.e., BPA was approximately 5 orders of magnitude less potent than 17β-estradiol at inducing estrogenic activity). EC_{50} values for other bisphenol compounds included 0.63% for BPA, 0.42 µM for bisphenol C, and 1.1 µM for bisphenol S.	Kitamura, Suzuki et al., 2005	Adequate.

Bisphenol F CASRN 620-92-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In an assay designed to evaluate estrogenic effects on the number of progesterone receptors (PgR) in MCF7 cells, 17β-estradiol, bisphenol F, and BPA each increased the concentration of PgR by approximately 10- to 15-fold.	Perez, Pulgar et al., 1998	Adequate.
	Cell Proliferation Assays		
	Weakly estrogenic in a transcriptional activation assay using human ER and HepG2 cells.	Cabaton, Dumont et al., 2009	Adequate.
	In an E-screen test for estrogenicity, bisphenol F, BPA, and bisphenol S increased proliferation of MCF-7 cells at concentrations in the range of 10^{-4} to 10^{-7} M. BPA appeared to be more effective than bisphenol S or bisphenol F.	Hashimoto, Moriguchi et al., 2001	Adequate.
	In an E-SCREEN test of MCF7 cell proliferation (an indicator of estrogenic activity), the proliferative potency of BPA was approximately 10^{-5} that of 17β-estradiol, suggestive of a weakly estrogenic effect for BPA. The potency of bisphenol F was somewhat less than that of BPA.	Perez, Pulgar et al., 1998	Adequate.

Bisphenol F CASRN 620-92-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In an E-screen test for estrogenicity, bisphenol F and BPA increased proliferation of MCF-7 cells with EC_{50} values of 84.8 nM and 410 nM, respectively, compared to an EC_{50} of 0.0045 nM for 17β-estradiol. The results indicate a weak estrogenic effect with bisphenol F exerting a more potent effect than BPA.	Stroheker, Picard et al., 2004	Adequate.
	In a proliferation assay of MCF-7 human breast cancer cells that contain ERα and ERβ and are known to proliferate in response to estrogens, BPA induced a proliferative response that was $1.0x10^{-3}$ that of 17β-estradiol. Proliferative values for other bisphenol compounds included $2.0x10^{-3}$ for BPA, $1.6x10^{-3}$ for bisphenol C, and $6.0x10^{-4}$ for bisphenol AP.	Coleman, Toscano et al., 2003	Adequate.
	In an assay that measured induction and secretion of pS2 in cultured MCF7 cells (ELSA-pS2 immunoradiometric assay), induction of pS2 by bisphenol F and BPA was approximately 1,000-fold less than that of 17β-estradiol.	Perez, Pulgar et al., 1998	Adequate.
	Androgen Assays		

Bisphenol F CASRN 620-92-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Bisphenol F and BPA induced androgenic effects in MDA-MB453 cells transfected with an AR responsive luciferase reporter gene; anti-androgenic effects were elicited in the presence of dihydrotestosterone. Relative potency of the androgenic and anti-androgenic effects elicited by bisphenol F was similar to that of BPA.	Stroheker, Picard et al., 2004	Adequate.
	In an ARE-luciferase reporter assay using a mouse fibroblast cell line (NIH3T3 cells), neither bisphenol F, BPA, bisphenol C, nor bisphenol S exerted an androgenic effect.	Kitamura, Suzuki et al., 2005	Adequate.
	In an ARE-luciferase reporter assay using a mouse fibroblast cell line (NIH3T3 cells), bisphenol F inhibited the androgenic activity of dihydrotestosterone. Anti-androgenic responses were elicited by BPA, bisphenol C, and bisphenol S as well.	Kitamura, Suzuki et al., 2005	Adequate.
	Bisphenol F induced an anti-androgenic response in a transcriptional activation assay at a concentration of 10^{-5}M.	Cabaton, Dumont et al., 2009	Adequate.

Bisphenol F CASRN 620-92-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	***In Vivo* Studies**		
	28-Day study with Crj:CD Sprague-Dawley rats (10/sex/dose), gavaged with 0, 20, 100, or 500 mg/kg-day: NOAEL = 500 mg/kg-day (endocrine/reproductive parameters). No changes in spermatological findings, estrous cycles, reproductive organ weight, or thyroid weight.	Higashihara, Shiraishi et al., 2007	Adequate.
	Exposure of immature female rats to bisphenol F (gavage dosing once daily for 4 days) resulted in a dose-dependent increase in uterine weight in immature female rats. LOAEL = 100 mg/kg-day (based on increased relative wet uterine weight NOAEL = 50 mg/kg-day There were no significant effects on uterine weight in BPA-treated immature female rats and no effects on uterine weight in bisphenol F- or BPA-treated ovariectromized rats.	Stroheker, Chagnon et al., 2003	Adequate.
	In an uterotrophic assay of rats subcutaneously injected with bisphenol F once daily for 3 days, an apparent estrogenic effect was evidenced by increased absolute and relative uterine weight. Similar effects were elicited by bisphenol S and bisphenol M.	Yamasaki, Noda et al., 2004	Adequate.

Bisphenol F CASRN 620-92-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In an uterotrophic assay in which immature female rats were injected with bisphenol F, bisphenol S, or bisphenol M subcutaneously for three consecutive days, observed changes in uterine weight indicated that bisphenol F, bisphenol S, and bisphenol M exerted both estrogenic and anti-estrogenic responses.	Akahori, Makai et al., 2008	Adequate.
Immunotoxicity	**No data located.**		
Immune System Effects			No data located.
ECOTOXICITY			
ECOSAR Class	Polyphenols		
Acute Toxicity	**MODERATE: Based on an experimental 48-hour EC_{50} of 56 mg/L in *Daphnia magna.***		
Fish LC_{50}	Fish 96-hour LC_{50} = 4.55 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	
	Fish 96-hour LC_{50} = 19.74 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

Bisphenol F CASRN 620-92-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid LC_{50}	*Daphnia magna* 48-hour EC_{50} = 56 mg/L 24-hour EC_{50} = 80 mg/L (Experimental)	Chen, Michihiko et al., 2002	Adequate.
	Daphnid 48-hour LC_{50} = 12.94 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid 48-hour LC_{50} = 13.0 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	
Green Algae EC_{50}	Green algae 96-hour EC_{50} = 1.37 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	
	Green algae 96-hour EC_{50} = 8.6 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Chronic Aquatic Toxicity	**HIGH: Based on an estimated ChV of 0.29 mg/L for green algae that is within the range of 0.1-1.0 mg/L.**		
Fish ChV	Fish 30-day ChV = 1.18 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	

Bisphenol F CASRN 620-92-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Fish 30-day ChV = 1.83 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid ChV	Daphnid ChV = 1.44 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid ChV = 4.56 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	
Green Algae ChV	Green algae ChV = 0.29 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	
	Green algae ChV = 3.78 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

Bisphenol F CASRN 620-92-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL FATE				
Transport		**Based on the Level III fugacity models incorporating the located experimental property data, bisphenol F is expected to partition primarily to soil. Bisphenol F is expected to exist in both neutral and anionic forms at environmentally-relevant pH, based on its measured pK_a. The neutral form of bisphenol F is expected to have low mobility in soil based on its estimated K_{oc}. The anionic form may be more mobile, as anions do not bind as strongly to organic carbon and clay due to their enhanced water solubility. However, leaching of bisphenol F through soil to groundwater is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that it will be nonvolatile from surface water. Volatilization from dry surfaces is also not expected based on its estimated vapor pressure. In the atmosphere, bisphenol F is expected to exist in both vapor and particulate phases, based on its estimated vapor pressure. Particulates will be removed from air by wet or dry deposition. Vapor-phase bisphenol F will be susceptible to atmospheric degradation processes.**		
	Henry's Law Constant ($atm\text{-}m^3/mole$)	$<1x10^{-8}$ (Estimated)	EPI	Cutoff value for nonvolatile compounds according to professional judgment.
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	$1.5x10^4$ (Estimated)	EPI	
	Level III Fugacity Model	Air = <1% (Estimated) Water = 15% Soil = 79% Sediment = 6.5%	EPI	

Bisphenol F CASRN 620-92-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**LOW: Bisphenol F degraded 100% after 2 weeks in a modified river die-away test (TOC-Handai Method). Complete mineralization was reported. Based on these data, the aerobic biodegradation half-life is expected to be <16 days. An anaerobic biodegradation test assessing primary degradation in concentrated pond sediment reported >80% after ca. 80 days with no lag period. A pure culture study evaluating the ability of a *Sphingobium yanoikuyae* strain to degrade bisphenol F suggested that the mechanism for biodegradation started at the bridging carbon between the two phenols via hydroxylation and subsequent oxidation to 4,4'-dihydroxybenzophenone. This degradation mechanism can occur for this BPA alternative because of the presence of labile benzylic hydrogens. Bisphenol F did not pass a ready biodegradability test (Japanese MITI), which reported only 1% degradation after 4 weeks, indicating that it may be resistant to biodegradation under more stringent conditions. Bisphenol F is not expected to undergo hydrolysis since it does not contain hydrolyzable functional groups. Absorption of light at environmentally relevant wavelengths indicates that it may be susceptible to direct photolysis by sunlight. The atmospheric half-life for the hydroxyl radical reaction of vapor phase bisphenol F is estimated to be 1.6 hours, although it is expected to exist in both the vapor and particulate phases in air. Based on these findings, biodegradation of bisphenol F is expected to be the main fate process in aquatic and terrestrial environments.**		
Water	**Aerobic Biodegradation**	100% after 2 weeks (Measured; TOC-Handai Method). Method similar to aerobic river die-away test. Used concentrated (10 times) river water microcosms diluted in "artificial water". Reported complete mineralization at TOC concentration of 10 mg/L.	Ike, Chen et al., 2006	Valid, nonguideline study demonstrating river water microcosms have the potential to biodegrade bisphenol F.

Bisphenol F CASRN 620-92-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Biodegradation efficiencies varied from 8% to 58% after 30 days, depending on the sampling site. A modified TOC-Handai Method was used, which is similar to aerobic river die-away test. Used concentrated seawater microcosms diluted in "artificial water". Resistance to seasonal variation was noted. Efficiencies varied from 75% to 100% after 30 days, depending on the sampling site using a sea-die away method. Purified seawater inoculums were used.	Danzl, Sei et al., 2009	Valid, nonguideline study demonstrating seawater microcosms have the potential to biodegrade bisphenol F.
		Sphingobium yanoikuyae strain FM-2 (isolated from river water) biodegraded bisphenol F. Reported mechanism suggested hydroxylation and subsequent oxidation at the bridging carbon to form the following metabolites: bis(4-hydroxyphenyl)methanol to 4,4'-dihydroxybenzophenone to 4-hydroxyphenyl-4-hydroxybenzoate to 4-hydroxybenzoate and 1,4-hydro-quinone, all of which are mineralized.	Inoue, Hara et al., 2008	Valid, pure culture study demonstrating biodegradation potential and mechanism.
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**	1% after 4 weeks (Measured in activated sludge). Japanese MITI test (OECD 301C) measuring BOD with test concentration of 100 mg/L and concentration of activated sludge inoculum = 30 mg/L	MITI, 1998	Adequate, guideline study.

Bisphenol F CASRN 620-92-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Anaerobic Biodegradation	>80% after ca. 80 days (Measured; no lag period). Anaerobic pond sediment condensed to twice its original concentration. TOC = 10 mg/L. Measured primary degradation only. No discussion of metabolites.	Ike, Chen et al., 2006	Valid nonguideline study, demonstrating anaerobic seawater sediments have potential to biodegrade bisphenol F.
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	1.6 hours (Estimated for hydroxyl radical reaction assuming a 12-hour day and a hydroxyl radical concentration of $1.5x10^6$ OH/cm^3)	EPI	
Reactivity	**Photolysis**	Susceptible to direct photolysis, with a reported UV absorption at 279 nm. Partial absorption at environmental wavelengths expected.	Lide and Milne, 1994; Professional judgment	Qualitative assessment based on functional groups.
	Hydrolysis	Not a significant fate process (Estimated)	Wolfe and Jeffers, 2000; Professional judgment	Substance does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.
	Pyrolysis			No data located.
Environmental Half-life		30 days	EPI, PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**LOW: The measured fish BCFs are <100.**		
	Fish BCF	6.6 (25 µg/L) (Measured); 11 (2.5 µg/L) (Measured)	MITI, 1998	Adequate, guideline study.
	BAF	28 (Estimated)	EPI	

Bisphenol F CASRN 620-92-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING			
Environmental Monitoring	Detected in landfill leachates (Öman and Hynning, 1993).		
Ecological Biomonitoring	No data located.		
Human Biomonitoring	This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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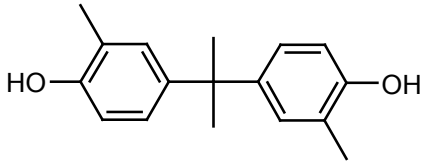
Bisphenol C



CASRN: 79-97-0

MW: 256.35

MF: $C_{17}H_{20}O_2$

Physical Forms:
Neat: Solid

Use: Developer for thermal paper

SMILES: Cc1cc(ccc1O)C(C)(C)c2ccc(c(c2)C)O

Synonyms: Phenol, 4,4'-(1-methylethylidene) bis[2-methyl-; Bisphenol C; 2,2-Bis(3-methyl-4-hydroxyphenyl)propane; 2,2-Bis(3-methyl-4-hydroxyphenyl)propane; 2,2-Bis(4-hydroxy-3-methylphenyl)propane; 2,2-Bis-(4-hydroxy-3-methylphenyl)propane; 3,3'-Dimethylbisphenol A; 3,3'-Dimethyldian; 4,4'-(1-Methylethylidene)bis(2-methylphenol); 4,4'-Isopropylidenebis(2-methylphenol); 4,4'-Isopropylidenebis[2-methylphenol]; 4,4'-isopropylidenedi-o-cresol

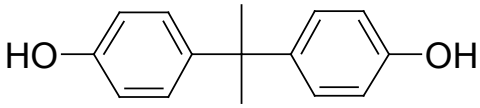
Polymeric: No
Oligomers: Not applicable

Metabolites, Degradates and Transformation Products: 4-hydroxy-3-methyl acetophenone, 4-hydroxy-3-methyl benzoic acid, and 2,2-bis[4-hydroxy-3-methylphenyl]-1-propanol

Analog: Bisphenol A (80-05-7)
Endpoint(s) using analog values: Acute toxicity, reproductive, developmental, repeated dose, skin sensitization, dermal irritation

Analog: Confidential analog (structure not available)
Endpoint(s) using analog values: eye irritation

Analog Structure:



Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)

Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2011).

Risk Assessments: None identified

Bisphenol C CASRN 79-97-0			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	138-140 (Measured)	Aldrich, 2009	Adequate; reported values that span a relatively narrow range and are consistent with those provided in other sources.
	140 (Measured)	Lide, 2008	Adequate.
Boiling Point (°C)	368 (Extrapolated from the reduced boiling point reported by Aldrich, 2009)	Professional judgment	The boiling point at 760 mm Hg was extrapolated from the measured boiling point at reduced pressure using a computerized nomograph.
	238-240 at 12 mm Hg (Measured)	Aldrich, 2009	Inadequate; value obtained at a reduced pressure.
Vapor Pressure (mm Hg)	$2.3x10^{-6}$ (Estimated from the reduced boiling point reported by Aldrich, 2009)	Professional judgment	The vapor pressure was extrapolated from the measured boiling point at reduced pressure using a computerized nomograph.
Water Solubility (mg/L)	4.7 (Estimated)	EPI	
Log K_{ow}	4.7 (Estimated)	EPI	
Flammability (Flash Point)			No data located.
Explosivity			No data located.
pH			No data located.
pK_a	10.5 (Estimated)	SPARC	
HUMAN HEALTH EFFECTS			
Toxicokinetics	**Bisphenol C as a neat material is estimated to not be absorbed through the skin and have poor skin absorption when in solution. Bisphenol C is expected to be absorbed via the lungs and gastrointestinal tract.**		
Dermal Absorption *in vitro*			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Not absorbed through the skin as neat material and has poor absorption in solution; can be absorbed through the lung and gastrointestinal tract (Estimated by analogy)	Professional judgment	Based on closely related confidential analog with similar structure, functional groups, and physical/chemical properties.
Acute Mammalian Toxicity		**LOW: Based on analogy to BPA, the acute oral and dermal toxicity hazard of bisphenol C is estimated to be low based on experimental data in animals for the analog. Data for exposure to the analog BPA via inhalation were inconclusive, as only a single concentration was tested and a LC_{50} was not provided.**		
Acute Lethality	**Oral**	Rat LD_{50} = 3,200->5,000 mg/kg bw (Estimated by analogy)	NTP, 1982; European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; multiple studies, some guideline studies.
		Mouse LD_{50} = 4,000-5,200 mg/kg bw (Estimated by analogy)	NTP, 1982; European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; multiple studies, some guideline studies.
	Dermal	Rabbit LD_{50} = 3,000-6,400 mg/kg bw (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; limited study details provided for multiple studies reported in secondary sources.
	Inhalation	No deaths among male and female F344 rats (10/sex) exposed to BPA dust at 0.17 mg/L (highest attainable concentration) for 6 hours; transient slight nasal tract epithelial damage was evident. (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; test guidelines were not reported in secondary sources.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Carcinogenicity		**MODERATE: Estimated using OncoLogic expert system which describes a concern for this compound as a potential carcinogen or tumorigenesis promoter arising from its structural similarity to estrogenic/androgenic compounds, using the "phenols and phenolic compounds" structural alert.**		
	OncoLogic Results	Moderate (Estimated) OncoLogic class: phenols and phenolic compounds	OncoLogic	OncoLogic SAR analysis using the phenols and phenolic compounds class.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
Genotoxicity		**MODERATE: Bisphenol C induced micronuclei in Chinese hamster V79 cells and human AG1522C fibroblasts, but was not mutagenic in one assay of *Salmonella typhimurium* strain TA1335 either with or without exogenous metabolic activity and did not induce chromosomal aberrations in Syrian hamster ovary cells.**		
	Gene Mutation *in vitro*	Negative; umu test in *S. typhimurium* TA1335 with and without metabolic activation	Chen, Michihiko et al., 2002	Adequate.
		Negative; gene mutation tests at the Na+/K+ ATPase locus and hprt locus of Syrian hamster embryo cells	Tsutsui, Tamura et al., 2000	Adequate.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Negative; chromosomal aberrations in Syrian hamster embryo cells	Tsutsui, Tamura et al., 2000	Adequate.
		Positive; induction of micronuclei in Chinese hamster V79 cells	Pfeiffer, Rosenberg et al., 1997	Adequate.
		Positive; induction of micronuclei in human AG1522C fibroblasts	Lehmann and Metzler, 2004	Adequate.
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.
	Other			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**MODERATE: Estimated based on analogy to BPA. Key studies identified by NTP for the analog BPA indicate that there are multiple distinct endpoints with NOAELs in the range of Moderate hazard concern and LOAELs in the range of Low hazard concern. At the target dose of 50 mg/kg-day (BPA), the NOAELs are on the margin of High and Moderate hazard, according to DfE criteria. Benchmark Dose (BMD) Modeling conducted by NTP, which interpolates between NOAEL and LOAEL values, yields values that further support a Moderate hazard designation.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	Potential for toxic effects to testes and ovaries (Estimated by analogy)	Professional judgment	Estimated based on located test data for a confidential analog.
		Potential for reproductive toxicity (Estimated by analogy)	Professional judgment	Estimated based on reported experimental data for the analog BPA.
		Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for 12% decreased terminal body weight in F_1 parental males Reproductive toxicity: Females: NOAEL = 50 mg/kg bw-day LOAEL = 500 mg/kg bw-day for decreases in number of implantation sites, delayed vaginal opening in F_1, F_2, F_3 offspring BMDLs (change of 1 standard deviation from control) reported for delayed vaginal opening (females)- F_1 = 176 mg/kg-day	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; adequate, guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		F_2 = 228 mg/kg-day F_3 = 203 mg/kg-day Males: NOAEL = 50 mg/kg bw-day, LOAEL = 500 mg/kg-day for delayed preputial separation in F_1 males BMDLs (change of 1 standard deviation from control) reported for delayed preputial separation (males)- F_1 = 163 mg/kg-day F_2 = 203 mg/kg-day F_3 = 189 mg/kg-day (Estimated by analogy)		

Bisphenol C CASRN 79-97-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for increased incidences of centrilobular hepatocellular hypertrophy in males and females Reproductive toxicity: NOAEL = 50 mg/kg bw-day LOAEL = 600 mg/kg bw-day for increased gestation length, decreased epididymal sperm concentration in F_1 males, increased incidence of gross ovarian cysts in F_1 and F_2 females BMD_1 (change of 1 standard deviation from control) reported for increased gestation length F_0 = 1144 mg/kg-day (BMDL = 599 mg/kg-day) F_1 = 772 mg/kg-day (BMDL = 531 mg/kg-day) BMD_{10s} (10% extra risk) reported for increased incidence of gross ovarian cysts F_0 = 225 mg/kg-day (BMDL = 141 mg/kg-day) F_1 = 202 mg/kg-day (BMDL = 120 mg/kg-day) (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; adequate, guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.
	Summary of Reproductive effects	Female effects: There is sufficient evidence in rats and mice that BPA caused female reproductive toxicity with subchronic or chronic oral exposures with a NOAEL of 50 mg/kg bw-day and	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; Classified by NTP-CERHR as having High Utility.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		a LOAEL of 500 mg/kg bw-day. Male effects: There is sufficient evidence in rats and mice that BPA causes male reproductive toxicity with subchronic or chronic oral exposures with a NOAEL of 50 mg/kg bw-day and a LOAEL of 500 mg/kg bw/day. (Estimated by analogy)		
		The joint FAO/WHO Expert Panel reviewed reproductive and developmental toxicity data for BPA located as of November 2010 and noted that most regulatory bodies reviewing the numerous studies on BPA have indicated an oral reproductive and developmental NOAEL of 50 mg/kg bw-day. (Estimated by analogy)	FAO/WHO, 2011	Based on the analog BPA.
Developmental Effects		**HIGH: Estimated based on analogy to BPA. The NTP-CERHR (2008) Expert Panel concluded that there is suggestive evidence that BPA causes neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01-0.2 mg/kg bw-day) following developmental exposures. The FAO/WHO (2011) Expert Panel also concluded that while there was broad agreement in a NOAEL of 50 mg/kg bw-day for developmental toxicity based on standard bioassays, specific targeted studies identified neurodevelopmental effects at low doses (<1 mg/kg bw-day), but the human relevance is less certain. There is great variation in results with different types of studies measuring different endpoints; developmental effects at lower doses cannot be ruled out. Taken together these findings support a hazard designation of High concern.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	with Reproduction/ Developmental Toxicity Screen			
	Summary of Developmental Effects	Potential for developmental neurotoxicity due to effects of thyroid toxicity (Estimated by analogy)	Professional judgment	Estimated based on located test data for a confidential analog.
		Potential for developmental toxicity (Estimated by analogy)	Professional judgment	Estimated based on reported experimental data for the analog BPA.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		The NTP-CERHR (2008) Expert Panel concluded that BPA: *Does not cause malformations or birth defects in rats or mice at levels up to the highest doses evaluated: 640 mg/kg-day (rats) and 1,250 mg/kg bw-day (mice). *Does not alter male or female fertility after gestational exposure up to doses of 450 mg/kg bw-day in the rat and 600mg/kg bw-day in the mouse (highest dose levels evaluated). *Does not permanently affect prostate weight at doses up to 475 mg/kg-day in adult rats or 600 mg/kg-day in mice. *Does not cause prostate cancer in rats or mice after adult exposure at up to 148 or 600 mg/kg-day, respectively. *Does change the age of puberty in male or female rats at high doses (ca. 475 mg/kg-day). And that rodent studies ***suggest*** that BPA: *Causes neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01-0.2 mg/kg/day). (Estimated by analogy)	NTP–CERHR, 2008; Professional judgment	Based on the analog BPA.

Bisphenol C CASRN 79-97-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		The joint FAO/WHO Expert Panel reviewed reproductive and developmental toxicity data for BPA located as of November 2010 and noted that most regulatory bodies reviewing the numerous studies on BPA have indicated an oral reproductive and developmental NOAEL of 50 mg/kg bw-day.	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert. (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on structural alert.
Repeated Dose Effects		**MODERATE: Estimated based on analogy to BPA, which produced histopathologic changes in the liver (centrilobular hepatocyte hypertrophy) from oral dosing at 50 mg/kg bw-day (NOAEL = 5 mg/kg bw-day) and there is uncertainty regarding the potential for BPA doses between the NOAEL of 5 mg/kg bw-day and the LOAEL of 50 mg/kg bw-day to cause adverse systemic effects. Furthermore, lesions in the nasal cavity of rats were reported following repeated inhalation exposure to BPA dust at 0.05 mg/L. These findings indicate a Moderate hazard potential for the oral and inhalation exposure routes.**		
		Potential for liver toxicity (Estimated by analogy)	Professional judgment	Estimated based on reported experimental data for the analog BPA.
		The FAO/WHO Expert Panel reviewed the located information regarding repeated-dose oral toxicity of BPA and concluded that results demonstrated effects on the liver, kidney, and body weight at doses of 50 mg/kg bw-day and higher and that the lowest NOAEL was 5 mg/kg-day, as identified in several studies. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.

Bisphenol C CASRN 79-97-0			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Parental systemic toxicity: NOAEL = 4.75 mg/kg bw-day LOAEL = 47.5 mg/kg bw-day for 12% decreased terminal body weight in F_1 parental males (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.
	Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for increased incidences of centrilobular hepatocellular hypertrophy in males and females (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.
	NOAEL = 0.01 mg/L LOAEL = 0.05 mg/L based on microscopic changes in the anterior portion of the nasal cavity (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA.
	NOAEL = None established LOAEL = 0.047 mg/L for decreased body weight gain, increased liver and kidney weight, unspecified "morphological changes" in liver, kidney, and lungs (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; single exposure level, insufficient study details in secondary sources.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Skin Sensitization		**MODERATE: Based on analogy to BPA, bisphenol C is estimated to be a skin sensitizer. Recent data from three BPA manufacturing facilities indicate that it does not elicit skin sensitization. However, results of some human studies suggest the possibility of a dermal sensitization response, although cross-sensitization was not ruled out. Most animal studies conducted on the analog were negative for dermal sensitization, although assays may not have been maximized. There is evidence of ear swelling in a photoallergy test in mice and moderate redness and swelling following repeated dermal exposure in rabbits. Based on suggestive evidence of skin sensitization in humans and mice for the analog, a Moderate hazard designation is warranted.**		
	Skin Sensitization	Potential for dermal sensitization (Estimated by analogy)	Professional judgment	Estimated based on reported experimental data for the analog BPA.
		Negative in a modified local lymph node assay of mice administered BPA epicutaneously on the ears at concentrations up to 30% on three consecutive days. (Estimated by analogy)	EINECS, 2010; Professional judgment	Based on the analog BPA; adequate, although the assay did not include concentrations >30%.
		Negative in a local lymph node assay modified to test for photoreactivity in mice administered BPA epicutaneously on the ears at concentrations up to 30% on three consecutive days and irradiated with UV light immediately following application. (Estimated by analogy)	EINECS, 2010; Professional judgment	Based on the analog BPA; adequate, although the assay did not include concentrations >30%.
		Negative in comprehensive medical surveillance data obtained from three BPA manufacturing plants for 875 employees examined for several years where workers were potentially exposed to other chemicals (phenol, acetone) that are not considered to be skin sensitizers. (Estimated by analogy)	EINECS, 2010; Professional judgment	Based on the analog BPA; adequate.
		Positive, rabbits; repeated dermal	NIOSH, 2010; Professional	Based on the analog BPA; adequate.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		application (30 times over 37 days) of BPA (pure powder) produced moderate swelling and redness. Skin turned yellow followed by dark pigmentation after day 15. (Estimated by analogy)	judgment	
		The Joint FAO/WHO Expert Meeting review of the toxicological aspects of BPA concludes that BPA is capable of producing a skin sensitization response in humans. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA; adequate.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**HIGH: Based on analogy to a confidential analog, bisphenol C is estimated to potentially cause severe irritation and corrosion to eyes.**		
	Eye Irritation	Potential for severe irritation and corrosion to eyes (Estimated by analogy)	Professional judgment	Estimated based on located test data for a confidential analog.
Dermal Irritation		**MODERATE: Bisphenol C is estimated to be slightly irritating to moderately irritating to rabbit skin based on test data for the analog BPA. NIOSH has assigned the analog, BPA, as a skin irritant.**		
	Dermal Irritation	Rabbit, nonirritating to slightly irritating when applied as undiluted or 10% aqueous suspension to intact or abraded skin. (Estimated by analogy)	European Commission, 2000; EINECS, 2010; NIOSH, 2010; Professional judgment	Based on the analog BPA; Adequate, study details provided for multiple studies indicate potential for BPA to cause dermal irritation.
		Rabbit, moderately irritating when applied as 40% solution in dimethyl sulfoxide under non-occlusive conditions. (Estimated by analogy)	European Commission, 2000; Professional judgment	Based on the analog BPA; adequate.
		Guinea pig, not irritating when applied as	European Commission, 2000;	Based on the analog BPA; adequate.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		5% solution in acetone for 24 hours under occlusive conditions. (Estimated by analogy)	Professional judgment	
Endocrine Activity		**Based on limited in vitro data it appears that Bisphenol C exhibits endocrine activity. *In vitro* assays demonstrate that bisphenol C can bind to estrogen receptors, elicit estrogen-induced gene transcription, and induce cell proliferation in MCF7 cancer cells. In an ARE-luciferase reporter assay using a mouse fibroblast cell line, bisphenol C did not elicit an androgenic response, but did inhibit the androgenic activity of dihydrotestosterone. Data located indicate that the *in vitro* endocrine activity of bisphenol C is approximately 3-5 orders of magnitude less than that of 17β-estradiol, suggesting that bisphenol C acts as a weak estrogen. Limited comparative *in vitro* data suggest that the endocrine activity of bisphenol C is similar in magnitude to that of BPA, bisphenol AP, and bisphenol F and somewhat more potent than bisphenol S. Bisphenol C elicited estrogenic and anti-estrogenic responses in a CARP-HEP/vitellogenin assay.**		
		Binding Assays		
		In a human ER binding assay, the relative binding affinity (RBA) of bisphenol C, was 0.129% compared to 126% for 17β-estradiol. RBAs for other bisphenol compounds included 0.195% for BPA, 0.0803% for bisphenol AP, 0.0719% for bisphenol F, and 0.0055% for bisphenol S. An RBA of 0.00473% was reported for PHBB.	METI, 2002	Adequate.
		In a competitive ER binding assay using human ERα, the RBA for bisphenol C was 1.68% that of 17β-estradiol. RBAs for other bisphenol compounds included 0.32% for BPA, 1.66% for bisphenol AP, and 0.09% for bisphenol F.	Coleman, Toscano et al., 2003	Adequate.
		Gene Transcription and Reporter Gene Assays		

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Bisphenol C exhibited evidence of estrogenic activity in a yeast (*Saccharomyces cerevisiae*) two-hybrid assay using ERα and the coactivator TIF2. Based on estrogenic activity that was 5 orders of magnitude lower than that of 17β-estradiol, bisphenol C was considered weakly estrogenic. Assessment of other bisphenols resulted in a ranking of relative potency as follows: bisphenol C ≥ BPA > bisphenol F > bisphenol S.	Chen, Michihiko et al., 2002	Adequate.
	Bisphenol C did not exhibit evidence of estrogenic activity in a yeast (*Saccharomyces cerevisiae*) two-hybrid assay using ERα and the coactivator TIF2.	Nishihara, Nishikawa et al., 2000	Adequate.
	In a reporter gene assay of estrogen-induced transcriptional activity, relative activity (RA) for bisphenol C was 0.00189% compared to 81.7% for 17β-estradiol. RAs for other bisphenol compounds included 0.00278% for BPA, 0.000639% for bisphenol F, 0.000254% for bisphenol S, and 0.000184% for bisphenol AP. An RA of 0.000592% was reported for PHBB.	METI, 2002	Adequate.
	In an ERE-luciferase reporter assay using MCF-7 cells, an EC_{50} was 0.42 µM for bisphenol C compared to an EC_{50} of $8.6x10^{-6}$ for 17β-estradiol (i.e., BPA was approximately 5 orders of magnitude less potent than 17β-estradiol	Kitamura, Suzuki et al., 2005	Adequate.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	at inducing estrogenic activity). EC_{50} values for other bisphenol compounds included 0.63 µM for BPA, 1.0 µM for bisphenol F, and 1.1 µM for bisphenol S		
	In an ER-mediated reporter gene expression assay, bisphenol C induced reporter gene expression at a relative activity (RA) of $4.9x10^{-4}$ that of 17β-estradiol. RAs for other bisphenol compounds included $5.3x10^{-4}$ for bisphenol F, $9.0x10^{-5}$ for bisphenol AP, and $2.75x10^{-3}$ for BPA.	Coleman, Toscano et al., 2003	Adequate.
	In an ERE-luciferase reporter assay using MCF-7 cells in the presence of 17β-estradiol, neither bisphenol C, BPA, bisphenol F, nor bisphenol S appeared to exert an anti-estrogenic effect	Kitamura, Suzuki et al., 2005	Adequate.
	In a proliferation assay of MCF-7 human breast cancer cells that contain ERα and ERβ and are known to proliferate in response to estrogens, bisphenol C induced a proliferative response that was $1.6x10^{-3}$ that of 17β-estradiol. Respective proliferative responses for other bisphenol compounds were $2.0x10^{-3}$ for BPA, $1.0x10^{-3}$ for bisphenol F, and $6.0x10^{-4}$ for bisphenol AP.	Coleman, Toscano et al., 2003	Adequate.
	In an ERE-luciferase reporter assay using MCF-7 cells in the presence of 17β-estradiol, neither bisphenol C, BPA, bisphenol F, nor bisphenol S appeared to exert an anti-estrogenic effect	Kitamura, Suzuki et al., 2005	Adequate.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Cell Proliferation Assays		
	In a proliferation assay of MCF-7 human breast cancer cells that contain ERα and ERβ and are known to proliferate in response to estrogens, bisphenol C induced a proliferative response that was $1.6x10^{-3}$ that of 17β-estradiol. Respective proliferative responses for other bisphenol compounds were $2.0x10^{-3}$ for BPA, $1.0x10^{-3}$ for bisphenol F, and $6.0x10^{-4}$ for bisphenol AP.	Coleman, Toscano et al., 2003	Adequate.
	Androgen Assays		
	In an ARE-luciferase reporter assay using a mouse fibroblast cell line (NIH3T3 cells), neither bisphenol C, BPA, bisphenol F, nor bisphenol S exerted an androgenic effect	Kitamura, Suzuki et al., 2005	Adequate.
	In an ARE-luciferase reporter assay using a mouse fibroblast cell line (NIH3T3 cells), bisphenol C inhibited the androgenic activity of dihydrotestosterone. Anti-androgenic responses were elicited by BPA, bisphenol F, and bisphenol S as well.	Kitamura, Suzuki et al., 2005	Adequate.
	Thyroid Assays		
	In an assay of thyroid hormonal activity whereby induction of growth hormone production is assessed in GH3 cells, neither bisphenol C nor BPA inhibited growth hormone production.	Kitamura, Suzuki et al., 2005	Adequate.
	Vitellogenin Assays		

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In a CARP-HEP/vitellogenin assay, bisphenol C and BPA induced vitellogenin production by up to 5 and 3%, respectively, of the vitellogenin production elicited by 17β-estradiol, indicating an estrogenic effect. In 17β-estradiol-induced preparations, bisphenol C inhibited vitellogenin production with a potency approximately one-hundredth that of the known estrogen antagonist tamoxifen, indicating an anti-estrogenic effect for bisphenol C.	Letcher, Sanderson et al., 2005	Adequate.
Immunotoxicity	**No data located.**		
Immune System Effects			No data located.
ECOTOXICITY			
ECOSAR Class	Polyphenols		
Acute Toxicity	**HIGH: Based on an experimental LC_{50} value for Daphnid (1.6 mg/L) and estimated acute toxicity values.**		
Fish LC_{50}	Fish 96-hour LC_{50} = 0.60 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	
	Fish 96-hour LC_{50} = 0.95 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid LC_{50}	*Daphnia magna* 48-hour EC_{50} = 1.6 mg/L; 24-hour EC_{50} = 4 mg/L (Experimental)	Chen, Michihiko et al., 2002	Adequate.
	Daphnid 48-hour LC_{50} = 0.77 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid 48-hour LC_{50} = 0.85 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	
Green Algae EC_{50}	Green algae 96-hour EC_{50} = 1.02 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Green algae 96-hour EC_{50} = 1.25 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	
Chronic Aquatic Toxicity	**HIGH: Estimated LC_{50} values for fish (neutral organics) <0.1 mg/L. All other estimated LC_{50} and EC_{50} values for neutral organics and polyphenol classes fall within 0.1 and 1.0.**		
Fish ChV	Fish ChV = 0.09 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Fish ChV = 0.12 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	
Daphnid ChV		Daphnid ChV = 0.12 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
		Daphnid ChV = 0.27 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	
Green Algae ChV		Green algae ChV = 0.13 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	
		Green algae ChV = 0.61 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version. 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
ENVIRONMENTAL FATE				
Transport		**If released to air, a vapor pressure of $2.3x10^{-6}$ mm Hg at 25°C indicates that bisphenol C will exist in both the vapor and particulate phases in the atmosphere. Particulate-phase bisphenol C will be removed from the atmosphere by wet or dry deposition. If released to soil, bisphenol C is expected to have low mobility based upon an estimated K_{oc} of >30,000. Volatilization from water surfaces is not expected to be an important fate process based upon this compound's estimated Henry's Law constant. Level III fugacity model results, which utilized estimated values as the input parameters, indicate that bisphenol C will partition primarily to soil and sediment.**		
	Henry's Law Constant	<$1x10^{-8}$ (Estimated)	EPI	Cutoff value for nonvolatile

Bisphenol C CASRN 79-97-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	(atm-m^3/mole)			compounds based on professional judgment.
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	>30,000 (Estimated)	EPI; U.S. EPA 2004; Professional judgment	Cutoff value for nonmobile compounds.
	Level III Fugacity Model	Air = <1% (Estimated) Water = 6% Soil = 63% Sediment = 31%	EPI	
Persistence		**MODERATE: Experimental studies indicate that bisphenol C may be removed from the environment by aerobic biodegradation. Bisphenol C has a measured primary biodegradation half-life in water of less than 2 weeks in a TOC Handai river die away method. Ultimate biodegradation will take longer based on experimental studies demonstrating 17% mineralization after 2 weeks (Ike, Chen et al, 2006). Although three bisphenol C degradation intermediates have been identified (Sakai, Yamanaka et al., 2007), the ultimate biodegradation data indicate that they do not persist in the environment. Bisphenol C lacks functional groups susceptible to hydrolysis and so hydrolysis is not an expected removal process. In addition, photolysis and anaerobic biodegradation have not been reported for bisphenol C.**		
Water	**Aerobic Biodegradation**	17% in 2 weeks (complete degradation) (Measured)	Ike, Chen et al., 2006	Adequate; valid nonguideline study demonstrating river water microcosms have the potential to biodegrade bisphenol C.
		58% in 2 weeks; % removal in a microcosm study (partial degradation) (Measured)	Ike, Chen et al., 2006	Supporting information presented; nonguideline study.
		94% in four days by *Sphingomonas* sp. Strain BP-7 (degradation intermediates detected) (Measured)	Sakai, Yamanaka et al., 2007	Adequate; valid nonguideline study using a pure culture inoculum supporting the potential for aerobic biodegradation.
		Degradation products 4-hydroxy-3-methyl acetophenone, 4-hydroxy-3-methyl benzoic acid, and 2,2-bis[4-hydroxy-3-methylphenyl]-	Lobos, Leib et al., 1992	Adequate, nonguideline study that provides supporting information on environmental persistence.

Bisphenol C CASRN 79-97-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		1-propanol identified; no biodegradation rate information included (Measured)		
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (anaerobic-methanogenic biodegradation probability model)	EPI	
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	1.3 hours (Estimated)	EPI	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	The substance does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.
	Hydrolysis	Not a significant fate process (Estimated)	Wolfe and Jeffers, 2000; Professional judgment	The substance does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.
	Pyrolysis			No data located.
Environmental Half-life		75 days (Estimated)	EPI; PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.

Bisphenol C CASRN 79-97-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Bioaccumulation		**MODERATE: The estimated fish BCF is <1,000.**		
	Fish BCF	620 (Estimated)	EPI	
	BAF	110 (Estimated)	EPI	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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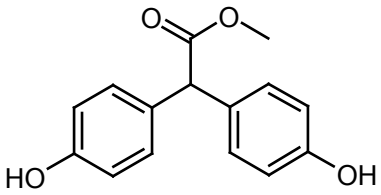
MBHA



CASRN: 5129-00-0

MW: 258.28

MF: $C_{15}H_{14}O_4$

Physical Forms:
Neat: Solid

Use: Developer for thermal paper

SMILES: O=C(OC)C(c(ccc(O)c1)c1)c(ccc(O)c2)c2

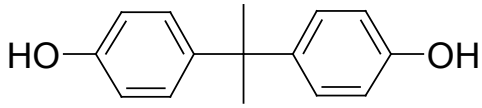
Synonyms: Benzeneacetic acid, 4-hydroxy-.alpha.-(4-hydroxyphenyl)-, methyl ester; Methyl bis(4-hydroxyphenyl)acetate

Polymeric: No
Oligomers: Not applicable

Metabolites, Degradates and Transformation Products: None identified

Analog: Bisphenol A (80-05-7)
Endpoint(s) using analog values: Acute toxicity, reproductive, developmental, repeated dose, skin and eye irritation, genotoxicity

Analog Structure:



Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)

Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2011).

Risk Assessments: None identified

MBHA CASRN 5129-00-0			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)			No data located.
Boiling Point (°C)	>300 (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for high boiling point compounds according to HPV assessment guidance.
Vapor Pressure (mm Hg)	$3.3x10^{-8}$ (Estimated)	EPI	
Water Solubility (mg/L)	360 (Estimated)	EPI	
Log K_{ow}	2.8 (Estimated)	EPI	
Flammability (Flash Point)			No data located.
Explosivity			No data located.
pH			No data located.
pK_a	9.7-9.9 (Estimated)	SPARC	

MBHA CASRN 5129-00-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**MBHA as a neat material is estimated to not be absorbed through the skin and will have poor skin absorption when in solution. MBHA is expected to be absorbed via the lungs and gastrointestinal tract. It is expected that MBHA will undergo ester hydrolysis by esterases in the body.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Not absorbed through the skin as neat material and has poor absorption in solution; can be absorbed through the lung and gastrointestinal tract (Estimated by analogy)	Professional judgment	Based on closely related confidential analog with similar structure, functional groups, and physical/chemical properties.
Acute Mammalian Toxicity		**LOW: The acute oral and dermal toxicity hazard of MBHA is estimated to be low based on experimental data in animals for the analog BPA. Data for exposure to the analog BPA via inhalation were inconclusive, as only a single concentration was tested and a LC_{50} was not provided.**		
Acute Lethality	**Oral**	Rat LD_{50} = 3,200->5,000 mg/kg bw (Estimated by analogy)	NTP, 1982; European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; multiple studies, some guideline studies.
		Mouse LD_{50} = 4,000-5,200 mg/kg bw (Estimated by analogy)	NTP, 1982; European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; multiple studies, some guideline studies.
	Dermal	Rabbit LD_{50} = 3,000-6,400 mg/kg bw (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; adequate by weight of evidence, multiple studies, although study details were not reported in secondary sources.
	Inhalation	No deaths among male and female F344 rats (10/sex) exposed to BPA dust at 0.17 mg/L (highest attainable concentration) for 6 hours; transient slight nasal tract epithelial damage was evident. (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; test guidelines were not reported in secondary sources.

MBHA CASRN 5129-00-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Carcinogenicity		**MODERATE: Estimated using OncoLogic expert system which describes a concern for this compound as a potential carcinogen or tumorigenesis promoter arising from its structural similarity to estrogenic/androgenic compounds, using the "phenols and phenolic compounds" structural alert.**		
	OncoLogic Results	Moderate (Estimated) OncoLogic class: phenols and phenolic compounds	OncoLogic	OncoLogic SAR analysis using the phenols and phenolic compounds class.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
Genotoxicity		**LOW: Based on analogy to BPA. FAO/WHO (2011) determined that: (1) the analog BPA is not a mutagen in *in vitro* test systems, (2) the analog BPA does not induce cell transformation, and (3) *in vivo* evidence for clastogenic effects induced by the analog BPA is inconsistent and inconclusive, although some *in vitro* studies have shown BPA to affect chromosomal structure in dividing cells. The conclusion of FAO/WHO (2011) is that the analog BPA is not likely to pose a genotoxic hazard to humans.**		
		Potential for mutagenicity (Estimated by analogy)	Professional judgment	Estimated based on reported experimental data for the analog BPA.

MBHA CASRN 5129-00-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Largely negative results in a variety of in vitro test systems, including studies with *Salmonella typhimurium*, Chinese hamster V79 cells, Syrian hamster embryo cells and mouse lymphoma cells. However, DNA damage was induced in MCF-7 and MDA-MB-231 cells, DNA adduct formation in Syrian hamster ovary cells and a number of positive findings have been reported for the potential for BPA to inhibit purified microtubule polymerization, affect the spindle apparatus, and produce aneuploidy in *in vitro* studies with Chinese hamster V79 cells or oocytes from Balb/c or MF1 mice. FAO/WHO Expert Panel concludes: BPA is not a mutagen in *in vitro* test systems, nor does it induce cell transformation. BPA has been shown to affect chromosomal structure in dividing cells in *in vitro* studies, but evidence for this effect in *in vivo* studies is inconsistent and inconclusive. BPA is not likely to pose a genotoxic hazard to humans. (Estimated by analogy)	FAO/WHO, 2011	Based on the analog BPA.

MBHA CASRN 5129-00-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**MODERATE: Based on analogy to BPA. Key studies identified by NTP for the analog BPA indicate there are multiple distinct endpoints with NOAELs in the range of Moderate hazard concern with LOAELs in the range of Low hazard concern. At the target dose of 50 mg/kg-day (BPA), the NOAELs are on the margin of High and Moderate hazard, according to DfE criteria. Benchmark Dose (BMD) Modeling conducted by NTP, which interpolates between NOAEL and LOAEL values, yields values that further support a Moderate hazard designation.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

MBHA CASRN 5129-00-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction and Fertility Effects	Potential for reproductive toxicity (Estimated by analogy)	Professional judgment	Estimated based on reported experimental data for the analog BPA.
		Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for 12% decreased terminal body weight in F_1 parental males Reproductive toxicity: Females: NOAEL = 50 mg/kg bw-day LOAEL = 500 mg/kg bw-day for decreases in number of implantation sites, delayed vaginal opening in F_1, F_2, F_3 offspring BMDLs (change of 1 standard deviation from control) reported for delayed vaginal opening (females)- F_1 = 176 mg/kg-day F_2 = 228 mg/kg-day F_3 = 203 mg/kg-day Males: NOAEL = 50 mg/kg bw-day, LOAEL = 500 mg/kg-day for delayed preputial separation in F_1 males BMDLs (change of 1 standard deviation from control) reported for delayed preputial separation (males)- F_1 = 163 mg/kg-day F_2 = 203 mg/kg-day F_3 = 189 mg/kg-day (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; adequate, guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.

MBHA CASRN 5129-00-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for increased incidences of centrilobular hepatocellular hypertrophy in males and females Reproductive toxicity: NOAEL = 50 mg/kg bw-day LOAEL = 600 mg/kg bw-day for increased gestation length, decreased epididymal sperm concentration in F_1 males, increased incidence of gross ovarian cysts in F_1 and F_2 females BMD_1 (change of 1 standard deviation from control) reported for increased gestation length F_0 = 1144 mg/kg-day (BMDL = 599 mg/kg-day) F_1 = 772 mg/kg-day (BMDL = 531 mg/kg-day) BMD_{10s} (10% extra risk) reported for increased incidence of gross ovarian cysts F_0 = 225 mg/kg-day (BMDL = 141 mg/kg-day) F_1 = 202 mg/kg-day (BMDL = 120 mg/kg-day) (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; adequate, guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.

MBHA CASRN 5129-00-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Summary of Reproductive Effects	Female effects: There is sufficient evidence in rats and mice that BPA caused female reproductive toxicity with subchronic or chronic oral exposures with a NOAEL of 50 mg/kg bw-day and a LOAEL of 500 mg/kg bw-day. Male effects: There is sufficient evidence in rats and mice that BPA causes male reproductive toxicity with subchronic or chronic oral exposures with a NOAEL of 50 mg/kg bw-day and a LOAEL of 500 mg/kg bw/day. (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA. Classified by NTP-CERHR as having High Utility.
		The joint FAO/WHO Expert Panel (2011) reviewed are productive and developmental toxicity data for BPA located as of November 2010 and noted that most regulatory bodies reviewing the numerous studies on BPA have indicated an oral reproductive and developmental NOAEL of 50 mg/kg bw-day. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.
Developmental Effects		**HIGH: Based on analogy to BPA. The NTP-CERHR (2008) Expert Panel concluded that there is suggestive evidence that BPA causes neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01-0.2 mg/kg bw-day) following developmental exposures. The FAO/WHO (2011) Expert Panel also concluded that while there was broad agreement in a NOAEL of 50 mg/kg bw-day for developmental toxicity based on standard bioassays, specific targeted studies identified neurodevelopmental effects at low doses (<1 mg/kg bw-day), but the human relevance is less certain. There is great variation in results with different types of studies measuring different endpoints; developmental effects at lower doses cannot be ruled out. Taken together these findings support a hazard designation of High concern.**		

MBHA CASRN 5129-00-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Summary of Developmental Effects	Potential for developmental toxicity (Estimated by analogy)	Professional judgment	Estimated based on reported experimental data for the analog BPA.

MBHA CASRN 5129-00-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		The NTP-CERHR (2008) Expert Panel concluded that BPA: *does not cause malformations or birth defects in rats or mice at levels up to the highest doses evaluated: 640 mg/kg bw-day (rats) and 1,250 mg/kg bw-day (mice). *does not alter male or female fertility after gestational exposure up to doses of 450 mg/kg bw-day in the rat and 600mg/kg bw-day in the mouse (highest dose levels evaluated). *does not permanently affect prostate weight at doses up to 475 mg/kg bw-day in adult rats or 600 mg/kg bw-day in mice. *does not cause prostate cancer in rats or mice after adult exposure at up to 148 or 600 mg/kg bw-day, respectively. *does change the age of puberty in male or female rats at high doses (ca. 475 mg/kg bw-day). And that rodent studies ***suggest*** that BPA: *causes neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01–0.2 mg/kg bw-day). (Estimated by analogy)	NTP–CERHR, 2008; Professional judgment	Based on the analog BPA.

MBHA CASRN 5129-00-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		The joint FAO/WHO (2011) Expert Panel reviewed reproductive and developmental toxicity data for BPA located as of November 2010 and noted that most regulatory bodies reviewing the numerous studies on BPA have indicated an oral reproductive and developmental NOAEL of 50 mg/kg bw-day. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert. (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on structural alert.
Repeated Dose Effects		**MODERATE: Estimated based on analogy to BPA, which produced histopathologic changes in the liver (centrilobular hepatocyte hypertrophy) from oral dosing at 50 mg/kg bw-day (NOAEL = 5 mg/kg bw-day) and there is uncertainty regarding the potential for BPA doses between the NOAEL of 5 mg/kg bw-day and the LOAEL of 50 mg/kg bw-day to cause adverse systemic effects. Furthermore, lesions in the nasal cavity of rats were reported following repeated inhalation exposure to BPA dust at 0.05 mg/L. These findings indicate a Moderate hazard concern for the oral and inhalation exposure routes.**		
		Potential for liver toxicity (Estimated by analogy)	Professional judgment	Estimated based on reported experimental data for the analog BPA.

MBHA CASRN 5129-00-0			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	The FAO/WHO (2011) Expert Panel reviewed the available information regarding repeated-dose oral toxicity of BPA and concluded that results demonstrated effects on the liver, kidney, and body weight at doses of 50 mg/kg bw-day and higher and that the lowest NOAEL was 5 mg/kg-day, as identified in several studies. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.
	Parental systemic toxicity: NOAEL = 4.75 mg/kg bw-day LOAEL = 47.5 mg/kg bw-day for 12% decreased terminal body weight in F_1 parental males (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.
	Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for increased incidences of centrilobular hepatocellular hypertrophy in males and females (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.
	NOAEL = 0.01 mg/L LOAEL = 0.05 mg/L based on microscopic changes in the anterior portion of the nasal cavity (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA.

MBHA CASRN 5129-00-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		NOAEL = None established LOAEL = 0.047 mg/L for decreased body weight gain, increased liver and kidney weight, unspecified "morphological changes" in liver, kidney, and lungs (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; single exposure level, insufficient study details in secondary sources.
Skin Sensitization		**LOW: Based on experimental data, MBHA is not a skin sensitizer in guinea pigs.**		
	Skin Sensitization	Not a skin sensitizer in maximization assay in guinea pigs	Kawaguchi Chemical Co., 2011	Conducted according to OECD guideline 406.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**MODERATE: Based on analogy to BPA. The analog BPA was slightly to highly irritating to rabbit eyes.**		
	Eye Irritation	Rabbit, slightly to highly irritating (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA. Adequate; multiple studies, weight of evidence indicates potential for BPA to cause eye irritation.
Dermal Irritation		**MODERATE: Based on analogy to BPA. The analog BPA was slightly irritating to moderately irritating to rabbit skin. NIOSH has assigned the analog, BPA as a skin irritant.**		
	Dermal Irritation	Rabbit, nonirritating to slightly irritating when applied as undiluted or 10% aqueous suspension to intact or abraded skin. (Estimated by analogy)	European Commission, 2000; EINECS, 2010; NIOSH 2010; Professional judgment	Based on the analog BPA. Adequate; multiple studies, weight of evidence indicates potential for BPA to cause dermal irritation.
		Rabbit, moderately irritating when applied as 40% solution in dimethyl sulfoxide under non-occlusive conditions. (Estimated by analogy)	European Commission, 2000; Professional judgment	Based on the analog BPA; adequate.

MBHA CASRN 5129-00-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Guinea pig, not irritating when applied as 5% solution in acetone for 24 hours under occlusive conditions. (Estimated by analogy)	European Commission, 2000; Professional judgment	Based on the analog BPA; adequate.
Endocrine Activity		**No data located.**		
				No data located.
Immunotoxicity		**No data located.**		
	Immune System Effects			No data located.
ECOTOXICITY				
ECOSAR Class		Polyphenols, esters		
Acute Toxicity		**HIGH: Estimated 96-hour LC_{50} for fish and 96-hour EC_{50} for algae are in the range of 1-10 mg/L.**		
Fish LC_{50}		Fish 96-hour LC_{50} = 8.80 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	
		Fish 96-hour LC_{50} = 13.0 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
		Fish 96-hour LC_{50} = 45.72 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

MBHA CASRN 5129-00-0			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid LC_{50}	Daphnid 48-hour LC_{50} = 24.24 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
	Daphnid 48-hour LC_{50} = 28.52 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	
	Daphnid 48-hour LC_{50} = 28.9 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Saltwater Invertebrate LC_{50}	Mysid shrimp 96-hour LC_{50} = 12.60 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
Green Algae EC_{50}	Green algae 96-hour EC_{50} = 1.88 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	
	Green algae 96-hour EC_{50} = 9.53 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
	Green algae 96-hour EC_{50} = 16.98 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

MBHA CASRN 5129-00-0			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Chronic Aquatic Toxicity	**HIGH: Estimated ChV for fish and ChV for algae are in the range of 0.1-1.0 mg/L.**		
Fish ChV	Fish 32/33-day ChV = 0.97 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
	Fish 30-day ChV = 2.41 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	
	Fish ChV = 4.27 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid ChV	Daphnid ChV = 3.050 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	
	Daphnid 21-day ChV = 12.60 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
	Daphnid 21-day ChV = 10.19 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	
Saltwater Invertebrate ChV	Mysid shrimp ChV = 194.76 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
Green Algae ChV	Green algae ChV = 0.450 mg/L (Estimated) ECOSAR: polyphenols	ECOSAR version 1.00	

MBHA CASRN 5129-00-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Green algae ChV = 3.07 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
		Green algae ChV = 7.05 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Earthworm Subchronic Toxicity		Earthworm 14-day LC_{50} = 1,922.81 mg/L (Estimated) ECOSAR: esters (MBHA may not be soluble enough to measure this predicted effect)	ECOSAR version 1.00	
ENVIRONMENTAL FATE				
Transport		**MBHA is expected to partition primarily to soil based on results from a level III fugacity model incorporating estimated property data. Based on its estimated pK_a, it is expected to exist primarily in the neutral form at environmentally-relevant pH, but anionic forms may be present at the upper-range of environmental pH. The neutral form of MBHA is expected to be moderately mobile in soil based on its estimated K_{oc}. The anionic form may have higher mobility, as anions do not bind as strongly to organic carbon and clay. However, leaching of MBHA through soil to groundwater is not expected to be an important transport mechanism. In the atmosphere, MBHA is expected to exist in the particulate phase, based on its estimated vapor pressure. Particulates will be removed from air by wet or dry deposition. If released to soil, MBHA is expected to bind strongly to soils with minimal migration to subsurface depths. It is not expected to migrate from water or soil surfaces to air. Release of particulates to the atmosphere will result in deposition to soil and water surfaces.**		
	Henry's Law Constant ($atm\text{-}m^3/mole$)	$<1x10^{-8}$ (Estimated)	EPI	Cutoff value for nonvolatile compounds based on professional judgment.

MBHA CASRN 5129-00-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	7,300 (Estimated)	EPI	
	Level III Fugacity Model	Air = <1% Water = 15 % Soil = 81% Sediment = 3% (Estimated)	EPI	
Persistence		**MODERATE: The persistence of MHBA is based on an estimated half-life of 30 days in soil. MBHA is expected to partition primarily to soil. Experimental biodegradation data for MBHA were not available. Results from biodegradation models estimate ultimate biodegradation in weeks and primary degradation in days-weeks. Biodegradation under anaerobic methanogenic conditions is not probable based on results from estimation models. MBHA does not contain chromophores that absorb light at environmentally-relevant wavelengths. Therefore, it is not expected to be susceptible to direct photolysis. Hydrolysis is expected to be negligible based on hydrolysis rate estimations. The atmospheric half-life of MBHA is estimated at 1.8 hours, although it is expected to exist primarily as a particulate in air. Biodegradation is expected to be the predominant fate pathway for MBHA in the environment.**		
Water	**Aerobic Biodegradation**	Days-weeks (primary survey model) Weeks (ultimate survey model)	EPI	
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (anaerobic-methanogenic biodegradation probability model)	EPI	
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	1.6 hours (Estimated)	EPI	

MBHA CASRN 5129-00-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	The substance does not contain functional groups that would be expected to absorb light at wavelengths >290 nm.
	Hydrolysis	Half-life at pH 8 = 200 days (Estimated) Half-life at pH 7 >1 year (Estimated)	EPI	
	Pyrolysis			No data located.
Environmental Half-life		30 days	EPI, PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**LOW: The estimated BCF is <100.**		
	Fish BCF	31 (Estimated)	EPI	
	BAF	6 (Estimated)	EPI	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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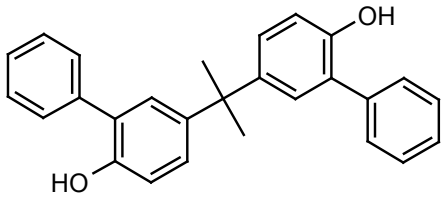
BisOPP-A



CASRN: 24038-68-4

MW: 380.49

MF: $C_{27}H_{24}O_2$

Physical Forms:
Neat: Solid

Use: Developer for thermal paper

SMILES: CC(C1=CC(C2=CC=CC=C2)=C(O)C=C1)(C)C3=CC(C4=CC=CC=C4)=C(O)C=C3

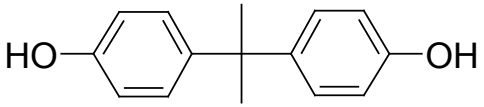
Synonyms: [1,1'-bisohenyl-2-ol]-2-ol, 5,5'(1-methylethylidene)bis-; 5,5'-Propane-2,2-diyldibiphenyl-2-ol; 4,4'-Isopropyllidenebis(2-phenylphenol); 2,2-Bis(2-hydroxy-5-biphenyl)propane

Polymeric: No
Oligomers: Not applicable

Metabolites, Degradates and Transformation Products: None

Analog: Bisphenol A (80-05-7)
Endpoint(s) using analog values: Acute toxicity, eye and dermal irritation, skin sensitization, reproductive and developmental toxicity, genotoxicity, repeated dose effects

Analog Structure:



Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)

Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2011).

Risk Assessments: None identified

BisOPP-A CASRN 24038-68-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	118 (Measured)	ChemSpider, 2010	Secondary source; study details and test conditions were not provided.
Boiling Point (°C)	>300 (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for high boiling point compounds according to HPV assessment guidance.
Vapor Pressure (mm Hg)	$<1x10^{-8}$ (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for nonvolatile compounds according to HPV assessment guidance.
Water Solubility (mg/L)	0.011 (Estimated)	EPI	
Log K_{ow}	7.2 (Estimated)	EPI	
Flammability (Flash Point)			No data located.
Explosivity			No data located.
pH			No data located.
pK_a	10.8-10.9 (Estimated)	SPARC	

BisOPP-A CASRN 24038-68-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**BisOPP-A is estimated not to be absorbed through the skin and poorly absorbed via the lungs and gastrointestinal tract based on data for structurally similar compounds.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Not absorbed through the skin and has poor absorption through the lung and gastrointestinal tract (Estimated by analogy)	Professional judgment	Based on closely related confidential analog with similar structure, functional groups, and physical/chemical properties.
Acute Toxicity		**LOW: Based on analogy to BPA. Potential for acute oral and dermal toxicity of bisOPP-A is estimated to be low based on experimental data in animals for the analog BPA. Data for exposure to the analog BPA via inhalation were inconclusive, as only a single concentration was tested and a LC_{50} was not provided.**		
Acute Lethality	**Oral**	Rat LD_{50} = 3,200>5,000 mg/kg bw (Estimated by analogy)	NTP, 1982; European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; multiple studies, some guideline studies.
		Mouse LD_{50} = 4,000-5,200 mg/kg bw (Estimated by analogy)	NTP, 1982; European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; multiple studies, some guideline studies.
	Dermal	Rabbit LD_{50} = 3,000-6,400 mg/kg bw (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA. Adequate; limited study details for multiple studies reported in secondary sources.
	Inhalation	No deaths among male and female F344 rats (10/sex) exposed to BPA dust at 0.17 mg/L (highest attainable concentration) for 6 hours; transient slight nasal tract epithelial damage was evident. (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; test guidelines were not reported in secondary sources.

BisOPP-A CASRN 24038-68-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Carcinogenicity		**MODERATE: Estimated using OncoLogic expert system, which describes a potential for this compound as a potential carcinogen or tumorigenesis promoter arising from its structural similarity to estrogenic/androgenic compounds. The "phenols and phenolic compounds" structural alert was used.**		
	OncoLogic Results	Moderate (Estimated) OncoLogic class: phenols and phenolic compounds	OncoLogic	OncoLogic SAR analysis using the phenols and phenolic compounds class.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
Genotoxicity		**LOW: Based on analogy to BPA. FAO/WHO (2011) determined that: (1) the analog BPA is not a mutagen in *in vitro* test systems, (2) does not induce cell transformation, and (3) *in vivo* evidence for clastogenic effects induced by the analog BPA is inconsistent and inconclusive, although some *in vitro* studies have shown BPA to affect chromosomal structure in dividing cells. FAO/WHO (2011) concluded that the analog BPA is not likely to pose a genotoxic hazard to humans.**		
		Potential for mutagenicity (Estimated by analogy)	Professional judgment	Estimated based on reported experimental data for the analog BPA.
		Largely negative results in a variety of in vitro test systems, including studies with *Salmonella typhimurium*, Chinese hamster V79 cells, Syrian hamster embryo cells and mouse lymphoma cells. However, DNA damage was induced in MCF-7 and MDA-MB-231 cells, DNA adduct formation in Syrian hamster ovary cells and a number of positive findings have been reported for the potential for BPA to inhibit purified microtubule polymerization, affect the spindle apparatus and produce aneuploidy in *in vitro* studies with Chinese hamster V79 cells or oocytes from Balb/c or MF1	FAO/WHO, 2011	Based on the analog BPA.

BisOPP-A CASRN 24038-68-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		mice. FAO/WHO Expert Panel concludes: BPA is not a mutagen in *in vitro* test systems, nor does it induce cell transformation. BPA has been shown to affect chromosomal structure in dividing cells in *in vitro* studies, but evidence for this effect in *in vivo* studies is inconsistent and inconclusive. BPA is not likely to pose a genotoxic hazard to humans. (Estimated by analogy)		
Reproductive Effects		**MODERATE: Estimated based on analogy to BPA. Key studies identified by NTP for the analog BPA indicate there are multiple distinct endpoints with NOAELs in the range of Moderate hazard concern with LOAELs in the range of Low hazard concern. At the target dose of 50 mg/kg-day (BPA), the NOAELs are on the margin of High and Moderate hazard, according to DfE criteria. Benchmark Dose (BMD) Modeling conducted by NTP, which interpolates between NOAEL and LOAEL values, yields values that further support a Moderate hazard designation.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	Potential for reproductive toxicity (Estimated by analogy)	Professional judgment	Estimated based on test data located for a confidential analog.

BisOPP-A CASRN 24038-68-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for 12% decreased terminal body weight in F_1 parental males Reproductive toxicity: Females: NOAEL = 50 mg/kg bw-day LOAEL = 500 mg/kg bw-day for decreases in number of implantation sites, delayed vaginal opening in F_1, F_2, F_3 offspring BMDLs (change of 1 standard deviation from control) reported for delayed vaginal opening (females)- F_1 = 176 mg/kg-day F_2 = 228 mg/kg-day F_3 = 203 mg/kg-day Males: NOAEL = 50 mg/kg bw-day, LOAEL = 500 mg/kg-day for delayed preputial separation in F_1 males BMDLs (change of 1 standard deviation from control) reported for delayed preputial separation (males)- F_1 = 163 mg/kg-day F_2 = 203 mg/kg-day F_3 = 189 mg/kg-day (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; adequate, guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.

BisOPP-A CASRN 24038-68-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for increased incidences of centrilobular hepatocellular hypertrophy in males and females Reproductive toxicity: NOAEL = 50 mg/kg bw-day LOAEL = 600 mg/kg bw-day for increased gestation length, decreased epididymal sperm concentration in F_1 males, increased incidence of gross ovarian cysts in F_1 and F_2 females BMD_1 (change of 1 standard deviation from control) reported for increased gestation length F_0 = 1144 mg/kg-day (BMDL = 599 mg/kg-day) F_1 = 772 mg/kg-day (BMDL = 531 mg/kg-day) BMD_{10s} (10% extra risk) reported for increased incidence of gross ovarian cysts F_0 = 225 mg/kg-day (BMDL = 141 mg/kg-day) F_1 = 202 mg/kg-day (BMDL = 120 mg/kg-day) (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; adequate, guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.

BisOPP-A CASRN 24038-68-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Summary of Reproductive Effects	Female effects: There is sufficient evidence in rats and mice that BPA caused female reproductive toxicity with subchronic or chronic oral exposures with a NOAEL of 50 mg/kg bw-day and a LOAEL of 500 mg/kg bw-day. Male effects: There is sufficient evidence in rats and mice that BPA causes male reproductive toxicity with subchronic or chronic oral exposures with a NOAEL of 50 mg/kg bw-day and a LOAEL of 500 mg/kg bw/day. (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; Classified by NTP-CERHR as having High Utility.
		The FAO/WHO Expert Panel reviewed reproductive and developmental toxicity data for BPA located as of November 2010 and noted that most regulatory bodies reviewing the numerous studies on BPA have indicated an oral reproductive and developmental NOAEL of 50 mg/kg bw-day. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.

BisOPP-A CASRN 24038-68-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Developmental Effects		**HIGH: Estimated based on analogy to BPA. The NTP-CERHR (2008) Expert Panel concluded that there is suggestive evidence that BPA causes neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01-0.2 mg/kg bw-day) following developmental exposures. The FAO/WHO (2011) Expert Panel also concluded that while there was broad agreement in a NOAEL of 50 mg/kg bw-day for developmental toxicity based on standard bioassays, specific targeted studies identified neurodevelopmental effects at low doses (<1 mg/kg bw-day), but the human relevance of these studies is less certain. There is great variation in results with different types of studies measuring different endpoints; developmental effects at lower doses cannot be ruled out. Taken together these findings support a hazard designation of High concern.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Summary of Developmental Effects	Potential for developmental toxicity (Estimated by analogy)	Professional judgment	Estimated based on test data located for a confidential analog.

BisOPP-A CASRN 24038-68-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		The NTP-CERHR Expert Panel concluded that BPA: *does not cause malformations or birth defects in rats or mice at levels up to the highest doses evaluated: 640 mg/kg bw-day (rats) and 1,250 mg/kg bw-day (mice). *does not alter male or female fertility after gestational exposure up to doses of 450 mg/kg bw-day in the rat and 600mg/kg bw-day in the mouse (highest dose levels evaluated). *does not permanently affect prostate weight at doses up to 475 mg/kg bw-day in adult rats or 600 mg/kg bw-day in mice. *does not cause prostate cancer in rats or mice after adult exposure at up to 148 or 600 mg/kg bw-day, respectively. *does change the age of puberty in male or female rats at high doses (ca. 475 mg/kg bw-day). And that rodent studies ***suggest*** that BPA: *causes neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01–0.2 mg/kg bw-day). (Estimated by analogy)	NTP–CERHR, 2008; Professional judgment	Based on the analog BPA.

BisOPP-A CASRN 24038-68-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		The FAO/WHO Expert Panel reviewed reproductive and developmental toxicity data for BPA located as of November 2010 and noted that most regulatory bodies reviewing the numerous studies on BPA have indicated an oral reproductive and developmental NOAEL of 50 mg/kg bw-day.	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert. (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on structural alert.
Repeated Dose Effects		**MODERATE: Estimated based on analogy to BPA which produced histopathologic changes in the liver (centrilobular hepatocyte hypertrophy) from oral dosing at 50 mg/kg bw-day (NOAEL = 5 mg/kg bw-day) and there is uncertainty regarding the potential for BPA doses between the NOAEL of 5 mg/kg bw-day and the LOAEL of 50 mg/kg bw-day to cause adverse systemic effects. Furthermore, lesions in the nasal cavity of rats were reported following repeated inhalation exposure to BPA dust at 0.05 mg/L. These findings indicate a moderate hazard potential for the oral and inhalation exposure routes.**		
		The FAO/WHO Expert Panel reviewed located information regarding repeated-dose oral toxicity of BPA and concluded that results demonstrated effects on the liver, kidney, and body weight at doses of 50 mg/kg bw-day and higher and that the lowest NOAEL was 5 mg/kg bw-day, as identified in several studies. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.

BisOPP-A CASRN 24038-68-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Parental systemic toxicity: NOAEL = 4.75 mg/kg bw-day LOAEL = 47.5 mg/kg bw-day for 12% decreased terminal body weight in F_1 parental males (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.
	Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for increased incidences of centrilobular hepatocellular hypertrophy in males and females (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.
	NOAEL = 0.01 mg/L LOAEL = 0.05 mg/L based on microscopic changes in the anterior portion of the nasal cavity (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA.
	NOAEL = None established LOAEL = 0.047 mg/L for decreased body weight gain, increased liver and kidney weight, unspecified "morphological changes" in liver, kidney, and lungs (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; single exposure level, insufficient study details in secondary sources.
Skin Sensitization	**MODERATE: Based on analogy to BPA, bisOPP-A is estimated to be a skin sensitizer. Recent data from three BPA manufacturing facilities indicated that the chemical does not elicit skin sensitization. However, results of some human studies suggested the possibility of a dermal sensitization response, although cross-sensitization was not ruled out. Most animal studies conducted on the analog were negative for dermal sensitization, although assays may not have been maximized. There is evidence of ear swelling in a photoallergy test in mice and moderate redness and swelling following repeated dermal exposure in rabbits. The Moderate hazard designation is based on suggestive evidence of skin sensitization in humans and mice for the analog.**		

BisOPP-A CASRN 24038-68-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Skin Sensitization	Negative in a modified local lymph node assay of mice administered BPA epicutaneously on the ears at concentrations up to 30% on 3 consecutive days. (Estimated by analogy)	EINECS, 2010; Professional judgment	Based on the analog BPA; adequate, although the assay did not include concentrations >30%.
		Negative in a local lymph node assay modified to test for photoreactivity in mice administered BPA epicutaneously on the ears at concentrations up to 30% on 3 consecutive days and irradiated with UV light immediately following application. (Estimated by analogy)	EINECS, 2010; Professional judgment	Based on the analog BPA; adequate, although the assay did not include concentrations >30%.
		Negative in comprehensive medical surveillance data obtained from three BPA manufacturing plants for 875 employees examined for several years where workers were potentially exposed to other chemicals (phenol, acetone) that are not considered to be skin sensitizers. (Estimated by analogy)	EINECS, 2010; Professional judgment	Based on the analog BPA; adequate.
		Positive, rabbits; repeated dermal application (30 times over 37 days) of BPA (pure powder) produced moderate swelling and redness. Skin turned yellow followed by dark pigmentation after day 15. (Estimated by analogy)	NIOSH, 2010; Professional judgment	Based on the analog BPA; adequate.
		The Joint FAO/WHO Expert Meeting review of the toxicological aspects of BPA concludes that BPA is capable of producing a skin sensitization response in humans. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.

BisOPP-A CASRN 24038-68-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**MODERATE: Based on analogy to BPA. BisOPP-A is estimated to be slightly to highly irritating to rabbit eyes based on test data for the analog BPA.**		
	Eye Irritation	Rabbit, slightly to highly irritating	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA. Adequate; study details provided for multiple studies indicate potential for BPA to cause eye irritation.
Dermal Irritation		**MODERATE: Based on analogy to BPA. BisOPP-A is estimated to be slightly to moderately irritating to rabbit and guinea pig skin based on test data for the analog and NIOSH identifying BPA as a skin irritant.**		
	Dermal Irritation	Rabbit, nonirritating to slightly irritating when applied as undiluted or 10% aqueous suspension to intact or abraded skin. (Estimated by analogy)	European Commission, 2000; EINECS, 2010; NIOSH, 2010; Professional judgment	Based on the analog BPA. Adequate, study details provided for multiple studies indicate potential for BPA to cause dermal irritation.
		Rabbit, moderately irritating when applied as 40% solution in dimethyl sulfoxide under non-occlusive conditions. (Estimated by analogy)	European Commission, 2000; Professional judgment	Based on the analog BPA; adequate.
		Guinea pig, not irritating when applied as 5% solution in acetone for 24 hours under occlusive conditions. (Estimated by analogy)	European Commission, 2000; Professional judgment	Based on the analog BPA; adequate.
Endocrine Activity		**No data located.**		
				No data located.
Immunotoxicity		**No data located.**		
	Immune System Effects			No data located.
ECOTOXICITY				
ECOSAR Class		Polyphenols		

BisOPP-A CASRN 24038-68-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Toxicity	**LOW: The log K_{ow} of 7.17 for this compound exceeds the SAR limitations to predict acute aquatic toxicity. No effects at saturation (NES) are predicted for these endpoints.**		
Fish LC_{50}	Fish 96-hour LC_{50} = 0.012 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	NES: The chemical may not be soluble enough to measure this predicted effect; the log K_{ow} of 7.17 for this chemical exceeds the SAR limitation for log K_{ow} of 7.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Fish 96-hour LC_{50} = 0.034 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	NES: The chemical may not be soluble enough to measure this predicted effect; the log K_{ow} of 7.17 for this chemical exceeds the SAR limitation for log K_{ow} of 7.0; NES are predicted for these endpoints.

BisOPP-A CASRN 24038-68-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid LC_{50}	Daphnid 48-hour LC_{50} = 0.013 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	NES: The chemical may not be soluble enough to measure this predicted effect; the log K_{ow} of 7.17 for this chemical exceeds the SAR limitation for log K_{ow} of 5.5; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid 48-hour LC_{50} = 0.017 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	NES: The chemical may not be soluble enough to measure this predicted effect; the log K_{ow} of 7.17 for this chemical exceeds the SAR limitation for log K_{ow} of 5.5; NES are predicted for these endpoints.

BisOPP-A CASRN 24038-68-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae EC_{50}	Green algae 96-hour LC_{50} = 0.048 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	NES: The chemical may not be soluble enough to measure this predicted effect; the log K_{ow} of 7.17 for this chemical exceeds the SAR limitation for log K_{ow} of 6.4; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Green algae 96-hour LC_{50} = 1.13 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	NES: The chemical may not be soluble enough to measure this predicted effect; the log K_{ow} of 7.17 for this chemical exceeds the SAR limitation for log K_{ow} of 6.4; NES are predicted for these endpoints.
Chronic Aquatic Toxicity	**HIGH: Based on estimated ChV values <0.1 mg/L for fish, Daphnid, and green algae.**		
Fish ChV	Fish ChV = 0.0010 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Fish 30-day ChV = 0.004 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	

BisOPP-A CASRN 24038-68-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid ChV		Daphnid ChV = 0.003 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
		Daphnid 21-day ChV = 0.005 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
Green Algae ChV		Green algae ChV = 0.041 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
		Green algae ChV = 0.045 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
ENVIRONMENTAL FATE				
Transport		**Evaluation of bisOPP-A transport is based entirely on QSAR estimations for fugacity (level III), disassociation constant (pK_a), K_{oc}, volatilization, and vapor pressure. It is expected to exist in neutral form at environmentally-relevant pH. BisOPP-A is expected to partition primarily to soil; therefore, leaching through soil to groundwater is not expected to be an important transport mechanism. In the atmosphere, bisOPP-A is expected to exist in the particulate phase, which will be deposited back to the soil and water surfaces through wet or dry deposition.**		
	Henry's Law Constant ($atm\text{-}m^3/mole$)	$<1x10^{-8}$ (Estimated)	EPI	Cutoff value for nonvolatile compounds, based on professional judgment.

BisOPP-A CASRN 24038-68-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Sediment/Soil Adsorption/ Desorption Coefficient – K_{oc}	>30,000 (Estimated)	EPI; U.S. EPA, 2004; Professional judgment	Cutoff value for nonmobile compounds.
	Level III Fugacity Model	Air = <1% Water = 2% Soil = 36% Sediment = 62% (Estimated)	EPI	
Persistence		**HIGH: The persistence of bisOPP-A is based on an estimated half-life of 340 days in soil. BisOPP-A is expected to partition primarily to soil. Experimental biodegradation data for bisOPP-A were not located. The biodegradation assessment for bisOPP-A is based entirely on QSARs of aerobic and anaerobic biodegradation. Results from these models estimate primary biodegradation in weeks and ultimate degradation in weeks-months. Biodegradation under anaerobic methanogenic conditions is estimated to be not probable. BisOPP-A does not contain functional groups that absorb light at environmentally-relevant wavelengths. Therefore, it is not expected to be susceptible to direct photolysis. It is not expected to undergo hydrolysis as it does not contain hydrolyzable functional groups. The atmospheric half-life of bisOPP-A is estimated to be 1.8 hours, although it is expected to exist primarily as a particulate in air. Based on the estimated data and qualitative assessments based on functional groups, biodegradation of bisOPP-A is expected to be the major removal process in the environment.**		
Water	**Aerobic Biodegradation**	Weeks (primary survey model) Weeks-months (ultimate survey model)	EPI	
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (anaerobic-methanogenic biodegradation probability model)	EPI	
	Soil Biodegradation w/ Product Identification			No data located.

BisOPP-A CASRN 24038-68-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	2 hours (Estimated assuming 12-hour day and hydroxyl radical concentration of 1.5x106 molecules/cm3)	EPI	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	The substance does not contain functional groups that would be expected to absorb light at wavelengths >290 nm.
	Hydrolysis	Not a significant fate process (Estimated)	Wolfe and Jeffers, 2000; Professional judgment	The substance does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.
	Pyrolysis			No data located.
Environmental Half-life		340 days (Estimated)	EPI; PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**MODERATE: The estimated fish BAF is <1,000. Although the BCF suggests a High potential hazard, the BAF model is anticipated to better account for metabolism of this substance.**		
	Fish BCF	11,000 (Estimated)	EPI	
	BAF	590 (Estimated)	EPI	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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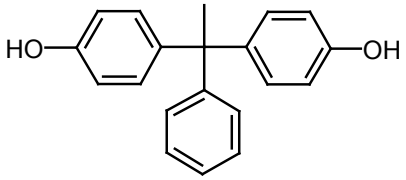
Bisphenol AP



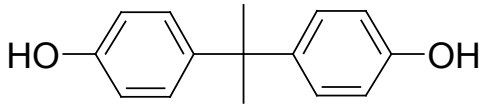
	CASRN: 1571-75-1
	MW: 290.36
	MF: $C_{20}H_{18}O_2$
	Physical Forms: **Neat:** Solid
	Use: Developer for thermal paper

SMILES: OC1=CC=C(C(C)(C2=CC=CC=C2)C3=CC=C(O)C=C3)C=C1

Synonyms: 4,4'-(α-methylbenzylidene)diphenol; 4,4′-(1-Phenylethylidene)bisphenol; phenol, 4,4'-(1-phenylethylidene)bis-

Polymeric: No
Oligomers: Not applicable

Metabolites, Degradates and Transformation Products: None

Analog: Bisphenol A (80-05-7) **Endpoint(s) using analog values:** Acute toxicity, dermal irritation, skin sensitization, reproductive and developmental toxicity, genotoxicity, repeated dose effects **Analog:** Confidential analog (structure not available) **Endpoint(s) using analog values:** Eye irritation, immunotoxicity	**Analog Structure:** 

Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)

Risk Phrases: 50/53 - Very toxic to aquatic organisms may cause long-term adverse effects in the aquatic environment (ESIS, 2011).

Risk Assessments: None identified

Bisphenol AP CASRN 1571-75-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	189	ChemSpider, 2010	Secondary source, consistent with other reported values.
	188-191 (Measured)	Aldrich, 2009	Adequate; measured by chemical supplier. Consistent with other reported values.
Boiling Point (°C)	>300 (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for high boiling compounds according to HPV assessment guidance.
Vapor Pressure (mm Hg)	$<1x10^{-8}$ (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for nonvolatile compounds according to HPV assessment guidance.
Water Solubility (mg/L)	1.1 (Estimated)	EPI	
Log K_{ow}	4.9 (Estimated)	EPI	
Flammability (Flash Point)			No data located.
Explosivity			No data located.
pH			No data located.
pK_a	9.9-10.1 (Estimated)	SPARC	

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Bisphenol AP, as a neat material, is estimated to not be absorbed through the skin and have poor skin absorption when in solution. Bisphenol AP is expected to have poor absorption via the lungs and gastrointestinal tract.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Not absorbed through the skin and has poor absorption to skin when in a solution; poor absorption through the lung and gastrointestinal tract. (Estimated by analogy)	Professional judgment	Based on closely related confidential analog with similar structure, functional groups, and physical/chemical properties.
Acute Mammalian Toxicity		**LOW: The acute oral and dermal toxicity hazard of bisphenol AP is estimated to be low based on analogy to BPA. Data for exposure to the analog BPA via inhalation were inconclusive, as only a single concentration was tested and a LC_{50} was not provided.**		
Acute Lethality	**Oral**	Rat LD_{50} = 3,200->5,000 mg/kg bw (Estimated by analogy)	NTP, 1982; European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; multiple studies, some guideline studies.
		Mouse LD_{50} = 4,000-5,200 mg/kg bw (Estimated by analogy)	NTP, 1982; European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; multiple studies, some guideline studies.
	Dermal	Rabbit LD_{50} = 3,000-6,400 mg/kg bw (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; limited study details for multiple studies reported in secondary sources.
	Inhalation	No deaths among male and female F344 rats (10/sex) exposed to BPA dust at 0.17 mg/L (highest attainable concentration) for 6 hours; transient slight nasal tract epithelial damage was evident. (Estimated by analogy)	EINECS, 2010; European Commission, 2000; Professional judgment	Based on the analog BPA; test guidelines were not reported in secondary sources.

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Carcinogenicity		**MODERATE: Estimated using OncoLogic expert system, which describes potential for this compound as a potential carcinogen or tumorigenesis promoter arising from its structural similarity to estrogenic/androgenic compounds, using the "phenols and phenolic compounds" structural alert**.		
	OncoLogic Results	Moderate (Estimated) OncoLogic class: phenols and phenolic compounds	OncoLogic	OncoLogic SAR analysis using the phenols and phenolic compounds class.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/ Carcinogenicity			No data located.
Genotoxicity		**LOW: Based on analogy to BPA. FAO/WHO (2011) determined that: (1) the analog BPA is not a mutagen in *in vitro* test systems, (2) does not induce cell transformation, and (3) *in vivo* evidence for clastogenic effects induced by the analog BPA is inconsistent and inconclusive although some in vitro studies have shown BPA to affect chromosomal structure in dividing cells. The conclusion of FAO/WHO (2011) is that the analog BPA is not likely to pose a genotoxic hazard to humans.**		
	Gene Mutation *in vitro*	Potential for mutagenicity (Estimated by analogy)	Professional judgment	Estimated based on located test data for a confidential analog with additional substituents.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Potential for mutagenicity; positive for chromosomal aberrations in Chinese hamster ovary (CHO) cells with metabolic activation (Estimated by analogy)	Professional judgment	Estimated based on located test data for a confidential analog with additional substituents.
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Other	Largely negative results in a variety of in vitro test systems, including studies with *Salmonella typhimurium*, Chinese hamster V79 cells, Syrian hamster embryo cells, and mouse lymphoma cells. However, DNA damage was induced in MCF-7 and MDA-MB-231 cells, DNA adduct formation in Syrian hamster ovary cells and a number of positive findings have been reported for the potential for BPA to inhibit purified microtubule polymerization, affect the spindle apparatus and produce aneuploidy in *in vitro* studies with Chinese hamster V79 cells or oocytes from Balb/c or MF1 mice. FAO/WHO Expert Panel concludes: BPA is not a mutagen in *in vitro* test systems, nor does it induce cell transformation. BPA has been shown to affect chromosomal structure in dividing cells in *in vitro* studies, but evidence for this effect in *in vivo* studies is inconsistent and inconclusive. BPA is not likely to pose a genotoxic hazard to humans. (Estimated by analogy)	FAO/WHO, 2011	Based on the analog BPA.
Reproductive Effects		**MODERATE: Estimated based on analogy to BPA. Key studies identified by NTP for the analog BPA indicate there are multiple distinct endpoints with NOAELs in the range of Moderate hazard concern with LOAELs in the range of Low hazard concern. At the target dose of 50 mg/kg-day (BPA), the NOAELs are on the margin of High and Moderate hazard, according to DfE criteria. Benchmark Dose (BMD) Modeling conducted by NTP, which interpolates between NOAEL and LOAEL values, yields values that further support a Moderate hazard designation.**		

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	Potential for toxic effects to prostate, testes and ovaries. Rat, 28-day oral study NOAEL = 5 mg/kg-day (Estimated by analogy)	Professional judgment	Estimated based on located test data for a confidential analog with additional substituents; a LOAEL for these effects was not identified.

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for 12% decreased terminal body weight in F_1 parental males Reproductive toxicity: Females: NOAEL = 50 mg/kg bw-day LOAEL = 500 mg/kg bw-day for decreases in number of implantation sites, delayed vaginal opening in F_1, F_2, F_3 offspring BMDLs (change of 1 standard deviation from control) reported for delayed vaginal opening (females)- F_1 = 176 mg/kg-day F_2 = 228 mg/kg-day F_3 = 203 mg/kg-day Males: NOAEL = 50 mg/kg bw-day, LOAEL = 500 mg/kg-day for delayed preputial separation in F_1 males BMDLs (change of 1 standard deviation from control) reported for delayed preputial separation (males)- F_1 = 163 mg/kg-day F_2 = 203 mg/kg-day F_3 = 189 mg/kg-day (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; adequate, guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for increased incidences of centrilobular hepatocellular hypertrophy in males and females Reproductive toxicity: NOAEL = 50 mg/kg bw-day LOAEL = 600 mg/kg bw-day for increased gestation length, decreased epididymal sperm concentration in F_1 males, increased incidence of gross ovarian cysts in F_1 and F_2 females BMD_1 (change of 1 standard deviation from control) reported for increased gestation length F_0 = 1144 mg/kg-day (BMDL = 599 mg/kg-day) F_1 = 772 mg/kg-day (BMDL = 531 mg/kg-day) BMD_{10s} (10% extra risk) reported for increased incidence of gross ovarian cysts F_0 = 225 mg/kg-day (BMDL = 141 mg/kg-day) F_1 = 202 mg/kg-day (BMDL = 120 mg/kg-day) (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; adequate, guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Summary of Reproductive Effects	Female effects: There is sufficient evidence in rats and mice that BPA caused female reproductive toxicity with subchronic or chronic oral exposures with a NOAEL of 50 mg/kg bw-day and a LOAEL of 500 mg/kg bw-day. Male effects: There is sufficient evidence in rats and mice that BPA causes male reproductive toxicity with subchronic or chronic oral exposures with a NOAEL of 50 mg/kg bw-day and a LOAEL of 500 mg/kg bw/day. (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; Classified by NTP-CERHR as having High Utility.
		The joint FAO/WHO Expert Panel reviewed reproductive and developmental toxicity data for BPA located as of November 2010 and noted that most regulatory bodies reviewing the numerous studies on BPA have indicated an oral reproductive and developmental NOAEL of 50 mg/kg bw-day. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.
Developmental Effects		**HIGH: Estimated based on analogy to BPA. The NTP-CERHR (2008) Expert Panel concluded that there is suggestive evidence that BPA causes neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01-0.2 mg/kg bw-day) following developmental exposures. The FAO/WHO (2011) Expert Panel also concluded that while there was broad agreement in a NOAEL of 50 mg/kg bw-day for developmental toxicity based on standard bioassays, specific targeted studies identified neurodevelopmental effects at low doses (<1 mg/kg bw-day), but the human relevance is less certain. There is great variation in results with different types of studies measuring different endpoints; developmental effects at lower doses cannot be ruled out. Taken together these findings support a hazard designation of High concern.**		

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Summary of Developmental Effects	The NTP-CERHR Expert Panel concluded that BPA: *does not cause malformations or birth defects in rats or mice at levels up to the highest doses evaluated: 640 mg/kg bw-day (rats) and 1,250 mg/kg bw-day (mice). *does not alter male or female fertility after gestational exposure up to doses of 450 mg/kg bw-day in the rat and 600mg/kg bw-day in the mouse (highest dose levels evaluated). *does not permanently affect prostate weight at doses up to 475 mg/kg bw-day in adult rats or 600 mg/kg bw-day in mice. *does not cause prostate cancer in rats or mice after adult exposure at up to 148 or 600 mg/kg bw-day, respectively. *does change the age of puberty in male or female rats at high doses (ca. 475 mg/kg bw-day). And that rodent studies ***suggest*** that BPA: *causes neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01-0.2 mg/kg bw-day). (Estimated by analogy)	NTP–CERHR, 2008; Professional judgment	Based on the analog BPA.

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		The joint FAO/WHO Expert Panel reviewed reproductive and developmental toxicity data for BPA located as of November 2010 and noted that most regulatory bodies reviewing the numerous studies on BPA have indicated an oral reproductive and developmental NOAEL of 50 mg/kg bw-day.	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert. (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on structural alert.
Repeated Dose Effects		**MODERATE: Estimated based on analogy to BPA, which produced histopathologic changes in the liver (centrilobular hepatocyte hypertrophy) from oral dosing at 50 mg/kg bw-day (NOAEL = 5 mg/kg bw-day) and there is uncertainty regarding the potential for BPA doses between the NOAEL of 5 mg/kg bw-day and the LOAEL of 50 mg/kg-day to cause adverse systemic effects. Furthermore, lesions in the nasal cavity of rats were reported following repeated inhalation exposure to BPA dust at 0.05 mg/L. These findings indicate a Moderate hazard potential for the oral and inhalation exposure routes. In addition, while no LOAEL was identified, data located for a confidential analog indicates the potential that bisphenol AP may cause toxic effects to the blood, liver, and kidney.**		
		Potential for toxic effects to blood, liver, and kidney Rat, 28-day oral study NOAEL = 5 mg/kg-day (Estimated by analogy)	Professional judgment	Estimated based on located test data for a confidential analog with additional substituents; a LOAEL for these effects was not identified.

Bisphenol AP CASRN 1571-75-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	The FAO/WHO Expert Panel reviewed the located information regarding repeated-dose oral toxicity of BPA and concluded that results demonstrated effects on the liver, kidney, and body weight at doses of 50 mg/kg bw-day and higher and that the lowest NOAEL was 5 mg/kg bw-day, as identified in several studies. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.
	Parental systemic toxicity: NOAEL = 4.75 mg/kg bw-day LOAEL = 47.5 mg/kg bw-day for 12% decreased terminal body weight in F_1 parental males (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.
	Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for increased incidences of centrilobular hepatocellular hypertrophy in males and females (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.
	NOAEL = 0.01 mg/L LOAEL = 0.05 mg/L based on microscopic changes in the anterior portion of the nasal cavity (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA.

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		NOAEL = None established LOAEL = 0.047 mg/L for decreased body weight gain, increased liver and kidney weight, unspecified "morphological changes" in liver, kidney, and lungs (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; single exposure level, insufficient study details in secondary sources.
Skin Sensitization		**MODERATE: Based on analogy to BPA, bisphenol AP is estimated to be a skin sensitizer. Recent data from three BPA manufacturing facilities indicate that it does not elicit skin sensitization. However, results of some human studies suggest the possibility of a dermal sensitization response, although cross-sensitization was not ruled out. Most animal studies conducted on the analog, BPA, were negative for dermal sensitization, although assays may not have been maximized. There is evidence of ear swelling in a photoallergy test in mice and moderate redness and swelling following repeated dermal exposure in rabbits. Based on suggestive evidence of skin sensitization in humans and mice for the analog, a Moderate hazard designation is warranted.**		
	Skin Sensitization	Negative in a modified local lymph node assay of mice administered BPA epicutaneously on the ears at concentrations up to 30% on 3 consecutive days. (Estimated by analogy)	EINECS, 2010; Professional judgment	Based on the analog BPA; adequate, although the assay did not include concentrations >30%.
		Negative in a local lymph node assay modified to test for photoreactivity in mice administered BPA epicutaneously on the ears at concentrations up to 30% on 3 consecutive days and irradiated with UV light immediately following application. (Estimated by analogy)	EINECS, 2010; Professional judgment	Based on the analog BPA; adequate, although the assay did not include concentrations >30%.

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Negative in comprehensive medical surveillance data obtained from three BPA manufacturing plants for 875 employees examined for several years where workers were potentially exposed to other chemicals (phenol, acetone) that are not considered to be skin sensitizers. (Estimated by analogy)	EINECS, 2010; Professional judgment	Based on the analog BPA; adequate.
		Positive, rabbits; repeated dermal application (30 times over 37 days) of BPA (pure powder) produced moderate swelling and redness. Skin turned yellow followed by dark pigmentation after day 15. (Estimated by analogy)	NIOSH, 2010; Professional judgment	Based on the analog BPA; adequate.
		The Joint FAO/WHO Expert Meeting review of the toxicological aspects of BPA concludes that BPA is capable of producing a skin sensitization response in humans. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**MODERATE: Based on confidential analog, bisphenol AP was moderately irritating to rabbit eyes. Bisphenol AP may potentially be irritating to eyes.**		
	Eye Irritation	Potential for irritation to eyes; caused moderate eye irritation in rabbits (Estimated by analogy)	Professional judgment	Estimated based on located test data for a confidential analog.
Dermal Irritation		**MODERATE: Based on analogy to BPA. Bisphenol AP is estimated to be slightly to moderately irritating to rabbit skin based on test data for the analog and NIOSH identifying BPA as a skin irritant.**		

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Dermal Irritation	Rabbit, nonirritating to slightly irritating when applied as undiluted or 10% aqueous suspension to intact or abraded skin. (Estimated by analogy)	European Commission, 2000; EINECS, 2010; NIOSH, 2010; Professional judgment	Based on the analog BPA; the details provided for multiple studies indicate potential for BPA to cause dermal irritation.
		Rabbit, moderately irritating when applied as 40% solution in dimethyl sulfoxide under non-occlusive conditions. (Estimated by analogy)	European Commission, 2000; Professional judgment	Based on the analog BPA; adequate.
		Guinea pig, not irritating when applied as 5% solution in acetone for 24 hours under occlusive conditions. (Estimated by analogy)	European Commission, 2000; Professional judgment	Based on the analog BPA; adequate.
Endocrine Activity		**Based on *in vitro* data, Bisphenol AP exhibits endocrine activity. *In vitro* assays indicate that bisphenol AP can bind to estrogen receptors, elicit estrogen-induced gene transcription, and induce cell proliferation in MCF7 cancer cells. Bisphenol AP appears to be similar to or somewhat less potent than BPA in its estrogenic responses *in vitro*.**		
		In a human ER binding assay, the relative binding affinity (RBA) of bisphenol AP was 0.0803% compared to 126% for 17β-estradiol. RBAs for other bisphenol compounds included 0.195% for BPA, 0.129% for bisphenol C, 0.0719% for bisphenol F, and 0.0055% for bisphenol S. An RBA of 0.00473% was reported for PHBB.	METI, 2002	Adequate.

Bisphenol AP CASRN 1571-75-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In a reporter gene assay of estrogen-induced transcriptional activity, relative activity (RA) for bisphenol AP was 0.000184% compared to 81.7% for 17β-estradiol. RAs for other bisphenol compounds included 0.00278% for BPA, 0.00189% for bisphenol C, 0.000639% for bisphenol F, and 0.000254% for bisphenol S. An RA of 0.000592% was reported for PHBB.	METI, 2002	Adequate.
	In a competitive ER binding assay using human ERα, the RBA for bisphenol AP was 1.66% that of 17β-estradiol. RBAs for other bisphenol compounds included 1.68% for bisphenol C, 0.32% for BPA, and 0.09% for bisphenol F.	Coleman, Toscano et al., 2003	Adequate.
	In an ER-mediated reporter gene expression assay, bisphenol AP induced reporter gene expression at a relative activity (RA) of $9.0x10^{-5}$ that of 17β-estradiol. RAs for other bisphenol compounds included $2.75x10^{-3}$ for BPA, $5.3x10^{-4}$ for bisphenol F, and $4.9x10^{-4}$ for bisphenol C.	Coleman, Toscano et al., 2003	Adequate.
	In a proliferation assay of MCF-7 human breast cancer cells that contain ERα and ERβ and are known to proliferate in response to estrogens, bisphenol AP induced a proliferative response that was $6.0x10^{-4}$ that of 17β-estradiol. Proliferative values for other bisphenol compounds included $2.0x10^{-3}$ for BPA, $1.6x10^{-3}$ for bisphenol C, and $1.0x10^{-3}$ for bisphenol F.	Coleman, Toscano et al., 2003	Adequate.

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Immunotoxicity		**Estimated based on analogy to confidential analog. There is uncertain potential for immunotoxicity based on effects to the spleen.**		
	Immune System Effects	Uncertain potential for toxic effects to adrenal glands and spleen. Rat, 28-day oral study NOAEL = 5 mg/kg-day (Estimated by analogy)	Professional judgment	Estimated based on located test data for a confidential analog with additional substituents; a LOAEL for these effects was not identified.
ECOTOXICITY				
ECOSAR Class		Phenols, poly		
Acute Toxicity		**HIGH: Based on estimated LC_{50} values for fish and Daphnid and EC_{50} value for algae, which are all <1.0 mg/L.**		
Fish LC_{50}		Fish 96-hour LC_{50} = 0.580 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
		Fish 96-hour LC_{50} = 0.851mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid LC_{50}		Daphnid 48-hour LC_{50} = 0.694 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
		Daphnid 48-hour LC_{50} = 0.774 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	

Bisphenol AP CASRN 1571-75-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae EC_{50}	Green algae 96-hour EC_{50} = 0.967 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Green algae 96-hour EC_{50} = 1.38 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
Chronic Aquatic Toxicity	**HIGH: Based on an estimated fish ChV of 0.076 mg/L.**		
Fish ChV	Fish ChV = 0.076 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Fish 30-day ChV = 0.110 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
Daphnid ChV	Daphnid ChV = 0.106 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Daphnid 21-day ChV = 0.243 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
Green Algae ChV		Green algae ChV = 0.134 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
		Green algae ChV = 0.590 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
ENVIRONMENTAL FATE				
Transport		**Evaluation of bisphenol AP transport is based entirely on QSAR estimations for fugacity (level III), disassociation constant (pK_a), K_{oc}, volatilization, and vapor pressure. Bisphenol AP is expected to exist in neutral form at environmentally-relevant pH. Bisphenol AP is expected to partition primarily to soil; therefore, leaching through soil to groundwater is not expected to be an important transport mechanism. In the atmosphere, bisphenol AP is expected to exist in the particulate phase which will be deposited back to the soil and water surfaces through wet or dry deposition.**		
	Henry's Law Constant (atm-m^3/mole)	$<1x10^{-8}$ (Estimated)	EPI	Cutoff value for nonvolatile compounds, based on professional judgment.
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	>30,000 (Estimated)	EPI; U.S. EPA, 2004	Cutoff value for nonmobile compounds.
	Level III Fugacity Model	Air = <1% Water = 2.4% Soil = 44% Sediment = 53% (Estimated)	EPI	

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**HIGH: The persistence of bisphenol AP is based on an estimated half-life of 75 days in soil. Bisphenol AP is expected to partition primarily to soil based on results from a Level III fugacity model. Evaluation of the persistence of bisphenol AP is based entirely on QSARs of aerobic and anaerobic biodegradation. Results from these models estimate primary biodegradation in days-weeks and ultimate degradation in weeks-months. Biodegradation under anaerobic methanogenic conditions is not probable. Bisphenol AP does not contain chromophores that absorb light at environmentally-relevant wavelengths. Therefore, it is not expected to be susceptible to direct photolysis. It is not expected to undergo hydrolysis as it does not contain hydrolyzable functional groups. The atmospheric half-life of bisphenol AP is estimated at 1.5 hours, although it is expected to exist primarily as a particulate in air. Based on the estimated data and qualitative assessments based on functional groups, biodegradation of bisphenol AP is expected to be the major removal process in the environment.**		
Water	**Aerobic Biodegradation**	Days-weeks (primary survey model) Weeks-months (ultimate survey model)	EPI	
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (anaerobic-methanogenic biodegradation probability model)	EPI	
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	1.5 hours	EPI	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	Substance does not contain functional groups that would be expected to absorb light at wavelengths >290 nm.
	Hydrolysis	Not a significant fate process (Estimated)	Wolfe and Jeffers, 2000; Professional judgment	Substance does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.

Bisphenol AP CASRN 1571-75-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Pyrolysis			No data located.
Environmental Half-life		75 days	EPI	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**MODERATE: The estimated BCF is <1,000.**		
	Fish BCF	750 (Estimated)	EPI	
	BAF	250 (Estimated)	EPI	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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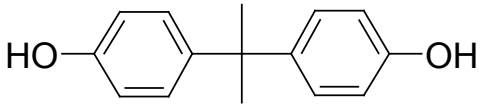
Substituted Phenolic Compound #1

	CASRN: Confidential CASRN
	MW: Confidential MW
	MF: Confidential MF
	Physical Forms: **Neat:** Solid
	Use: Developer for thermal paper
SMILES: This mixture containing confidential material is not amenable to the generation of a single SMILES notation.	
Synonyms:	
Polymeric: No **Oligomers:** Not applicable	
Metabolites, Degradates and Transformation Products: None identified	
Analog: Bisphenol A (80-05-7) **Endpoint(s) using analog values:** Acute toxicity, eye and skin irritation, skin sensitization, reproductive and developmental toxicity, repeated dose effects	**Analog Structure:** 
Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)	
Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2011).	
Risk Assessments: None identified	

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	171.5 (Measured)	Lide, 2008	Adequate; selected value for assessment.
	171-172 (Measured)	O'Neil et al., 2010	Adequate; reported values, which span a relatively narrow range, are consistent with those provided in other sources.
Boiling Point (°C)	>300 (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for high boiling point compounds according to HPV assessment guidance.
Vapor Pressure (mm Hg)	$<1x10^{-8}$ (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for nonvolatile compounds according to HPV assessment guidance.
Water Solubility (mg/L)	180 (Estimated)	EPI	
	Appreciably soluble in water	O'Neil et al., 2010	Inadequate; qualitative, nonspecific value.
	Very soluble in water	Lide, 2008	
Log K_{ow}	3.4 (Estimated)	EPI	
Flammability (Flash Point)	208°C (Measured)	Alfa Aesar, 2010	Adequate.
Explosivity			No data located.
pH			No data located.
pK_a	4.7; 10 (Estimated)	SPARC	
HUMAN HEALTH EFFECTS			
Toxicokinetics	**As a neat material, this substituted phenolic compound is estimated to not be absorbed through the skin and have poor skin absorption when in solution. This compound is expected to be moderately absorbed via the lungs and gastrointestinal tract.**		
Dermal Absorption *in vitro*			No data located.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Not absorbed through the skin as neat material and has poor absorption in solution; can be moderately absorbed through the lung and gastrointestinal tract (Estimated by analogy)	Professional judgment	Based on closely related confidential analog with similar structure, functional groups, and physical/chemical properties.
Acute Mammalian Toxicity		**LOW: Based on analogy to BPA. The acute oral and dermal toxicity hazard of this substituted phenolic compound is estimated to be low based on experimental data in animals for a closely related substance. Data for exposure to the analog BPA via inhalation were inconclusive, as only a single concentration was tested and a LC_{50} was not provided.**		
Acute Lethality	**Oral**	Rat LD_{50} = 3,200->5,000 mg/kg bw (Estimated by analogy)	NTP, 1982; European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; multiple studies, some guideline studies.
		Mouse LD_{50} = 4,000-5,200 mg/kg bw (Estimated by analogy)	NTP, 1982; European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; multiple studies, some guideline studies.
	Dermal	Rabbit LD_{50} = 3,000-6,400 mg/kg bw (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; adequate by weight of evidence, multiple studies, although study details were not reported in secondary sources.
	Inhalation	No deaths among male and female F344 rats (10/sex) exposed to BPA dust at 0.17 mg/L (highest attainable concentration) for 6 hours; transient slight nasal tract epithelial damage was evident. (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; test guidelines were not reported in secondary sources.
Carcinogenicity		**MODERATE: Estimated using OncoLogic expert system, which describes a concern for this compound as a potential carcinogen or tumorigenesis promoter arising from its structural similarity to estrogenic/androgenic compounds, using the "phenols and phenolic compounds" structural alert.**		
	OncoLogic Results	Moderate (Estimated) OncoLogic class: phenols and phenolic compounds	OncoLogic	OncoLogic SAR analysis using the phenols and phenolic compounds class.
	Carcinogenicity (Rat and Mouse)			No data located.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Combined Chronic Toxicity/ Carcinogenicity			No data located.
Genotoxicity		**LOW: This compound was not mutagenic in one assay that included several strains of *Salmonella typhimurium* and did not induce micronuclei in peripheral bone marrow of male B6C3F1 mice *in vivo*.**		
	Gene Mutation *in vitro*	Negative, Ames assay (standard plate) in *S. typhimurium* strains TA97, TA98, TA100, and TA1535 with and without metabolic activation	NTP, 2010	Adequate.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*			No data located.
	Chromosomal Aberrations *in vivo*	Negative, micronucleus assay of peripheral bone marrow and blood in B6C3F1 mice (males only)	*Mutat. Res.,* 2008 (Sanitized)	Adequate.
	DNA Damage and Repair			No data located.
	Other			No data located.
Reproductive Effects		**MODERATE: Based on analogy to BPA. Key studies identified by NTP for the analog BPA indicate there are multiple distinct endpoints with NOAELs in the range of Moderate hazard concern with LOAELs in the range of Low hazard concern. At the target dose of 50 mg/kg-day (BPA), the NOAELs are on the margin of High and Moderate hazard, according to DfE criteria. Benchmark Dose (BMD) Modeling conducted by NTP, which interpolates between NOAEL and LOAEL values, yields values that further support a Moderate hazard designation.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction and Fertility Effects	Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for 12% decreased terminal body weight in F_1 parental males Reproductive toxicity: Females: NOAEL = 50 mg/kg bw-day LOAEL = 500 mg/kg bw-day for decreases in number of implantation sites, delayed vaginal opening in F_1, F_2, F_3 offspring BMDLs (change of 1 standard deviation from control) reported for delayed vaginal opening (females)- F_1 = 176 mg/kg-day F_2 = 228 mg/kg-day F_3 = 203 mg/kg-day Males: NOAEL = 50 mg/kg bw-day, LOAEL = 500 mg/kg-day for delayed preputial separation in F_1 males BMDLs (change of 1 standard deviation from control) reported for delayed preputial separation (males)- F_1 = 163 mg/kg-day F_2 = 203 mg/kg-day F_3 = 189 mg/kg-day (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; adequate, guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for increased incidences of centrilobular hepatocellular hypertrophy in males and females Reproductive toxicity: NOAEL = 50 mg/kg bw-day LOAEL = 600 mg/kg bw-day for increased gestation length, decreased epididymal sperm concentration in F_1 males, increased incidence of gross ovarian cysts in F_1 and F_2 females BMD_1 (change of 1 standard deviation from control) reported for increased gestation length F_0 = 1144 mg/kg-day (BMDL = 599 mg/kg-day) F_1 = 772 mg/kg-day (BMDL = 531 mg/kg-day) BMD_{10s} (10% extra risk) reported for increased incidence of gross ovarian cysts F_0 = 225 mg/kg-day (BMDL = 141 mg/kg-day) F_1 = 202 mg/kg-day (BMDL = 120 mg/kg-day) (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; adequate, guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Summary of Reproductive Effects	Female effects: There is sufficient evidence in rats and mice that BPA caused female reproductive toxicity with subchronic or chronic oral exposures with a NOAEL of 50 mg/kg bw-day and a LOAEL of 500 mg/kg bw-day. Male effects: There is sufficient evidence in rats and mice that BPA causes male reproductive toxicity with subchronic or chronic oral exposures with a NOAEL of 50 mg/kg bw-day and a LOAEL of 500 mg/kg bw/day. (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA. Classified by NTP-CERHR as having High Utility.
		The joint FAO/WHO Expert Panel reviewed reproductive and developmental toxicity data for BPA located as of November 2010 and noted that most regulatory bodies reviewing the numerous studies on BPA have indicated an oral reproductive and developmental NOAEL of 50 mg/kg bw-day. (Estimated by analogy)	FAO/WHO, 2011	Based on the analog BPA.
Developmental Effects		**HIGH: Estimated based on analogy to BPA. The NTP-CERHR (2008) Expert Panel concluded that there is suggestive evidence that BPA causes neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01-0.2 mg/kg bw-day) following developmental exposures. The FAO/WHO (2011) Expert Panel also concluded that while there was broad agreement in a NOAEL of 50 mg/kg bw-day for developmental toxicity based on standard bioassays, specific targeted studies identified neurodevelopmental effects at low doses (<1 mg/kg bw-day), but the human relevance is less certain. There is great variation in results with different types of studies measuring different endpoints; developmental effects at lower doses cannot be ruled out. Taken together these findings support a hazard designation of High concern.**		

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Summary of Developmental Effects	The NTP-CERHR (2008) Expert Panel concluded that BPA: *does not cause malformations or birth defects in rats or mice at levels up to the highest doses evaluated: 640 mg/kg bw-day (rats) and 1,250 mg/kg bw-day (mice). *does not alter male or female fertility after gestational exposure up to doses of 450 mg/kg bw-day in the rat and 600 mg/kg bw-day in the mouse (highest dose levels evaluated). *does not permanently affect prostate weight at doses up to 475 mg/kg bw-day in adult rats or 600 mg/kg bw-day in mice. *does not cause prostate cancer in rats or mice after adult exposure at up to 148 or 600 mg/kg bw-day, respectively. *does change the age of puberty in male or female rats at high doses (ca. 475 mg/kg bw-day). And that rodent studies ***suggest*** that BPA: *causes neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01–0.2 mg/kg bw-day). (Estimated by analogy)	NTP–CERHR, 2008; Professional judgment	Based on the analog BPA.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		The joint FAO/WHO (2011) Expert Panel reviewed reproductive and developmental toxicity data for BPA located as of November 2010 and noted that most regulatory bodies reviewing the numerous studies on BPA have indicated an oral reproductive and developmental NOAEL of 50 mg/kg bw-day. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert. (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on structural alert.
Repeated Dose Effects		**MODERATE: Estimated based on analogy to BPA, which produced histopathologic changes in the liver (centrilobular hepatocyte hypertrophy) from oral dosing at 50 mg/kg bw-day (NOAEL = 5 mg/kg bw-day) and there is uncertainty regarding the potential for BPA doses between the NOAEL of 5 mg/kg bw-day and the LOAEL of 50 mg/kg bw-day to cause adverse systemic effects. Furthermore lesions in the nasal cavity of rats were reported following repeated inhalation exposure to BPA dust at 0.05 mg/L. These findings indicate a Moderate hazard concern for the oral and inhalation exposure routes.**		
		The FAO/WHO (2011) Expert Panel reviewed the available information regarding repeated-dose oral toxicity of BPA and concluded that results demonstrated effects on the liver, kidney, and body weight at doses of 50 mg/kg bw-day and higher and that the lowest NOAEL was 5 mg/kg-day, as identified in several studies. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Parental systemic toxicity: NOAEL = 4.75 mg/kg bw-day LOAEL = 47.5 mg/kg bw-day for 12% decreased terminal body weight in F_1 parental males (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.
	Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for increased incidences of centrilobular hepatocellular hypertrophy in males and females (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.
	NOAEL = 0.01 mg/L LOAEL = 0.05 mg/L based on microscopic changes in the anterior portion of the nasal cavity (Estimated by analogy)	EINECS, 2010; European Commission, 2000; Professional judgment	Based on the analog BPA.
	NOAEL = None established LOAEL = 0.047 mg/L for decreased body weight gain, increased liver and kidney weight, unspecified “morphological changes” in liver, kidney, and lungs (Estimated by analogy)	EINECS, 2010; European Commission, 2000; Professional judgment	Based on the analog BPA; single exposure level, insufficient study details in secondary sources.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Skin Sensitization		**MODERATE: Based on analogy to BPA, this substituted phenolic compound is estimated to be a skin sensitizer. Recent data from three BPA manufacturing facilities indicate that it does not elicit skin sensitization. However, results of some human studies suggest the possibility of a dermal sensitization response, although cross-sensitization was not ruled out. Most animal studies conducted on the analog were negative for dermal sensitization, although assays may not have been maximized. There is evidence of ear swelling in a photoallergy test in mice and moderate redness and swelling following repeated dermal exposure in rabbits. Based on suggestive evidence of skin sensitization in humans and mice for the analog, a Moderate hazard designation is warranted.**		
	Skin Sensitization	Negative in a modified local lymph node assay of mice administered BPA epicutaneously on the ears at concentrations up to 30% on 3 consecutive days. (Estimated by analogy)	EINECS, 2010; Professional judgment	Based on the analog BPA; adequate, although the assay did not include concentrations >30%.
		Negative in a local lymph node assay modified to test for photoreactivity in mice administered BPA epicutaneously on the ears at concentrations up to 30% on three consecutive days and irradiated with UV light immediately following application. (Estimated by analogy)	EINECS, 2010; Professional judgment	Based on the analog BPA; adequate, although the assay did not include concentrations >30%.
		Negative in comprehensive medical surveillance data obtained from three BPA manufacturing plants for 875 employees examined for several years where workers were potentially exposed to other chemicals (phenol, acetone) that are not considered to be skin sensitizers. (Estimated by analogy)	EINECS, 2010; Professional judgment	Based on the analog BPA; adequate.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Positive, rabbits; repeated dermal application (30 times over 37 days) of BPA (pure powder) produced moderate swelling and redness; skin turned yellow followed by dark pigmentation after day 15. (Estimated by analogy)	NIOSH, 2010; Professional judgment	Based on the analog BPA; adequate.
		The Joint FAO/WHO Expert Meeting review of the toxicological aspects of BPA concludes that BPA is capable of producing a skin sensitization response in humans. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**MODERATE: Based on analogy to BPA. The analog BPA was slightly to highly irritating to rabbit eyes.**		
	Eye Irritation	Rabbit, slightly to highly irritating	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA. Adequate; multiple studies, weight of evidence indicates potential for BPA to cause eye irritation.
Dermal Irritation		**MODERATE: This substituted phenolic compound is estimated to be slightly irritating to moderately irritating based on test data for the analog BPA.**		
	Dermal Irritation	Rabbit, nonirritating to slightly irritating when applied as undiluted or 10% aqueous suspension to intact or abraded skin. (Estimated by analogy)	European Commission, 2000; EINECS, 2010; NIOSH, 2010; Professional judgment	Based on the analog BPA. Adequate; multiple studies, weight of evidence indicates potential for BPA to cause dermal irritation.
		Rabbit, moderately irritating when applied as 40% solution in dimethyl sulfoxide under non-occlusive conditions. (Estimated by analogy)	European Commission, 2000; Professional judgment	Based on the analog BPA; adequate.
		Guinea pig, not irritating when applied as 5% solution in acetone for 24-hours under occlusive conditions. (Estimated by analogy)	European Commission, 2000; Professional judgment	Based on the analog BPA; adequate.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Endocrine Activity	**This compound exhibited a weakly positive ER binding affinity in one *in vitro* assay.**		
	The proprietary phenolic compound exhibited weak ER binding activity in preparations from uteri of ovariectomized Sprague-Dawley rats as evidenced by a relative binding affinity (RBA) that was 0.0007% of the binding affinity of 17β-estradiol. RBAs for other tested chemicals included 0.008% for BPA, 0.003% for PHBB and 0.0009% for bisphenol F.	Blair, Fang et al., 2000	Adequate.
Immunotoxicity	**No data located.**		
Immune System Effects			No data located.
ECOTOXICITY			
ECOSAR Class	Phenols, poly – acid		
Acute Toxicity	**HIGH: Based on an estimated 96-hour EC_{50} of 7.67 (ECOSAR class: neutral organics) for green algae.**		
Fish LC_{50}	Fish 96-hour LC_{50} = 14.75 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Fish 96-hour LC_{50} = 41.53 mg/L (Estimated) ECOSAR: phenols, poly - acid	ECOSAR version 1.00	
Daphnid LC_{50}	Daphnid 48-hour LC_{50} = 10.07 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Daphnid 48-hour LC_{50} = 103.05 mg/L (Estimated) ECOSAR: phenols, poly - acid	ECOSAR version 1.00	
Green Algae EC_{50}	Green algae 96-hour EC_{50} = 7.67 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Green algae 96-hour EC_{50} = 18.35 mg/L (Estimated) ECOSAR: phenols, poly - acid	ECOSAR version 1.00	
Chronic Aquatic Toxicity	**MODERATE: Based on ECOSAR-estimated data for fish, Daphnid, and green algae.**		
Fish ChV	Fish ChV = 1.36 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Fish 30-day ChV = 10.16 mg/L (Estimated) ECOSAR: phenols, poly - acid	ECOSAR version 1.00	
Daphnid ChV	Daphnid ChV = 1.19 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Daphnid 21-day ChV = 35.44 mg/L (Estimated) ECOSAR: phenols, poly - acid	ECOSAR version 1.00	
Green Algae ChV		Green algae ChV = 3.34 mg/L (Estimated) ECOSAR: phenols, poly - acid	ECOSAR version 1.00	
		Green algae ChV = 3.58 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
ENVIRONMENTAL FATE				
Transport		**Based on the Level III fugacity models incorporating the available experimental property data, this substituted phenolic compound is expected to partition primarily to soil where it is expected to be immobile in based on its estimated K_{oc}. Estimated volatilization half-lives indicate it will be nonvolatile from surface water. Volatilization from dry surface is also not expected based on its estimated vapor pressure. In the atmosphere, this substituted phenolic compound is expected to exist solely in the particulate phase, based on its estimated vapor pressure. Particulates may be removed from air by wet or dry deposition.**		
	Henry's Law Constant (atm-m^3/mole)	<$1x10^{-8}$ (Estimated)	EPI	Cutoff value for nonvolatile compounds based on professional judgment.
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	8,900 (Estimated)	EPI	
	Level III Fugacity Model	Air = <1% (Estimated) Water = 15% Soil = 81% Sediment = 4%	EPI	

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**MODERATE: Evaluation of the persistence of this compound is based entirely on QSARs in the compartment that this compound is most likely to be found, soil. Results from these models estimate a persistence half-life in soil of 30 days. The biodegradation models estimate primary biodegradation in days-weeks and ultimate degradation in weeks. Based on these data, the biodegradation half-life is expected to be <60 days. Biodegradation under anaerobic methanogenic conditions is not probable. This compound is not expected to undergo hydrolysis since it does not contain hydrolyzable functional groups. The atmospheric half-life of this compound is estimated at 1.5 hours, although it is expected to exist primarily in the particulate phase in air. Based on the estimated data and qualitative assessments based on functional groups, biodegradation of this compound is expected to be the primary removal process in the environment.**		
Water	**Aerobic Biodegradation**	Days-weeks (primary survey model) Weeks (ultimate survey model)	EPI	
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (anaerobic-methanogenic biodegradation probability model)	EPI	
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	1.5 hours (Estimated)	EPI	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	Substance does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Hydrolysis	Not a significant fate process (Estimated)	Wolfe and Jeffers, 2000; Professional judgment	Substance does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.
	Pyrolysis			No data located.
Environmental Half-life		30 days (Estimated)	EPI; PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**LOW: The fish BCF and BAF estimates are <100.**		
	Fish BCF	3.2 (Estimated)	EPI	
	BAF	84 (Estimated)	EPI	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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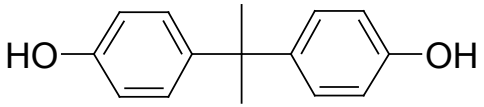
Substituted Phenolic Compound #2

	CASRN: Confidential CASRN
	MW: Confidential MW
	MF: Confidential MF
	Physical Forms: **Neat:** Solid
	Use: Developer for thermal paper
SMILES: This confidential material is not amenable to the generation of a single SMILES notation.	
Synonyms: None	
Polymeric: No **Oligomers:** Not applicable	
Metabolites, Degradates and Transformation Products: None identified	
Analog: Bisphenol A (80-05-7) **Endpoint(s) using analog values:** Acute toxicity, eye and skin irritation, skin sensitization, reproductive and developmental toxicity, genotoxicity, repeated dose effects	**Analog Structure:** 
Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)	
Risk Phrases: R43 - May cause sensitization by skin contact; 62 Possible risk of impaired fertility; 51/53 - Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (ESIS, 2011).	
Risk Assessments: None identified	

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	138 (Measured)	Chemspider, 2010	Adequate; secondary source, study details and test conditions were not provided; selected value for assessment.
	135-139 (Measured)	Aldrich, 2009	Adequate; measured by chemical supplier, consistent with other reported values.
Boiling Point (°C)	>300 (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for high boiling point compounds according to HPV assessment guidance.
Vapor Pressure (mm Hg)	$<1x10^{-8}$ (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for nonvolatile compounds according to HPV assessment guidance.
Water Solubility (mg/L)	0.12 (Estimated)	EPI	
Log K_{ow}	6.3 (Estimated)	EPI	
Flammability (Flash Point)			No data located.
Explosivity			No data located.
pH			No data located.
pK_a	10 (Estimated)	SPARC	

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Substituted phenolic compound #2 is estimated to not be absorbed through the skin and have poor absorption when in solution via the lungs and gastrointestinal tract.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Not absorbed through the skin and has poor absorption through the lung and gastrointestinal tract (Estimated by analogy)	Professional judgment	Based on closely related confidential analog with similar structure, functional groups, and physical/chemical properties.
Acute Mammalian Toxicity		**LOW: Based on analogy to BPA. The acute oral and dermal toxicity hazard of substituted phenolic compound #2 is estimated to be low based on experimental data in animals for a closely related substance. Data for exposure to the analog BPA via inhalation were inconclusive, as only a single concentration was tested and a LC_{50} was not provided.**		
Acute Lethality	**Oral**	Rat LD_{50} = 3,200-5,000 mg/kg bw (Estimated by analogy)	NTP, 1982; European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; multiple studies, some guideline studies.
		Mouse LD_{50} = 4,000-5,200 mg/kg bw (Estimated by analogy)	NTP, 1982; European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; multiple studies, some guideline studies.
	Dermal	Rabbit LD_{50} = 3,000-6,400 mg/kg bw (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; adequate by weight of evidence, multiple studies, although study details were not reported in secondary sources.
	Inhalation	No deaths among male and female F344 rats (10/sex) exposed to BPA dust at 0.17 mg/L (highest attainable concentration) for 6 hours; transient slight nasal tract epithelial damage was evident. (Estimated by analogy)	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA; test guidelines were not reported in secondary sources.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Carcinogenicity		**MODERATE: Estimated using OncoLogic expert system, which describes a concern for this compound as a potential carcinogen or tumorigenesis promoter arising from its structural similarity to estrogenic/androgenic compounds, using the "phenols and phenolic compounds" structural alert**.		
	OncoLogic Results	Moderate (Estimated) OncoLogic class: phenols and phenolic compounds	OncoLogic	OncoLogic SAR analysis using the phenols and phenolic compounds class.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/ Carcinogenicity			No data located.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Genotoxicity		**LOW: Based on analogy to BPA. FAO/WHO (2011) determined that: (1) the analog BPA is not a mutagen in *in vitro* test systems, (2) the analog BPA does not induce cell transformation, and (3) *in vivo* evidence for clastogenic effects induced by the analog BPA is inconsistent and inconclusive although some *in vitro* studies have shown BPA to affect chromosomal structure in dividing cells. The conclusion of FAO/WHO (2011) is that the analog BPA is not likely to pose a genotoxic hazard to humans.**		
		Largely negative results in a variety of in vitro test systems, including studies with *Salmonella typhimurium*, Chinese hamster V79 cells, Syrian hamster embryo cells, and mouse lymphoma cells. However, DNA damage was induced in MCF-7 and MDA-MB-231 cells, DNA adduct formation in Syrian hamster ovary cells and a number of positive findings have been reported for the potential for BPA to inhibit purified microtubule polymerization, affect the spindle apparatus and produce aneuploidy in *in vitro* studies with Chinese hamster V79 cells or oocytes from Balb/c or MF1 mice. FAO/WHO Expert Panel concludes: BPA is not a mutagen in *in vitro* test systems, nor does it induce cell transformation. BPA has been shown to affect chromosomal structure in dividing cells in *in vitro* studies, but evidence for this effect in *in vivo* studies is inconsistent and inconclusive. BPA is not likely to pose a genotoxic hazard to humans. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**MODERATE: Based on analogy to BPA. Key studies identified by NTP for the analog BPA indicate there are multiple distinct endpoints with NOAELs in the range of Moderate hazard concern with LOAELs in the range of Low hazard concern. At the target dose of 50 mg/kg-day (BPA), the NOAELs are on the margin of High and Moderate hazard, according to DfE criteria. Benchmark Dose (BMD) Modeling conducted by NTP, which interpolates between NOAEL and LOAEL values, yields values that further support a Moderate hazard designation.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction and Fertility Effects	Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for 12% decreased terminal body weight in F_1 parental males Reproductive toxicity: Females: NOAEL = 50 mg/kg bw-day LOAEL = 500 mg/kg bw-day for decreases in number of implantation sites, delayed vaginal opening in F_1, F_2, F_3 offspring BMDLs (change of 1 standard deviation from control) reported for delayed vaginal opening (females)- F_1 = 176 mg/kg-day F_2 = 228 mg/kg-day F_3 = 203 mg/kg-day Males: NOAEL = 50 mg/kg bw-day, LOAEL = 500 mg/kg-day for delayed preputial separation in F_1 males BMDLs (change of 1 standard deviation from control) reported for delayed preputial separation (males)- F_1 = 163 mg/kg-day F_2 = 203 mg/kg-day F_3 = 189 mg/kg-day (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; adequate, guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for increased incidences of centrilobular hepatocellular hypertrophy in males and females Reproductive toxicity: NOAEL = 50 mg/kg bw-day LOAEL = 600 mg/kg bw-day for increased gestation length, decreased epididymal sperm concentration in F_1 males, increased incidence of gross ovarian cysts in F_1 and F_2 females BMD_1 (change of 1 standard deviation from control) reported for increased gestation length F_0 = 1144 mg/kg-day (BMDL = 599 mg/kg-day) F_1 = 772 mg/kg-day (BMDL = 531 mg/kg-day) BMD_{10s} (10% extra risk) reported for increased incidence of gross ovarian cysts F_0 = 225 mg/kg-day (BMDL = 141 mg/kg-day) F_1 = 202 mg/kg-day (BMDL = 120 mg/kg-day) (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; adequate, guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Summary of Reproductive Effects	Female effects: There is sufficient evidence in rats and mice that BPA caused female reproductive toxicity with subchronic or chronic oral exposures with a NOAEL of 50 mg/kg bw-day and a LOAEL of 500 mg/kg bw-day. Male effects: There is sufficient evidence in rats and mice that BPA causes male reproductive toxicity with subchronic or chronic oral exposures with a NOAEL of 50 mg/kg bw-day and a LOAEL of 500 mg/kg bw/day. (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA. Classified by NTP-CERHR as having High Utility.
		The joint FAO/WHO Expert Panel reviewed reproductive and developmental toxicity data for BPA located as of November 2010 and noted that most regulatory bodies reviewing the numerous studies on BPA have indicated an oral reproductive and developmental NOAEL of 50 mg/kg bw-day. (Estimated by analogy)	FAO/WHO, 2011	Based on the analog BPA.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Developmental Effects		**HIGH: Based on analogy to BPA. The NTP-CERHR (2008) Expert Panel concluded that there is suggestive evidence that BPA causes neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01-0.2 mg/kg bw-day) following developmental exposures. The FAO/WHO (2011) Expert Panel also concluded that while there was broad agreement in a NOAEL of 50 mg/kg bw-day for developmental toxicity based on standard bioassays, specific targeted studies identified neurodevelopmental effects at low doses (<1 mg/kg bw-day), but the human relevance is less certain. There is great variation in results with different types of studies measuring different endpoints; developmental effects at lower doses cannot be ruled out. Taken together these findings support a hazard designation of High concern.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Summary of Developmental Effects	The NTP-CERHR (2008) Expert Panel concluded that BPA: *does not cause malformations or birth defects in rats or mice at levels up to the highest doses evaluated: 640 mg/kg bw-day (rats) and 1,250 mg/kg bw-day (mice). *does not alter male or female fertility after gestational exposure up to doses of 450 mg/kg bw-day in the rat and 600mg/kg bw-day in the mouse (highest dose levels evaluated). *does not permanently affect prostate weight at doses up to 475 mg/kg bw-day in adult rats or 600 mg/kg bw-day in mice. *does not cause prostate cancer in rats or mice after adult exposure at up to 148 or 600 mg/kg bw-day, respectively. *does change the age of puberty in male or female rats at high doses (ca. 475 mg/kg bw-day). And that rodent studies ***suggest*** that BPA: *causes neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01-0.2 mg/kg bw-day). (Estimated by analogy)	NTP–CERHR, 2008; Professional judgment	Based on the analog BPA.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		The joint FAO/WHO (2011) Expert Panel reviewed reproductive and developmental toxicity data for BPA located as of November 2010 and noted that most regulatory bodies reviewing the numerous studies on BPA have indicated an oral reproductive and developmental NOAEL of 50 mg/kg bw-day. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert. (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on structural alert.
Repeated Dose Effects		**MODERATE: Estimated based on analogy to BPA, which produced histopathologic changes in the liver (centrilobular hepatocyte hypertrophy) from oral dosing at 50 mg/kg bw-day (NOAEL = 5 mg/kg bw-day) and there is uncertainty regarding the potential for BPA doses between the NOAEL of 5 mg/kg bw-day and the LOAEL of 50 mg/kg bw-day to cause adverse systemic effects. Furthermore, lesions in the nasal cavity of rats were reported following repeated inhalation exposure to BPA dust at 0.05 mg/L. These findings indicate a Moderate hazard concern for the oral and inhalation exposure routes.**		

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	The FAO/WHO (2011) Expert Panel reviewed the available information regarding repeated-dose oral toxicity of BPA and concluded that results demonstrated effects on the liver, kidney, and body weight at doses of 50 mg/kg bw-day and higher and that the lowest NOAEL was 5 mg/kg bw-day, as identified in several studies. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.
	Parental systemic toxicity: NOAEL = 4.75 mg/kg bw-day LOAEL = 47.5 mg/kg bw-day for 12% decreased terminal body weight in F_1 parental males (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.
	Parental systemic toxicity: NOAEL = 5 mg/kg bw-day LOAEL = 50 mg/kg bw-day for increased incidences of centrilobular hepatocellular hypertrophy in males and females (Estimated by analogy)	NTP-CERHR, 2008; Professional judgment	Based on the analog BPA; guideline study as reported in the secondary source. Classified by NTP-CERHR as having High Utility.
	NOAEL = 0.01 mg/L LOAEL = 0.05 mg/L based on microscopic changes in the anterior portion of the nasal cavity (Estimated by analogy)	EINECS, 2010; European Commission, 2000; Professional judgment	Based on the analog BPA.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		NOAEL = None established LOAEL = 0.047 mg/L for decreased body weight gain, increased liver and kidney weight, unspecified "morphological changes" in liver, kidney, and lungs (Estimated by analogy)	EINECS, 2010; European Commission, 2000; Professional judgment	Based on the analog BPA; single exposure level, insufficient study details in secondary sources.
Skin Sensitization		**MODERATE: Based on analogy to BPA, substituted phenolic compound #2 is estimated to be a skin sensitizer. Recent data from three BPA manufacturing facilities indicate that it does not elicit skin sensitization. However, results of some human studies suggest the possibility of a dermal sensitization response, although cross-sensitization was not ruled out. Most animal studies conducted on the analog were negative for dermal sensitization, although assays may not have been maximized. There is evidence of ear swelling in a photoallergy test in mice and moderate redness and swelling following repeated dermal exposure in rabbits. Based on suggestive evidence of skin sensitization in humans and mice for the analog, a Moderate hazard designation is warranted.**		
	Skin Sensitization	Negative in a modified local lymph node assay of mice administered BPA epicutaneously on the ears at concentrations up to 30% on 3 consecutive days. (Estimated by analogy)	EINECS, 2010; Professional judgment	Based on the analog BPA; adequate, although the assay did not include concentrations >30%.
		Negative in a local lymph node assay modified to test for photoreactivity in mice administered BPA epicutaneously on the ears at concentrations up to 30% on 3 consecutive days and irradiated with UV light immediately following application. (Estimated by analogy)	EINECS, 2010; Professional judgment	Based on the analog BPA; adequate, although the assay did not include concentrations >30%.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Negative in comprehensive medical surveillance data obtained from three BPA manufacturing plants for 875 employees examined for several years where workers were potentially exposed to other chemicals (phenol, acetone) that are not considered to be skin sensitizers. (Estimated by analogy)	EINECS, 2010; Professional judgment	Based on the analog BPA; adequate.
		Positive, rabbits; repeated dermal application (30 times over 37 days) of BPA (pure powder) produced moderate swelling and redness. Skin turned yellow followed by dark pigmentation after day 15. (Estimated by analogy)	NIOSH, 2010; Professional judgment	Based on the analog BPA; adequate.
		The Joint FAO/WHO Expert Meeting review of the toxicological aspects of BPA concludes that BPA is capable of producing a skin sensitization response in humans. (Estimated by analogy)	FAO/WHO, 2011; Professional judgment	Based on the analog BPA.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**MODERATE: Based on analogy to BPA. Substituted phenolic compound #2 is estimated to be slightly to highly irritating to rabbit eyes based on test data for the analog BPA.**		
	Eye Irritation	Rabbit, slightly to highly irritating	European Commission, 2000; EINECS, 2010; Professional judgment	Based on the analog BPA. Adequate; multiple studies, weight of evidence indicates potential for BPA to cause eye irritation.
Dermal Irritation		**MODERATE: Substituted phenolic compound #2 is estimated to be slightly irritating to moderately irritating to rabbit skin based on test data for the analog BPA. NIOSH has assigned the analog BPA as a skin irritant.**		

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Dermal Irritation	Rabbit, nonirritating to slightly irritating when applied as undiluted or 10% aqueous suspension to intact or abraded skin. (Estimated by analogy)	European Commission, 2000; EINECS, 2010; NIOSH, 2010; Professional judgment	Based on the analog BPA. Adequate; multiple studies, weight of evidence indicates potential for BPA to cause dermal irritation.
		Rabbit, moderately irritating when applied as 40% solution in dimethyl sulfoxide under non-occlusive conditions. (Estimated by analogy)	European Commission, 2000; Professional judgment	Based on the analog BPA; adequate.
		Guinea pig, not irritating when applied as 5% solution in acetone for 24 hours under occlusive conditions. (Estimated by analogy)	European Commission, 2000; Professional judgment	Based on the analog BPA; adequate.
Endocrine Activity		**Substituted phenolic compound #2 is capable of eliciting an estrogenic response in rats injected with substituted phenolic compound #2 subcutaneously, as evidenced by increased uterine weight. Substituted phenolic compound #2 did not bind to estrogen receptors in one *in vitro* assay and did not elicit androgenic or anti-androgenic responses in another in vitro assay.**		
		In a uterotrophic assay in which immature female rats were injected with bisphenol F, bisphenol S, or substituted phenolic compound #2 subcutaneously for 3 consecutive days, observed changes in uterine weight indicated that bisphenol F, bisphenol S, and substituted phenolic compound #2 exerted both estrogenic and anti-estrogenic responses.	Akahori et al., 2008	Adequate.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In a uterotrophic assay of rats subcutaneously injected with bisphenol F once daily for 3 days, an apparent estrogenic effect was evidenced by increased absolute and relative uterine weight. Similar effects were elicited by bisphenol S and substituted phenolic compound #2.	*Toxicol. Lett.* 2004 (Sanitized)	Adequate.
	In a human ER binding assay, the relative binding affinity (RBA) of substituted phenolic compound #2 was 0.175% relative to 17β-estradiol (set at 100%). RBAs for other bisphenol compounds included 0.0719% for bisphenol F and 0.0055% for BPA.	*Toxicol. Lett.* 2004 (Sanitized)	Adequate.
	In an ERE-luciferase reporter assay using MCF-7 cells, substituted phenolic compound #2 did not appear to elicit an estrogenic response (EC_{50} >1,000 µM). EC_{50} values for other bisphenol compounds included 0.63% for BPA, 0.42 µM for bisphenol C, 1.0 µM for bisphenol F, and 1.1 µM for bisphenol S.	*Toxicol. Sci.,* 2005 (Sanitized)	Adequate.
	In an ERE-luciferase reporter assay using MCF-7 cells in the presence of 17β-estradiol, neither substituted phenolic compound #2, BPA, bisphenol C, bisphenol F, nor bisphenol S, appeared to exert an anti-estrogenic effect.	*Toxicol. Sci.,* 2005 (Sanitized)	Adequate.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		In an ARE-luciferase reporter assay using NIH3T3 cells without expressing AR, substituted phenolic compound #2 did not elicit an androgenic response or an anti-androgenic response in the presence of dihydrotestosterone.	*Toxicol. Sci.,* 2005 (Sanitized)	Adequate although actual data were not shown in study report.
Immunotoxicity		**No data located.**		
	Immune System Effects			No data located.
ECOTOXICITY				
ECOSAR Class		Phenols, Poly		
Acute Toxicity		**HIGH: Based on estimated 96-hour LC_{50} for fish, 48-hour LC_{50} for Daphnid, and 96-hour EC_{50} for green algae (neutral organics).**		
Fish LC_{50}		Fish 96-hour LC_{50} = 0.067 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
		Fish 96-hour LC_{50} = 0.106 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
Daphnid LC_{50}		Daphnid 48-hour LC_{50} = 0.065 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Daphnid 48-hour LC_{50} = 0.078 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
Green Algae EC_{50}	Green algae 96-hour EC_{50} = 0.16 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Chemical may not be sufficiently soluble to measure this predicted effect. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Green algae 96-hour EC_{50} = 1.24 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	Chemical may not be sufficiently soluble to measure this predicted effect.
Chronic Aquatic Toxicity	**HIGH: Based on estimated ChVs for fish, Daphnid, and green algae.**		
Fish ChV	Fish ChV = 0.006 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Fish 30-day ChV = 0.016 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid ChV	Daphnid ChV = 0.013 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid ChV = 0.023 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
Green Algae ChV	Green algae ChV = 0.066 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
	Green algae ChV = 0.126 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Chemical may not be sufficiently soluble to measure this predicted effect. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL FATE				
Transport		**The transport evaluation for substituted phenolic compound #2 is based on available experimental and estimated physical and chemical properties. Based on the Level III fugacity models incorporating the available experimental property data, substituted phenolic compound #2 is expected to partition to sediment and soil. Additionally, substituted phenolic compound #2 is expected to have low mobility in soil based on its estimated K_{oc} therefore, leaching of substituted phenolic compound #2 through soil to groundwater is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that it will be nonvolatile from surface water. In the atmosphere, substituted phenolic compound #2 is expected to exist in the particulate phase, based on its estimated vapor pressure. Particulates will be removed from air by wet or dry deposition.**		
	Henry's Law Constant (atm-m^3/mole)	<$1x10^{-8}$ (Estimated)	EPI	Cutoff value for nonvolatile compounds based on professional judgment.
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	>30,000 (Estimated)	EPI; U.S. EPA, 2004	Cutoff value for nonmobile compounds.
	Level III Fugacity Model	Air = <1% (Estimated) Water = 1% Soil = 42% Sediment = 57%	EPI	
Persistence		**HIGH: Evaluation of the persistence of substituted phenolic compound #2 is based entirely on QSARs of aerobic and anaerobic biodegradation. Results from these models estimate ultimate biodegradation in months and primary degradation in weeks. Biodegradation under anaerobic methanogenic conditions is not probable based on results from estimation models. Substituted phenolic compound #2 does not contain chromophores that absorb light at wavelengths >290 nm. Therefore, it is not expected to be susceptible to direct photolysis. It is not expected to undergo hydrolysis as it does not contain hydrolyzable functional groups. The atmospheric half-life of substituted phenolic compound #2 is estimated at 1.4 hours, although it is expected to exist primarily as a particulate in air. Therefore, biodegradation is expected to be the main degradation pathway for substituted phenolic compound #2.**		
Water	**Aerobic Biodegradation**	Weeks (primary survey model) Months (ultimate survey model)	EPI	

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (Anaerobic-methanogenic biodegradation probability model)	EPI	
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	1.4 hours (Estimated)	EPI	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	Substance does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.
	Hydrolysis	Not a significant fate process (Estimated)	Wolfe and Jeffers, 2000; Professional judgment	Substance does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.
	Pyrolysis			No data located.
Environmental Half-life		>180 days (Estimated)	EPI; PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**HIGH: The estimated BAF and fish BCF values are >5,000.**		
	Fish BCF	6,200 (Estimated)	EPI	
	BAF	9,100 (Estimated)	EPI	
	Metabolism in fish			No data located.

PROPRIETARY SUBSTITUTED PHENOLIC COMPOUND #2			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL MONITORING AND BIOMONITORING			
Environmental Monitoring	No data located.		
Ecological Biomonitoring	No data located.		
Human Biomonitoring	This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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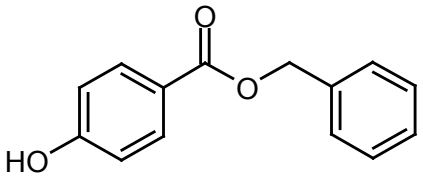
PHBB



	CASRN: 94-18-8
	MW: 228.25
	MF: $C_{14}H_{12}O_3$
	Physical Forms: **Neat:** Solid
	Use: Developer for thermal paper

SMILES: c1(C(OCc2ccccc2)=O)ccc(O)cc1

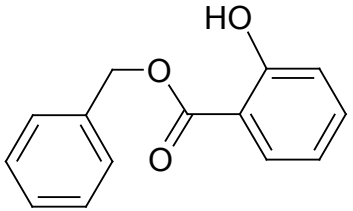
Synonyms: Benzoic acid, 4-hydroxy-, phenylmethyl ester; Benzyl 4-hydroxybenzoate; Benzyl p-hydroxybenzoate; Benzyl parahydroxybenzoate; Benzylparaben; Phenylmethyl 4-hydroxybenzoate; AI3-02955; Benzyl Parasept; Benzyl Tegosept; Nipabenzyl; Parosept; Solbrol Z; p-Hydroxybenzoic acid benzyl ester

Polymeric: No
Oligomers: Not applicable

Metabolites, Degradates and Transformation Products: Hydrolysis products - 4-hydroxybenzoic acid (99-96-7) and benzyl alcohol (100-51-6)

Analog: Benzyl-2-hydroxybenzoate (118-58-1)
Endpoint(s) using analog values: Aerobic biodegradation, persistence, and genotoxicity

Analog Structure:



Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)

Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2011).

Risk Assessments: None identified

PHBB CASRN 94-18-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	111 (Measured)	PhysProp	Adequate; consistent values reported in secondary source.
	110–112 (Measured)	CIR, 1986	Adequate; valid, nonguideline study.
Boiling Point (°C)	>300 (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for high boiling point compounds according to HPV assessment guidance.
Vapor Pressure (mm Hg)	$3.8x10^{-6}$ (Estimated)	EPI	
Water Solubility (mg/L)	60 at 25 ºC (Measured)	Thomas, 2006	Nonguideline study reported in secondary source. Although the value is consistent with other reported properties, the pH of the measurement was not reported, and was interpreted as pH 7.
Log K_{ow}	3.56 (Measured)	PhysProp	Adequate; nonguideline study reported in secondary source. Value is consistent with other reported properties.
Flammability (Flash Point)			No data located.
Explosivity			No data located.
pH			No data located.
pK_a	7.8 (Estimated)	SPARC	

PHBB CASRN 94-18-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**PHBB is estimated to not be absorbed through the skin as neat material and has moderate absorption through skin when in solution. PHBB can be absorbed through the lung and gastrointestinal tract. Although not readily hydrolyzed, PHBB is expected to undergo ester hydrolysis by esterases in the body and produce the metabolites benzyl alcohol and p-hydroxybenzoic acid.**		
Dermal Absorption *in vitro*		At 24 hours following application of PHBB to human skin (*in vitro*), recoveries in the receptor medium as parent compound and its hydrolysis product (4-hydroxybenzoic acid) were 17 and 2.4%, respectively. Hydrolysis of PHBB to 4-hydroxybenzoic acid in the human skin was catalyzed by carboxylesterases, particularly human carboxylesterase 2.	Jewell, Prusakiewicz et al., 2007	Adequate.
		20% dermal absorption *in vitro* (Estimated by analogy)	Professional judgment	Based on a confidential study on a closely related analog.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal, Inhaled**	Trace amounts of PHBB (in conjugated form) were detected in the urine of 39/100 demographically-diverse adult volunteers with no known occupational exposure to PHBB.	Ye, Bishop et al., 2006	Adequate.
		Following ingestion of PHBB (2 g/day for 5 days) by two volunteers, analysis of the urine revealed that 6% of the administered dose was eliminated unchanged; 87% was eliminated as the sulfate conjugate of the ester. Only small quantities of PHBB metabolites (4-hydroxybenzoic acid, benzyl alcohol, benzoic acid, 4-hydroxyhippuric acid, and hippuric acid) were detected.	Sabalitschka and Neufeld-Crzellitzer, 1954 (as cited in CIR 1986, 2008)	Adequate.

PHBB CASRN 94-18-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Not absorbed through the skin as neat material and has moderate absorption through skin when in solution. Can be absorbed through the lung and gastrointestinal tract. PHBB is expected to undergo ester hydrolysis by esterases in the body and produce benzyl alcohol and p-hydroxybenzoic acid. (Estimated by analogy)	Professional judgment	Based on closely related confidential analog with similar structure, functional groups, and physical/chemical properties.
		93% absorbed in gastrointestinal tract (Estimated by analogy)	Professional judgment	Based on a confidential study on a closely related analog.
Acute Mammalian Toxicity		**LOW: Based on experimental data in which no overt clinical signs of toxicity or death occurred as result of acute oral exposure of laboratory animals to doses 2,000-10,000 mg/kg, although the information located was limited to summary statements in secondary sources that did not include important study details. No data were located regarding the hazard of acute inhalation or dermal exposure.**		
Acute Lethality	**Oral**	No deaths or clinical signs of toxicity were observed in slc-ddy mice administered 10,000 mg/kg PHBB via gavage.	Sabalitschka, 1933 (as cited in CIR, 1986)	Inadequate; details are missing as this is a review on various animal toxicity studies.
		No deaths occurred when Charles River CD rats were given 5,000 mg/kg PHBB.	CTFA, 1985 (as cited in CIR, 1986, 2008)	Adequate.
		No signs of toxicity were evident in guinea pigs fed 2,000 mg PHBB/day for an unspecified period.	Sabalitschka and Neufeld-Crzellitzer, 1954 (as cited in CIR, 1986, 2008)	Adequate.
	Dermal			No data located.
	Inhalation			No data located.
Carcinogenicity		**MODERATE: Estimated to have potential for carcinogenicity based on the benzyl alcohol hydrolysis product. Potential for carcinogenicity is dependent on the rate of hydrolysis and oxidation of the alcohol to an aldehyde. Also, there is uncertainty due to the lack of data located for this substance. Carcinogenic effects cannot be ruled out.**		
	OncoLogic Results			No data located.

PHBB CASRN 94-18-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Carcinogenicity (Rat and Mouse)	Potential for carcinogenicity (Estimated)	Professional judgment	Estimated based on professional judgment and concern for the benzyl alcohol hydrolysis product; concern is dependent on the rate of hydrolysis and oxidation of the alcohol to an aldehyde.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
Genotoxicity		**MODERATE: Estimated to have potential for genotoxicity based on the benzyl alcohol hydrolysis product; potential is dependent on the rate of hydrolysis and oxidation of the alcohol to an aldehyde. This endpoint was also evaluated by analogy to measured data for the closely related compound benzyl-2 hydroxybenzoate. These chemicals differ only by the position of the hydroxyl grouped (ortho vs. para), which is not anticipated to result in significant differences in the mechanistic interpretation of this end point. In addition, there is uncertainty due to the lack of data for this substance. Carcinogenic effects cannot be ruled out.**		
	Gene Mutation *in vitro*	No data for PHBB. An analog (benzyl 2-hydroxybenzoate) did not induce mutations in *Salmonella typhimurium* strains TA 98, TA100, TA1535, or TA1537 with and without metabolic activation.	Zeiger, Anderson et al., 1987	Adequate.
		Uncertain concern for mutagenicity based on the benzyl alcohol hydrolysis product (Estimated by analogy)	Professional judgment	Estimated based on test data located for a hydrolysis product benzyl alcohol and is dependent on the rate of hydrolysis and oxidation of the alcohol to an aldehyde.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*			No data located.
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.

PHBB CASRN 94-18-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Other (Mitotic Gene Conversion)			No data located.
Reproductive Effects		**LOW: Estimated to have low potential for reproductive effects based on no identified structural alerts and expert judgment.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	No potential for reproductive effects (Estimated)	Expert judgment	Estimated based on expert judgment and because no structural alerts were identified.
	Reproduction and Fertility Effects			No data located.
Developmental Effects		**MODERATE: Estimated to have potential for developmental effects based on the 4-hydroxybenzoic acid hydrolysis product and professional judgment.**		
	Reproduction/ Developmental Toxicity Screen	Potential for developmental effects (Estimated)	Professional judgment	Estimated based on the 4-hydroxybenzoic acid hydrolysis product.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert. (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on the phenol structural alert.

PHBB CASRN 94-18-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects		**LOW: Estimated to have low potential for repeated dose effects based on no identified structural alerts and expert judgment.**		
		No signs of toxicity were evident in guinea pigs fed 1,000 mg PHBB/day for 19 days.	Ishizeki, Ayoama et al., 1955 (as cited in CIR, 1986)	Inadequate; details are missing as this is a review on various animal toxicity studies. Test methodology appears not to be standard with only a 19-day exposure duration period.
		Low potential for repeated dose effects (Estimated)	Expert judgment	Estimated to have low potential for repeated dose effects based on expert judgment and because no structural alerts were identified.
Skin Sensitization		**MODERATE: Potential for skin sensitization based on close structural analog and based on concerns for the 4-hydroxybenzoic acid hydrolysis product.**		
	Skin Sensitization	Contact dermatitis has been observed in several studies of large numbers of eczematous patients or single case reports of patients with dermal disorders topically administered products containing mixed 4-hydroxybenzoates that typically included PHBB. The overall rate of allergic reactions is in the range of 1%. Among patients sensitized to mixed 4-hydroxybenzoate substances, patch testing for sensitivity to individual 4-hydroxy benzoate substances reveal significant cross-sensitization potential and the lowest frequency of sensitization to PHBB compared to the other 4-hydroxybenzoates.	Bandmann, Calnan et al., 1972 (as cited in CIR, 1986, 2008); Meynadier, Meynadier et al., 1982 (as cited in CIR, 1986, 2008); Romaguera and Grimalt, 1980 (as cited in CIR, 1986, 2008); Rudner, 1978 (as cited in CIR, 1986, 2008); Menné and Hjorth, 1988; Würbach, Schubert et al., 1993; Tosi, Fanti et al., 1989	Inadequate; patients were sensitized to mixed 4-hydroxybenzoates prior to patch testing of individual 4-hydroxybenzoates and cross-sensitization was apparent.

PHBB CASRN 94-18-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Potential for dermal sensitization (Estimated by analogy)	Professional judgment	Estimated based on reported experimental data for a confidential analog and for the 4-hydroxybenzoic acid hydrolysis product.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**VERY LOW: PHBB is not an eye irritant.**		
	Eye Irritation	Negative for ocular irritation in New Zealand rabbits (n = 3) 1, 24, 48 and 72 hours after instillation of 100 mg into the conjunctival sac.	CTFA, 1985 (as cited in CIR, 1986)	Adequate.
Dermal Irritation		**VERY LOW: PHBB is not a skin irritant.**		
	Dermal Irritation	Negative for skin irritation in New Zealand rabbits when applied under occlusive conditions to intact and abraded skin at 500 mg.	European Economic Commission, 1984 (as cited in CIR, 1986)	Inadequate; details are missing as this is a review on various animal toxicity studies.
		Negative for skin irritation/corrosion in rabbits when 500 mg PHBB was applied under semi-occlusive conditions.	CTFA, 1985 (as cited in CIR 1986, 2008)	Adequate.

PHBB CASRN 94-18-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Endocrine Activity	**Based on primarily *in vitro* test data, PHBB exhibits endocrine activity. PHBB exhibited estrogenic and anti-estrogenic activity in various test systems.**		
	PHBB demonstrated estrogen agonistic properties both *in vitro* and *in vivo* by displacing 17β-estradiol from cytosolic ER of MCF-7 human breast cancer cells, increasing expression of a stably transfected estrogen-responsive reporter gene in MCF-7 cells, increasing the growth of estrogen-dependent MCF-7 cells (which could be inhibited by pure anti-estrogen ICI182 780 indicating that the growth effects were ER mediated), increasing the growth of a second estrogen-dependent human breast cancer cell line ZR-75-1 but not the estrogen insensitive MDA-MB-231 line, and by inducing increased uterine weight in immature mice receiving three daily dermal applications of PHBB to unshaven dorsal skin (NOAEL = 10mg, LOAEL = 33 mg).	Darbre, Byford et al., 2003	Adequate.
	Receptor Binding Assays		
	PHBB exhibited weak ER binding activity in preparations from uteri of ovariectomized Sprague-Dawley rats. Relative binding affinity (RBA) = 0.003% of the binding affinity of 17β-estradiol. An RBA of 0.008% was observed for BPA.	Blair, Fang et al., 2000	Adequate.
	In a rat uterine cytosolic ER-competitive binding assay, results for PHBB, bisphenol S, and BPA indicated a weak affinity for ER.	Laws, Yavanhxay et al., 2006	Adequate.

PHBB CASRN 94-18-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In a human ER binding assay, the relative binding affinity (RBA) of PHBB was 0.00473% compared to 126% for 17β-estradiol. RBAs for bisphenol compounds included 0.195% for BPA, 0.129% for bisphenol C, 0.0803% for bisphenol AP, 0.0719% for bisphenol F, and 0.0055% for bisphenol S.	METI, 2002	Adequate.
	PHBB did not elicit an estrogenic response in a receptor binding assay with human ERα or ERβ.	Schultis and Metzger, 2004	Adequate.
	Gene Transcription and Reporter Gene Assays		
	PHBB exhibited estrogenic activity approximately 4,000-fold less than that of 17β-estradiol in an *in vitro* recombinant yeast estrogen assay. The estrogenic activities of BPA and bisphenol F were 10,000-fold and 9,000-fold less than that of 17β-estradiol.	Miller, Wheals et al., 2001	Adequate.
	PHBB exhibited estrogenic activity in multiple *in vitro* assays. Compared to the activity of 17β-estradiol, the relative activity (RA) values were E-Screen RA (relative to $= 1.0x10^{-4}$ for the E-screen assay, $6.0x10^{-5}$ for the LYES-assay, and $3.7x10^{-4}$ for the YES-assay.	Schultis and Metzger, 2004	Adequate.

PHBB CASRN 94-18-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In a reporter gene assay of estrogen-induced transcriptional activity, relative activity (RA) for PHBB was 0.000592% compared to 81.7% for 17β-estradiol. RAs for bisphenol compounds included 0.00278% for BPA, 0.00189% for bisphenol C, 0.000639% for bisphenol F, 0.000254% for bisphenol S, and 0.000184% for bisphenol AP.	METI, 2002	Adequate.
	PHBB exhibited estrogenic activity in *in vitro* yeast two-hybrid assays incorporating human or medaka ERα. hER α assay: RA (relative to 17β-estradiol)= $1.1x10^{-4}$ MedER α assay: RA = $3.3x10^{-3}$	Terasaki, Kamata et al., 2009b	Adequate.
	PHBB exhibited estrogenic activity in a hERα competitive enzyme-linked immunosorbent assay (ER-ELISA). RBA (relative to DES) = $8.1x10^{-4}$	Terasaki, Kamata et al., 2009b	Adequate.
	PHBB showed relatively high estrogenic activity in an ER yeast reporter assay.	Ozaki, Shinohara et al., 2007	Adequate.
	Cell Proliferation Assays		
	PHBB was estrogenic in an E-screen (MCF-7 proliferation assay) and inhibited aromatase activity in microsomes derived from a human placenta. Inhibition of aromatase activity results in decreased conversion of testosterone into estrogens suggestive of an anti-estrogenic effect.	van Meeuwen, van Son et al., 2008	Adequate.
	Thyroid Assays		

PHBB CASRN 94-18-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		PHBB did not exhibit thyroid hormone receptor binding in a yeast two-hybrid assay system with TRα and coactivator TIF-2.	Kitagawa, Takatori et al., 2003	Adequate.
Immunotoxicity		**No data located.**		
	Immune System Effects			No data located.
ECOTOXICITY				
ECOSAR Class		Phenols, esters		
Acute Toxicity		**HIGH: Based on experimental data for fish and Daphnid with LC_{50} values between 1.0 and 10 mg/L.**		
Fish LC_{50}		Fathead minnow, static conditions 48-hour LC_{50} = 3.3 mg/L (Experimental)	Dobbins, Usenko et al., 2009	Adequate; follows standardized acute and subchronic tests for freshwater fish.
		Fish 96-hour LC_{50} = 2.452 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.00	
		Fish 96-hour LC_{50} = 3.98 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
		Fish 96-hour LC_{50} = 8.42 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid LC_{50}		*Daphnia magna*, static conditions 48-hour LC_{50} = 4.0 mg/L (Experimental)	Dobbins, Usenko et al., 2009	Adequate; follows standardized acute and subchronic tests for daphnia.
		Daphnia magna, acute immobilization test. 48-hour EC_{50} = 6.6 mg/L (Experimental)	Terasaki, Makino et al., 2009a	Adequate.

PHBB CASRN 94-18-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Daphnid 48-hour LC_{50} = 1.559 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.00	
	Daphnid 48-hour LC_{50} = 6.69 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
	Daphnid 48-hour LC_{50} = 5.86 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Saltwater Invertebrate LC_{50}	Mysid shrimp 96-hour LC_{50} = 2.526 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
Green Algae EC_{50}	Green algae 96-hour EC_{50} = 2.411 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
	Green algae 96-hour EC_{50} = 6.16 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.00	
	Green algae 96-hour EC_{50} = 4.79 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

PHBB CASRN 94-18-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Chronic Aquatic Toxicity	**HIGH: Based on an estimated fish 30-day ChV of 0.029 mg/L (ECOSAR class: phenol). The ECOSAR phenol class resulted in the lowest estimated chronic toxicity value. Experimental studies located for fish and Daphnid were of insufficient exposure duration to be utilized to assign the hazard concern.**		
Fish ChV	Fathead minnow, static-renewal conditions, 7-day LOEC-growth = 1.7 mg/L (Experimental)	Dobbins, Usenko et al., 2009	Inadequate; exposure duration only 7 days.
	Fish 30-day ChV = 0.293 mg/L (Estimated) ECOSAR: phenol	ECOSAR version 1.00	
	Fish 60-day ChV = 0.007 mg/L (Estimated) ECOSAR: phenol	ECOSAR version 1.00	
	Fish 32/33-d-day ChV = 0.246 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
	Fish ChV = 0.772 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid ChV	*Daphnia magna*, static-renewal conditions, 10-day LOEC (growth) = 0.1 mg/L 10-day LOEC (reproduction) = 2.0 mg/L (Experimental)	Dobbins, Usenko et al., 2009	Inadequate; exposure duration only 10 days.
	Daphnid 21-day ChV = 0.296 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.00	

PHBB CASRN 94-18-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Daphnid 21-day ChV = 2.825 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
	Daphnid ChV = 0.714 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Saltwater Invertebrate ChV	Mysid shrimp ChV = 7.231 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
Green Algae ChV	Green algae ChV = 1.010 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
	Green algae ChV = 2.84 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.00	
	Green algae ChV = 2.31 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Earthworm Subchronic Toxicity	Earthworm 14-day LC_{50} = 48.812 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.00	

PHBB CASRN 94-18-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Earthworm 14-day LC_{50} = 934.7 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
ENVIRONMENTAL FATE				
Transport		**The transport evaluation for PHBB is based on located experimental data and estimated physical/chemical properties. Based on the Level III fugacity models incorporating the located experimental property data, PHBB is expected to partition primarily to soil. It is expected to exist in both neutral and anionic forms at environmentally-relevant pH, based on its estimated pK_a. The neutral form of PHBB is expected to have moderate mobility in soil based on its estimated K_{oc}. The anionic form may have more mobility, as anions do not bind as strongly to organic carbon and clay due to their enhanced water solubility. However, leaching of PHBB through soil to groundwater is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that it will be nonvolatile from surface water. In the atmosphere, PHBB is expected to exist in both vapor and particulate phases, based on its estimated vapor pressure. Particulates will be removed from air by wet or dry deposition. Vapor-phase PHBB will be susceptible to atmospheric degradation processes.**		
	Henry's Law Constant ($atm\text{-}m^3/mole$)	$2.9x10^{-10}$ (Estimated)	EPI	
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	3,200 (Estimated)	EPI	
	Level III Fugacity Model	Air = <1% Water = 16% Soil = 83% Sediment = 1.6% (Estimated)	EPI	

PHBB CASRN 94-18-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**LOW: No experimental data were located regarding the persistence of PHBB and it was evaluated using measured biodegradation data for the analog benzyl-2-hydroxybenzoate. These chemicals differ only by the position of the hydroxyl group (ortho vs. para) and this is not anticipated to result in a different mechanistic interpretation of this endpoint. Estimates based on this analog are expected to be superior to those based solely on modeling. The analog benzyl-2-hydroxybenzoate passed two ready biodegradability tests, one that met the 10-day window in an activated sludge inoculum and one that did not meet the 10-day window in a secondary effluent inoculum. Based on these data, the environmental persistence of PHBB is estimated to be Low. PHBB is not expected to undergo hydrolysis based on estimated half-lives of >1 year at pH 7 and 8. PHBB does not absorb light at environmentally significant wavelengths, and is not expected to be susceptible to direct photolysis. The atmospheric half-life for the vapor-phase hydroxyl radical reaction of PHBB is estimated at 7.5 hours. This is an important removal process for vapor-phase PHBB in the atmosphere. However, it is also expected to exist in the particulate form in the atmosphere. Biodegradation of PHBB is expected to be the primary removal process in aquatic and terrestrial environments.**		
Water	**Aerobic Biodegradation**	Days (primary survey model); Weeks (ultimate survey model)	EPI	
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**	87% after 28 days; readily biodegradable, 10-day window met (Estimated by analogy to benzyl-2-hydroxybenzoate in activated sludge inoculum)	HPV Robust Summary, 2003	Adequate; PHBB and benzyl-2-hydroxybenzoate are closely related structures that differ only by position of the hydroxyl group. Benzyl-2-hydroxybenzoate data are for a guideline study.
		62% after 28 days; 10-day window not met. (Estimated by analogy to benzyl-2-hydroxybenzoate in secondary effluent inoculum during an ISO 14593 Carbon Dioxide Evolution Test)	HPV Robust Summary, 2003	Adequate; PHBB and benzyl-2-hydroxybenzoate are closely related structures that differ only by position of the hydroxyl group. Benzyl-2-hydroxybenzoate data are for a guideline study.

PHBB CASRN 94-18-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Anaerobic Biodegradation			No data located.
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	7.5 hours (Estimated)	EPI	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	The substance does not contain functional groups that would be expected to absorb light at wavelengths >290 nm.
	Hydrolysis	Half-life >1 year (Estimated at pH = 8 and pH =7)	EPI	Hydrolysis products expected: 4-hydroxybenzoic acid (99-96-7) and benzyl alcohol (100-51-6).
	Pyrolysis			No data located.
Environmental Half-life		30 days	EPI; PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**LOW: The estimated fish BAF is <100. Although the BCF is estimated to be 100, the BAF model is anticipated to better account for metabolism for this substance.**		
	Fish BCF	100 (Estimated)	EPI	
	BAF (upper trophic)	9.8 (Estimated)	EPI	
	Metabolism in Fish			No data located.

PHBB CASRN 94-18-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL MONITORING AND BIOMONITORING			
Environmental Monitoring	No data located.		
Ecological Biomonitoring	No data located.		
Human Biomonitoring	PHBB and its metabolites have been detected in human urine biological samples (CIR, 1986; Ye, 2006). This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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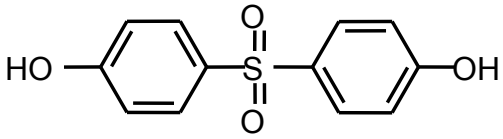
Bisphenol S



	CASRN: 80-09-1
	MW: 250.27
	MF: $C_{12}H_{10}O_4S$
	Physical Forms: **Neat:** Solid
	Use: Developer for thermal paper
SMILES: O=S(=O)(c1ccc(O)cc1)c2ccc(O)cc2	
Synonyms: Phenol, 4,4'-sulfonylbis-; bis(4-hydroxyphenyl)sulfone; 1,1'-Sulfonylbis(4-hydroxybenzene); 2,4'-Sulfonyldiphenol; 4,4'-Bisphenol S; 4,4'-Dihydroxydiphenyl sulfone; 4,4'-Sulfonylbisphenol; 4,4'-Sulfonyldiphenol; 4-Hydroxyphenyl sulfone; Bis(4-hydroxyphenyl) sulfone; Bis(p-hydroxyphenyl) sulfone; Diphone C; p,p'-Dihydroxydiphenyl sulfone	
Polymeric: No **Oligomers:** Not applicable	
Metabolites, Degradates and Transformation Products: None	
Analog: None **Endpoint(s) using analog values:** Not applicable	**Analog Structure:** Not applicable
Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)	
Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2011).	
Risk Assessments: None identified	

Bisphenol S CASRN 80-09-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	240.5 (Measured)	Lide, 2008	Adequate.
	245-248 (Measured)	ECHA, 2011	Adequate; reported values, which span a relatively narrow range, are consistent with other sources.
	242-247 (Measured)	ECHA, 2011	Adequate; reported values, which span a relatively narrow range, are consistent with other sources.
Boiling Point (°C)	>300 (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for high boiling point compounds according to HPV assessment guidance; decomposition is anticipated to occur before the melting point is reached.
	315 decomposition temperature Boiling point of the test item could not be determined, OECD 103 (Measured)	ECHA, 2011	Inadequate; nonspecific value.
Vapor Pressure (mm Hg)	$<1x10^{-8}$ (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for nonvolatile compounds according to HPV assessment guidance.
Water Solubility (mg/L)	$1.1x10^{3}$ (Measured) Reported as 1.1 g/L at 20°C	ECHA, 2011	Adequate, nonguideline study reported in secondary source; value is consistent with other reported properties.
	$<2x10^{3}$ (Measured)	HSNO, 2010	Inadequate; sufficient details were not provided to assess the quality of this study.
Log K_{ow}	1.2 OECD Method 117 (Measured)	ECHA, 2011	Adequate guideline study.
Flammability (Flash Point)	≥400°C auto-flammability/self-ignition temperature DIN 51 794 (Measured)	ECHA, 2011	Adequate guideline study.

Bisphenol S CASRN 80-09-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Not highly flammable EU Method A.10 (Measured)	ECHA, 2011	
Explosivity				No data located.
pH				No data located.
pK_a		8 OECD Method 112 (Measured)	ECHA, 2011	Adequate, guideline study.
HUMAN HEALTH EFFECTS				
Toxicokinetics		**No toxicokinetic data located.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**			No data located.
Acute Mammalian Toxicity		**LOW: The weight of evidence indicates that the acute oral toxicity of bisphenol S is low. A reported acute oral LD_{50} of 1,600 mg/kg for the mouse could not be verified because no study details were available. Located data suggest a low hazard concern for acute dermal exposure. No data were located regarding the acute inhalation hazard.**		
Acute Lethality	**Oral**	Rat oral LD_{50} >5,000 mg/kg	ECHA, 2011	Adequate guideline study (OECD 401); no deaths at limit dose of 5,000 mg/kg.
		Wistar rat (male) LD_{50} = 2,830 mg/kg	ECHA, 2011	Adequate guideline comparable to OECD guideline 401; the LD_{50} value supports other reported results.
		Rat oral LD_{50} = 4,556 mg/kg	BIOFAX Industrial Bio-Test Laboratories, Inc., 1974, cited in CHEMID	Although no study details were provided in the secondary source, the LD_{50} value supports other reported results.
		Rat (male, female; strain unspecified) LD_{50} = 2,540 mg/kg (females) LD_{50} = >3,200 mg/kg (males)	Eastman Kodak, 1991	Although study details were lacking in the study summary, the LD_{50} value supports other reported results.

Bisphenol S CASRN 80-09-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Sprague-Dawley rat (male, female) LD_{50} >2,000 mg/kg	ECHA, 2011	Although the secondary source indicated that the study followed OECD guideline 401, it was noted that only an abstract of the study was located.
		Wistar rat (gender unspecified) A single dosed rat died following a single oral dose of 10,000 mg/kg; a single rat given 7,000 mg/kg survived	Monsanto Company, 1945 (OTS0555048)	Although insufficient numbers of animals were assessed, the results support study results for rats.
		Mouse (gender, strain unspecified) LD_{50} = 1,600 mg/kg	Eastman Kodak, 1991	This value could not be verified because the study summary provides only the LD_{50} value for the mouse.
		Albino rabbit (gender unspecified) One of two rabbits died following a single oral dose of 7,000 mg/kg; a single rabbit given 4,700 mg/kg survived	Monsanto Company, 1945 (OTS0555048)	Although insufficient numbers of animals were assessed, the results support study results for rats.
	Dermal	Rabbit dermal LD_{50} >10,250 mg/kg	BIOFAX Industrial Bio-Test Laboratories, Inc., 1974, cited in CHEMID	Although limited study information was located, the high dose suggests a low hazard concern for the dermal exposure route.
		Guinea pig (strain and gender unspecified) dermal LD_{50} >1,000 mg/kg	Eastman Kodak, 1991	Inadequate, limited study information located.
	Inhalation			No data located.
Carcinogenicity		**MODERATE: Estimated using OncoLogic expert system which describes a concern for this compound as a potential carcinogen or tumorigenesis promoter arising from its structural similarity to estrogenic/androgenic compounds, using the "phenols and phenolic compounds" structural alert**.		
	OncoLogic Results	Moderate (Estimated) OncoLogic class: phenols and phenolic compounds	OncoLogic	OncoLogic SAR analysis using the phenols and phenolic compounds class.
	Carcinogenicity (Rat and Mouse)			No data located.

Bisphenol S CASRN 80-09-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Combined Chronic Toxicity/ Carcinogenicity			No data located.
Genotoxicity		**MODERATE: Bisphenol S did not induce gene mutations in several *in vitro* assays and did not induce chromosomal aberrations *in vivo* in a mammalian erythrocyte micronucleus assay in NMRI mice or in Chinese hamster ovary (CHO) cells *in vitro* in the presence of exogenous metabolic activation. However, bisphenol S did induce chromosomal aberrations in CHO cells *in vitro* in the absence of exogenous metabolic activation (at a noncytotoxic concentration). The positive result in the *in vitro* assay and negative result in the *in vivo* test suggest an equivocal response and therefore a Moderate hazard concern.**		
	Gene Mutation *in vitro*	Negative, mouse lymphoma L5178Y (TK+/TK-) cells, with and without metabolic activation	CCRIS, 2010	Adequate.
		Negative, Ames assay (standard plate) in *Salmonella typhimurium* strains TA98, TA100, TA1537, TA1535, and TA1538 with and without metabolic activation	CCRIS, 2010	Adequate.
		Negative, Salmonella/microsome test, *S. typhimurium* strains TA1535, TA100, TA1537, and TA98 with and without metabolic activation	Miles Inc., 1992; ECHA, 2011	Adequate guideline study (OECD 471).
		Negative, Ames assay (preincubation) in *S. typhimurium* strains TA98, TA100, TA1537, and TA1535, and *Escherichia coli* WP2UVRA with and without metabolic activation	CCRIS, 2010; ECHA, 2011	Adequate guideline study (OECD 471).
		Negative, umu test in *S. typhimurium* strain TA1335	Chen, Michihiko et al., 2002	Adequate.
		Negative, CHO HGPRT mutation assay, with and without metabolic activation	Amoco Corp., 1991a; ECHA, 2011	Adequate.
	Gene Mutation *in vivo*			No data located.

Bisphenol S CASRN 80-09-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Chromosomal Aberrations *in vitro*	Positive, chromosomal aberrations in CHO cytogenetics assay, without metabolic activation, negative with metabolic activation. Results were obtained in the absence of cytotoxicity.	Amoco Corp., 1991b; ECHA, 2011	Adequate guideline study (similar to OECD 473).
	Chromosomal Aberrations *in vivo*	Negative, did not produce chromosomal aberrations *in vivo* in a mammalian erythrocyte micronucleus assay in male NMRI mice (5/group) administered bisphenol S via single gavage dose at dose levels up to 2,000 mg/kg.	ECHA, 2011	Adequate guideline study (OECD 474).
	DNA Damage and Repair			No data located.
	Other (Mitotic Gene Conversion)			No data located.
Reproductive Effects		**MODERATE: In a reproduction/developmental toxicity screening test, oral exposure of parental rats to bisphenol S resulted in marked systemic effects and the NOAEL for reproductive effects is 60 mg/kg-day (prolonged estrous cycle, decreased fertility index and decreased number of live offspring). Based on the NOAEL for reproductive effects, a Moderate hazard designation is selected.**		

Bisphenol S CASRN 80-09-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction/ Developmental Toxicity Screen	In a reproduction/developmental toxicity screening test, groups of Sprague-Dawley rats (12/sex/group) were administered bisphenol S by gavage at 0, 10, 60, or 300 mg/kg bw-day (males for 45 days and females from 14 days before mating to LD 3). The mid dose caused parental gross- and histo-pathological changes in cecum of both sexes. The high dose caused decreased body weight gain and food consumption in females, increased relative liver weight in males, hypertrophy of hepatocytes in both sexes, prolonged estrous cycle, decreased fertility index, and decreased number of live offspring on LD 4. Parental toxicity: NOAEL = 10 mg/kg bw-day LOAEL = 60 mg/kg bw-day for effects on cecum (distension, diffuse hyperplasia of mucosal epithelium) Reproductive toxicity: NOAEL = 60 mg/kg bw-day LOAEL = 300 mg/kg bw-day for prolonged estrous cycle, decreased fertility index, and decreased number of live offspring on LD 4.	ECHA, 2011	Adequate guideline study (OECD 421) reported in a secondary source.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects			No data located.

Bisphenol S CASRN 80-09-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Developmental Effects		**MODERATE: In a reproduction/developmental toxicity screening test, oral exposure of parental rats to bisphenol S resulted in marked systemic effects and decreased number of live offspring (PND 4) at the highest dose level (300 mg/kg-day), with a NOAEL of 60 mg/kg-day. Based on the NOAEL, a Moderate hazard designation is selected.**		
	Reproduction/ Developmental Toxicity Screen	In a reproduction/developmental toxicity screening test, groups of Sprague-Dawley rats (12/sex/group) were administered bisphenol S by gavage at 0, 10, 60, or 300 mg/kg bw-day (males for 45 days and females from 14 days before mating to LD 3). The mid dose caused parental gross- and histo-pathological changes in cecum of both sexes. The high dose caused decreased body weight gain and food consumption in females, increased relative liver weight in males, hypertrophy of hepatocytes in both sexes, prolonged estrous cycle, decreased fertility index, and decreased number of live offspring on LD 4. No changes attributable to the compound were observed in parameters including the sex ratio, the live birth index, body weight, viability index on day 4, anogenital distance, external or necropsy findings. Parental toxicity: NOAEL = 10 mg/kg bw-day LOAEL = 60 mg/kg bw-day for effects on cecum (distension, diffuse hyperplasia of mucosal epithelium) Reproductive toxicity: NOAEL = 60 mg/kg bw-day LOAEL = 300 mg/kg bw-day for prolonged estrous cycle, decreased	ECHA, 2011	Adequate guideline study (OECD 421) reported in a secondary source.

Bisphenol S CASRN 80-09-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		fertility index, and decreased number of live offspring on LD 4.		
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert. (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on structural alert.
Repeated Dose Effects		**HIGH: Among two adequately-designed, repeated-dose oral studies in rats, one study identified a NOAEL of 10 mg/kg-day and a LOAEL of 60 mg/kg-day for systemic effects and the other study identified a NOAEL of 40 mg/kg-day and a LOAEL of 200 mg/kg-day for systemic effects. Based on uncertainty as to the potential systemic toxicity in the range of 40 to 60 mg/kg-day, a High hazard designation is selected. It should be noted that because the standard criteria thresholds are for 90-day studies, the 28-day study was evaluated using modified criteria at 3 times the threshold values.**		
		In a repeated-dose oral study, Sprague-Dawley rats (6/sex/dose group) were administered bisphenol S by gavage at 0, 40, 200, or 1,000 mg/kg bw-day. No treatment-related effects were seen at low dose. Effects at the 200 mg/kg bw-day dose level included decreased body weight gain in females, increased incidences of proteinuria in males and females and urobilinogen in males, increased kidney weight in males, and increased incidences of hyperplasia and necrosis in cecal mucosal epithelium of	ECHA, 2011	Adequate 28-day repeat dose toxicity guideline study; this study will be evaluated using modified criteria at 3 times the thresholds because the standard thresholds are based on 90-day studies.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	males and females. NOAEL = 40 mg/kg bw-day LOAEL = 200 mg/kg-bw-day		
	In a reproduction/developmental toxicity screening test, groups of Sprague-Dawley rats (12/sex/group) were administered bisphenol S by gavage at 0, 10, 60, or 300 mg/kg bw-day (males for 45 days and females from 14 days before mating to LD 3). The mid dose caused parental gross- and histo-pathological changes in cecum of both sexes. The high dose caused decreased body weight gain and food consumption in females, increased relative liver weight in males, and hypertrophy of hepatocytes in both sexes. NOAEL = 10 mg/kg bw-day LOAEL = 60 mg/kg bw-day for effects on cecum (distension, diffuse hyperplasia of mucosal epithelium)	ECHA, 2011	Adequate guideline study (OECD 421).
	In a 13-day oral (dietary) study in rats, increases in red blood cell count, hemoglobin concentrations, and hematocrit were observed; histopathologic examinations revealed cytoplasmic basophilia of the renal distal convoluted tubule epithelium. Decreased weight gain, decreased absolute liver and kidney weight, and atrophy in adipose tissue may have been secondary effects of decreased food consumption. NOAEL = 97 mg/kg-day LOAEL = 810 mg/kg-day	Eastman Kodak, 1991	Inadequate; exposure duration only 13 days.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Skin Sensitization		**LOW: Studies on guinea pigs and mice indicate that bisphenol S not a likely skin sensitizer.**		
	Skin Sensitization	Negative for skin sensitization, guinea pig	Eastman Kodak, 1991	Limited study details.
		Negative for skin sensitization, mouse local lymph node assay	ECHA, 2011	Adequate guideline study (OECD 429).
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: Bisphenol S was non-irritating to mildly irritating to rabbit eyes.**		
	Eye Irritation	Slightly irritating, rabbit	Eastman Kodak, 1991	Limited study details.
		Mildly irritating, rabbit	Monsanto, 1991	Limited study details.
		Nonirritating, rabbit	ECHA, 2011	Adequate guideline study (OECD 405).
Dermal Irritation		**LOW: Bisphenol S was slightly irritating to guinea pig skin and not irritating to rabbit skin.**		
	Dermal Irritation	Slight skin irritant, guinea pig	Eastman Kodak, 1991	Limited study details.
		Non-irritant, rabbit	Monsanto, 1991	Adequate.
		Non-irritant, rabbit	ECHA, 2011	Adequate guideline study (OECD 404).
Endocrine Activity		**Based on limited data, it appears that bisphenol S exhibits endocrine activity. *In vitro* assays demonstrate that bisphenol S can bind to estrogen receptors (ER), elicit estrogen-induced gene transcription, and induce cell proliferation in MCF7 cancer cells, and inhibit the androgenic activity of dihydrotestosterone. In an ARE-luciferase reporter assay using a mouse fibroblast cell line, bisphenol S did not elicit an androgenic response, but did inhibit the androgenic activity of dihydrotestosterone. Located data indicate that the *in vitro* endocrine activity of bisphenol S is approximately 5-7 orders of magnitude less than that of 17β-estradiol, suggesting that bisphenol S acts as a weak estrogen. Comparative *in vitro* data suggest that the endocrine activity of bisphenol S is somewhat less than that of BPA, bisphenol AP, bisphenol C, and bisphenol F. Limited *in vivo* data suggest the potential for estrogenic activity.**		

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In a human ER binding assay, the relative binding affinity (RBA) of bisphenol S was 0.0055% relative to 17β-estradiol (set at 100%). RBAs for other bisphenol compounds included 0.175% for bisphenol M and 0.0719% for bisphenol F.	Yamasaki, Noda et al., 2004	Adequate.
	In a human ER binding assay, the RBA of bisphenol S was 0.0055% compared to 126% for 17β-estradiol. RBAs for other bisphenol compounds included 0.195% for BPA, 0.129% for bisphenol C, 0.0803% for bisphenol AP, and 0.0719% for bisphenol F. A RBA of 0.00473% was reported for PHBB.	METI, 2002	Adequate.
	In a rat uterine cytosolic ER-competitive binding assay, results for bisphenol S, BPA, and PHBB indicated a weak affinity for ER.	Laws, Yavanhxay et al., 2006	Adequate.
	Gene Transcription and Reporter Gene Assays		
	Bisphenol S exhibited evidence of estrogenic activity in a yeast (*Saccharomyces cerevisiae*) two-hybrid assay using ERα and the coactivator TIF2. Based on estrogenic activity that was approximately 7 orders of magnitude lower than that of 17β-estradiol, bisphenol S was considered less estrogenic than BPA which was considered weakly estrogenic (5 orders of magnitude less active than 17β-estradiol). Assessment of other bisphenols resulted in a ranking of	Chen, Michihiko et al., 2002	Adequate.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	relative potency as follows: bisphenol C ≥ BPA > bisphenol F > bisphenol S.		
	In a yeast two-hybrid assay using β-galactosidase activity as a measure of estrogenic activity, bisphenol S did not appear to elicit an estrogenic response but a weakly estrogenic response was elicited by BPA.	Nishihara, Nishikawa et al., 2000	Adequate.
	In yeast two-hybrid systems (reporter gene assay) using β-galactosidase activity as a measure of estrogenic activity, an estrogenic response was elicited by bisphenol S only in the presence of exogenous metabolic activation; estrogenic responses were elicited by BPA and bisphenol F both in the absence and presence of exogenous metabolic activation.	Hashimoto and Nakamura, 2000; Hashimoto, Moriguchi et al., 2001	Adequate.
	In a reporter gene assay of estrogen-induced transcriptional activity, relative activity (RA) for bisphenol S was 0.000254% compared to 81.7% for 17β-estradiol. RAs for other bisphenol compounds included 0.00278% for BPA, 0.00189% for bisphenol C, 0.000639% for bisphenol F, and 0.000184% for bisphenol AP. An RA of 0.000592% was reported for PHBB.	METI, 2002	Adequate.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In an ERE-luciferase reporter assay using MCF-7 cells, an EC_{50} was 1.1 µM for bisphenol S compared to an EC_{50} of $8.6x10^{-6}$ for 17β-estradiol (i.e., BPA was approximately 5 orders of magnitude less potent than 17β-estradiol at inducing estrogenic activity). EC_{50} values for other bisphenol compounds included 0.63 µM for BPA, 0.42 µM for bisphenol C, and 1.0 µM for bisphenol F.	Kitamura, Suzuki et al., 2005	Adequate.
	In an E-screen test for estrogenicity, bisphenol S, BPA, and bisphenol F increased proliferation of MCF-7 cells at concentrations in the range of 10^{-4} to 10^{-7} M. BPA appeared to be more effective than bisphenol S or bisphenol F.	Hashimoto, Moriguchi et al., 2001	Adequate.
	In an ERE-luciferase reporter assay using MCF-7 cells in the presence of 17β-estradiol, neither bisphenol S, BPA, bisphenol C, nor bisphenol F appeared to exert an anti-estrogenic effect	Kitamura, Suzuki et al., 2005	Adequate.
	Cell Proliferation Assays		
	In a cell proliferation assay using human breast cancer MCF-7 cells, bisphenol S elicited a proliferative response comparable to that of BPA.	Kuruto-Niwa, Nowaza et al., 2005	Adequate.
	Androgen Activity		

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In an ARE-luciferase reporter assay using a mouse fibroblast cell line (NIH3T3 cells), bisphenol S inhibited the androgenic activity of dihydrotestosterone. Anti-androgenic responses were elicited by BPA, bisphenol C, and bisphenol F as well.	Kitamura, Suzuki et al., 2005	Adequate.
	In an ARE-luciferase reporter assay using a mouse fibroblast cell line (NIH3T3 cells), neither bisphenol S, BPA, bisphenol C, nor bisphenol F exerted an androgenic effect	Kitamura, Suzuki et al., 2005	Adequate.
	***In Vivo* Studies**		
	In an uterotrophic assay of rats subcutaneously injected with bisphenol S once daily for 3 days, an apparent estrogenic effect was evidenced by increased absolute and relative uterine weight. Similar effects were elicited by bisphenol F and bisphenol M.	Yamasaki, Noda et al., 2004	Adequate.
Immunotoxicity	**No data located.**		
Immune System Effects			No data located.
ECOTOXICITY			
ECOSAR Class	Phenols, poly		
Acute Toxicity	**MODERATE: Based on an experimental 48-hour LC_{50} value of 55 mg/L for Daphnid.**		
Fish LC_{50}	Fish (species unspecified) 96-hour LC_{50} >100 mg/L (Experimental, nominal)	ECHA, 2011	Adequate guideline study (OECD 203), although information regarding measured test substance concentrations was not located.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Oryzias latipes (orange-red killifish) 96-hour LC_{50} >500 mg/L (semi-static) (Experimental, nominal)	ECHA, 2011	Adequate guideline study (Japanese Industrial Standard JIS K 0102-1986-71), although information regarding measured test substance concentrations was not located.
	Fish 96-hour LC_{50} = 38 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Fish 96-hour LC_{50} = 38 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.11	
Daphnid LC_{50}	*Daphnia magna* (water flea) 48-hour EC_{50} = 55 mg/L 24-hour EC_{50} = 76 mg/L (Experimental)	Chen, Michihiko et al., 2002; ECHA, 2011	Adequate guideline study (OECD 202), although information regarding measured test substance concentrations was not located.
	Daphnid (water flea) 96-hour LC_{50} = 45 mg/L NOEC = 10 mg/L (Experimental)	Eastman Kodak, 1991	Adequate, non guideline study, although information regarding measured test substance concentrations was not located.
	Daphnia sp. (water flea) 48-hour EC_{50} = 100 mg/L (Experimental)	ECHA, 2011	Adequate guideline study (OECD 202), although information regarding measured test substance concentrations was not located.

Bisphenol S CASRN 80-09-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Daphnid 48-hour LC_{50} = 195 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid 48-hour LC_{50} = 195 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.11	
Green Algae EC_{50}	*Desmodesmus subspicatus* (green algae) 72-hour EC_{50} = 106 mg/L (growth) 72-hour NOEC = 10 mg/L (Measured; static conditions)	ECHA, 2011	Adequate guideline study (OECD 201).
	Green algae 72-hour EC_{50} = 65 mg/L (growth) 72-hour NOEC = 4.6 mg/L (Experimental)	ECHA, 2011	Adequate guideline study (OECD 201); secondary source noted that test substance concentrations were measured, but did not indicate whether nominal or measured concentrations were used for effect levels.
	Green algae 96-hour EC_{50} = 2.29 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

Bisphenol S CASRN 80-09-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Green algae 96-hour EC_{50} = 2.3 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.11	
Chronic Aquatic Toxicity	**MODERATE: The measured EC_{50} value for Daphnid is 14 mg/L while the measured NOEC is 2.7mg/L. Using a conservative approach, the unidentified LOEC for chronic toxicity in Daphnid is assumed to fall between 2.7 and 14 mg/L, which partly spans across the range of values that indicate a Moderate hazard concern (1-10 mg/L).**		
Fish ChV	Fish 30-day ChV = 12.58 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Fish 30-day ChV = 13 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.11	
Daphnid ChV	*Daphnia* sp. (water flea) 21-day EC_{50} = 14 mg/L (reproduction) 21-day NOEC = 2.7 mg/L (Experimental)	ECHA, 2011	Adequate guideline study (OECD 211), although information regarding measured test substance concentrations was not located.
	Daphnid ChV = 18.31 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae ChV		Green algae ChV = 0.88 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
		Green algae ChV = 0.88 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.11	
ENVIRONMENTAL FATE				
Transport		**The transport evaluation for bisphenol S is based on located experimental and estimated physical and chemical properties. Based on the Level III fugacity models incorporating the located experimental property data, bisphenol S is expected to partition primarily to soil. It is expected to exist in both neutral and anionic forms at environmentally-relevant pH, based on its measured pKa. The neutral form of bisphenol S is expected to have slight mobility in soil based on its estimated K_{oc}. The anionic form may be more mobile, as anions do not bind as strongly to organic carbon and clay due to their enhanced water solubility. However, leaching of bisphenol S through soil to groundwater is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that it will be nonvolatile from surface water. In the atmosphere, bisphenol S is expected to exist in the particulate phase, based on its estimated vapor pressure. Particulates will be removed from air by wet or dry deposition.**		
	Henry's Law Constant ($atm\text{-}m^3/mole$)	$<1x10^{-8}$ (Estimated)	EPI	Cutoff value for nonvolatile compounds based on professional judgment.
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	1800 (Estimated)	EPI	
	Level III Fugacity Estimations	Air = 0% (Estimated) Water = 16% Soil = 83% Sediment = 1%	EPI	

Bisphenol S CASRN 80-09-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**MODERATE: Degradation of bisphenol S did not occur in a river die-away test and bisphenol S did not pass a Japanese MITI ready biodegradability test (OECD TG 301C), which reported 0% degradation after 4 weeks. However in a nonguideline, less-stringent test, results indicate potential for biodegradation under aerobic conditions. The persistence of bisphenol S is supported by an estimated half-life of 30 days in soil. Bisphenol S is expected to partition primarily to soil. Bisphenol S may degrade under anaerobic conditions with approximately 60% removal measured after 70 days in anoxic bottles with pond sediment. However, it is not expected to significantly partition to sediment and removal under anaerobic conditions is not anticipated to be a significant fate process. Bisphenol S is not expected to undergo hydrolysis since it does not contain hydrolyzable functional groups. Bisphenol S does not absorb UV light at environmentally significant wavelengths. The vapor phase reaction of bisphenol S with atmospheric hydroxyl radicals is estimated at 8.8 hours, although it is expected to exist primarily in the particulate phase in air. Considerations of all these factors indicate that the persistence concern is Moderate for bisphenol S.**		
Water	**Aerobic Biodegradation**	Bisphenol S aerobic degradation was not detected after 2 weeks; degradation based on TOC decrease in river water and measured with HPLC (Measured)	Ike, Chen et al., 2006	Adequate nonguideline study.
		This study measured the degradation of BPA, bisphenol F, and bisphenol S in seawater. Degradation of bisphenol S was not detected in seawater. This study used TOC Handai and river die-away methods. (Measured)	Danzl, Sei et al., 2009	Adequate nonguideline study.
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**	Ready Test: MITI-I (OECD 301C) No biodegradation detected; Bisphenol S for 4 weeks with 100 mg/L in 30 mg/L activated sludge BOD 0%; TOC 0% (Measured)	MITI, 1998	Adequate guideline study.
	Anaerobic Biodegradation	Not probable (anaerobic-methanogenic biodegradation probability model)	EPI	

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation	Anaerobic degradation of bisphenol S was detected by HPLC analysis. Approximately 60% of bisphenol S was removed after 70 days in anoxic bottles with pond sediment (Measured)	Ike, Chen et al., 2006	Adequate, nonguideline study.
Air	**Atmospheric Half-life**	8.8 hours (Estimated)	EPI	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	Substance does not contain functional groups that would be expected to absorb light at wavelengths >290 nm
	Hydrolysis	Not a significant fate process (Estimated)	Wolfe and Jeffers, 2000; Professional judgment	Substance does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.
	Pyrolysis			No data located.
Environmental Half-life		30 days (Estimated)	EPI; PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**LOW: The low concern for bioaccumulation was based on two experimental BCF values. Both values are well below the low criteria cutoff of 100.**		
	Fish BCF	A BCF of <2.2 at a concentration of 50 µg/L after 6 weeks in carp (*Cyprinus carpio*); OECD 305C (Measured)	MITI, 1998	Adequate guideline study.
		A BCF of <0.2 at a concentration of 500 µg/L after 6 weeks in carp (*Cyprinus carpio*); OECD 305C (Measured)	MITI, 1998	Adequate guideline study.
	BAF	1.8 (Estimated)	EPI	

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING			
Environmental Monitoring	No data located.		
Ecological Biomonitoring	No data located.		
Human Biomonitoring	BPS was detected in human urine samples from general populations of the United States, China, India, Japan, Korea, Kuwait, Malaysia and Vietnam (Liao, Liu, et al., 2012). This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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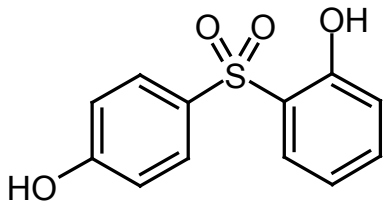
2,4-BPS



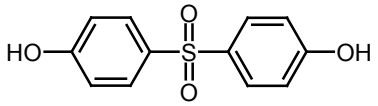
	CASRN: 5397-34-2
	MW: 250.3
	MF: $C_{12}H_{10}O_4S$
	Physical Forms: **Neat:** Solid
	Use: Developer for thermal paper

SMILES: O=S(=O)(c1ccc(O)cc1)c1c(O)cccc1

Synonyms: Phenol, 2-[(4-hydroxyphenyl)sulfonyl]-; 2,4'-Dihydroxydiphenyl sulfone; 2,4'-Sulfonyldiphenol; 2-((4-Hydroxyphenyl)sulfonyl)phenol; 4,2'-Dihydroxydiphenyl sulfone; O,P-Dihydroxydiphenyl sulfone; Phenol, 2,4'-sulfonyldi-; o-((4-Hydroxyphenyl)sulphonyl)phenol

Polymeric: No
Oligomers: Not applicable

Metabolites, Degradates and Transformation Products: None

Analog: Bisphenol S (80-09-1) **Endpoint(s) using analog values:** Boiling point, Acute lethality (oral and dermal); Irritation (eye, dermal); dermal sensitization, repeated dose effects, reproductive and developmental toxicity	**Analog Structure:** 

Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)

Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2011).

Risk Assessments: None identified

2,4-BPS CASRN 5397-34-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES				
Melting Point (°C)		184	ChemSpider, 2010	Secondary source; study details and test conditions were not provided.
Boiling Point (°C)		>300 (Estimated)	EPI; U.S. EPA, 1999	Decomposition may occur before the boiling point is reached based on the experimental decomposition temperature of 315°C for the analog bisphenol S. Cutoff value for high boiling point compounds according to HPV assessment guidance.
Vapor Pressure (mm Hg)		$<1x10^{-8}$ (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for nonvolatile compounds according to HPV assessment guidance.
Water Solubility (mg/L)		$1.7x10^{3}$ (Estimated)	EPI	
Log K_{ow}		1.7 (Estimated)	EPI	
Flammability (Flash Point)				No data located.
Explosivity				No data located.
pH				No data located.
pK_a		7.6; 8.2 (Estimated)	SPARC	Estimates are for pK_1 and pK_2.
HUMAN HEALTH EFFECTS				
Toxicokinetics		**2,4-BPS as a neat material is estimated to not be absorbed through the skin and will have poor skin absorption when in solution. 2,4-BPS is expected to be absorbed via the lungs and gastrointestinal tract.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Not absorbed through the skin as neat material and has poor absorption in solution; can be absorbed through the lung and gastrointestinal tract (Estimated by analogy)	Professional judgment	Based on closely related confidential analog with similar structure, functional groups, and physical/chemical properties.

2,4-BPS CASRN 5397-34-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Mammalian Toxicity		**LOW: Estimated based on analogy to bisphenol S. The weight of evidence indicates that the acute oral toxicity of the analog bisphenol S is low. Located data suggest a low hazard concern for acute dermal exposure to this analog. No data were located regarding the acute inhalation hazard.**		
Acute Lethality	**Oral**	Rat oral LD_{50} >5,000 mg/kg (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; using the analog bisphenol S. Data are for an adequate guideline study (OECD 401). No deaths at limit dose of 5,000 mg/kg.
		Wistar rat (male) LD_{50} = 2,830 mg/kg (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; using the analog bisphenol S. Data are for an adequate guideline comparable to OECD guideline 401. The LD_{50} value supports other reported results.
		Rat oral LD_{50} = 4,556 mg/kg (Estimated by analogy)	BIOFAX Industrial Bio-Test Laboratories, Inc., Data Sheets. Vol. 601-05501, 1974, cited in CHEMID, 2010; Professional judgment	Adequate; using the analog bisphenol S. Although no study details were provided in the secondary source, the LD_{50} value supports other reported results.
		Rat oral LD_{50} = 2,540 mg/kg (females) and >3,200 mg/kg (males) (Estimated by analogy)	Eastman Kodak, 1991; Professional judgment	Adequate; using the analog bisphenol S. Although study details were lacking in the study summary, the LD_{50} value supports other reported results.
		Sprague-Dawley rat (male, female) LD_{50} >2,000 mg/kg (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; using the analog bisphenol S. Although the secondary source indicated that the study followed OECD guideline 401, it was noted that only an abstract of the study was located.
	Dermal	Guinea pig dermal LD_{50} >1,000 mg/kg (Estimated by analogy)	Eastman Kodak, 1991; Professional judgment	Adequate; using the analog bisphenol S. Data are for an adequate, nonguideline study.
	Inhalation			No data located.

2,4-BPS CASRN 5397-34-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Carcinogenicity		**MODERATE: Estimated using OncoLogic expert system, which describes a potential for this compound as a potential carcinogen or tumorigenesis promoter arising from its structural similarity to estrogenic/androgenic compounds. The "phenols and phenolic compounds" structural alert was used.**		
	OncoLogic Results	Moderate (Estimated) OncoLogic class: phenols and phenolic compounds	OncoLogic	OncoLogic SAR analysis using the phenols and phenolic compounds class.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
Genotoxicity		**MODERATE: 2,4-BPS did not cause genetic mutations in *Salmonella typhimurium*, but did cause chromosomal aberrations in Chinese hamster ovary (CHO) cells *in vitro*. Based on evidence of mutagenicity in animal cells, Moderate hazard is designated.**		
	Gene Mutation *in vitro*	Negative for gene mutations in *S. typhimurium* strains TA98, TA100, TA1535, and TA1538 with and without metabolic activation, and TA1537 with exogenous metabolic activation; positive in TA1537 without exogenous metabolic activation, but only at cytotoxic concentration.	NICCA USA Inc., 1996	Adequate; guideline (OECD 473).
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Positive for chromosomal aberrations in CHO cells with and without metabolic activation.	NICCA USA Inc., 1996	Adequate; guideline (OECD 473).
	Chromosomal Aberrations *in vivo*			
	DNA Damage and Repair			No data located.
	Other (Mitotic Gene Conversion)			No data located.

2,4-BPS CASRN 5397-34-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**MODERATE: Estimated based on analogy to bisphenol S. In a reproductive/developmental toxicity screening test, oral exposure of parental rats to the analog bisphenol S resulted in marked systemic and the NOAEL for reproductive effects is 60 mg/kg-day (prolonged estrous cycle, decreased fertility index and decreased number of live offspring). Based on the NOAEL for reproductive effects, a Moderate hazard designation is selected.**		
	Reproduction/ Developmental Toxicity Screen	Parental toxicity: NOAEL = 10 mg/kg bw-day LOAEL = 60 mg/kg bw-day Reproductive toxicity: NOAEL = 60 mg/kg bw-day LOAEL = 300 mg/kg bw-day (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; using the analog bisphenol S. Data are for an adequate guideline study (OECD 421) reported in a secondary source.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	Potential for reproductive toxicity (Estimated by analogy)	Professional judgment	Estimated based on reported experimental data for the analog bisphenol S.
Developmental Effects		**MODERATE: Estimated based on analogy to bisphenol S. In a reproductive/developmental toxicity screening test, oral exposure of parental rats to the analog bisphenol S resulted in marked systemic effects and decreased number of live offspring (PND 4) at the highest dose level (300 mg/kg-day) with a NOAEL of 60 mg/kg-day. Based on the NOAEL, a Moderate hazard designation is selected.**		
	Reproduction/ Developmental Toxicity Screen	Parental toxicity: NOAEL = 10 mg/kg bw-day LOAEL = 60 mg/kg bw-day Reproductive toxicity: NOAEL = 60 mg/kg bw-day LOAEL = 300 mg/kg bw-day (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; using the analog bisphenol S. Data are for an adequate guideline study (OECD 421) reported in a secondary source.
		Potential for developmental toxicity (Estimated by analogy)	Professional judgment	Estimated based on reported experimental data for the analog bisphenol S.

2,4-BPS CASRN 5397-34-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert. (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on structural alert.
Repeated Dose Effects		**HIGH: Based on analogy to bisphenol S. Among two adequately-designed repeated-dose oral studies in rats, one study identified a NOAEL of 10 mg/kg-day and a LOAEL of 60 mg/kg-day for systemic effects and the other study identified a NOAEL of 40 mg/kg-day and a LOAEL of 200 mg/kg-day for systemic effects following exposure to the analog bisphenol S. Based on uncertainty as to the potential systemic toxicity in the range of 40-60 mg/kg-day, a High hazard designation is selected.**		
		In a repeated-dose oral study, Sprague-Dawley rats, NOAEL = 40 mg/kg bw-day LOAEL = 200 mg/kg-bw-day (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; using the analog bisphenol S. Data are for an adequate 28-day repeat dose toxicity guideline study.
		In a reproduction/developmental toxicity screening test, Sprague-Dawley rats, NOAEL = 10 mg/kg bw-day LOAEL = 60 mg/kg bw-day (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; using the analog bisphenol S. Data are for an adequate guideline study (OECD 421).
Skin Sensitization		**LOW: Not considered a skin sensitizer for guineas pig based on analog data for bisphenol S.**		
	Skin Sensitization	Negative for skin sensitization, guinea pig (Estimated by analogy)	Eastman Kodak, 1991; Professional judgment	Adequate; using the analog bisphenol S. Data are for an adequate study with limited details.

2,4-BPS CASRN 5397-34-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Negative for skin sensitization, mouse local lymph node assay (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; using the analog bisphenol S. Data are for an adequate guideline study (OECD 429).
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: Estimated based on analogy to bisphenol S. The analog bisphenol S was nonirritating to mildly irritating to rabbit eyes.**		
	Eye Irritation	Slight eye irritant, rabbit (Estimated by analogy)	Eastman Kodak, 1991; Professional judgment	Adequate; using the analog bisphenol S. Data are for an adequate, nonguideline study.
		Mild eye irritant, rabbit (Estimated by analogy)	Monsanto, 1991; Professional judgment	Adequate; using the analog bisphenol S. Data are for an adequate, nonguideline study.
		Nonirritating, rabbit (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; using the analog bisphenol S. Data are for an adequate guideline study (OECD 405).
Dermal Irritation		**LOW: Estimated based on analogy to bisphenol S. The analog bisphenol S was slightly irritating to guinea pig skin, and not irritating to rabbit skin.**		
	Dermal Irritation	Slight skin irritant, guinea pig (Estimated by analogy)	Eastman Kodak, 1991; Professional judgment	Adequate; using the analog bisphenol S. Data are for an adequate, nonguideline study.
		Non-irritant, rabbit (Estimated by analogy)	Monsanto, 1991; Professional judgment	Adequate; using the analog bisphenol S, data are for an adequate, nonguideline study.
		Non-irritant, rabbit (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; using the analog bisphenol S. Data are for an adequate guideline study (OECD 404).
Endocrine Activity		**No data located.**		
				No data located.

2,4-BPS CASRN 5397-34-2			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Immunotoxicity	**No data located.**		
Immune System Effects			No data located.
ECOTOXICITY			
ECOSAR Class	Phenols, Poly		
Acute Toxicity	**MODERATE: Based on estimated 96-hour EC_{50} of 2.3 mg/L for green algae.**		
Fish LC_{50}	Fish 96-hour LC_{50} = 37.91 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
	Fish 96-hour LC_{50} = 383.85 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid LC_{50}	Daphnid 48-hour LC_{50} = 196.26 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
	Daphnid 48-hour LC_{50} = 212.23 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Green Algae EC_{50}	Green algae 96-hour EC_{50} = 2.29 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	

2,4-BPS CASRN 5397-34-2			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Green algae 96-hour EC_{50} = 79.15 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Chronic Aquatic Toxicity	**HIGH: Based on estimated a ChV value of 0.88 mg/L for green algae.**		
Fish ChV	Fish 30-day ChV = 12.64 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
	Fish ChV = 36.72 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid ChV	*Daphnia* sp. (water flea) 21-day EC_{50} = 14 mg/L (reproduction) 21-day NOEC = 2.7 mg/L (Estimated by analogy) (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; using the analog bisphenol S. Data are for an adequate guideline study (OECD 211).
	Daphnid ChV = 18.42 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid 21-day ChV = 74.99 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	

2,4-BPS CASRN 5397-34-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae ChV		Green algae ChV = 0.88 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
		Green algae ChV = 26.85 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
ENVIRONMENTAL FATE				
Transport		**2,4-BPS is expected to exist in both neutral and anionic forms at environmentally-relevant pH, based on its estimated pK_a. The neutral form of 2,4-BPS is expected to have moderate mobility in soil based on its estimated K_{oc}. The anionic form may be more mobile although leaching of 2,4-BPS through soil to groundwater is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that it will be nonvolatile from surface water. Volatilization from dry surface is also not expected based on its estimated vapor pressure. In the atmosphere, 2,4-BPS is expected to exist solely in the particulate phase, based on its estimated vapor pressure. Particulates may be removed from air by wet or dry deposition. Level III fugacity models incorporating the located experimental property data, indicate that the unionized form of 2,4-BPS is expected to partition primarily to soil.**		
	Henry's Law Constant ($atm\text{-}m^3/mole$)	$<1x10^{-8}$ (Estimated)	EPI	Cutoff value for nonvolatile compounds based on professional judgment.
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	$1.9x10^3$ (Estimated)	EPI	
	Level III Fugacity Model	Air = <1% (Estimated) Water = 16% Soil = 83% Sediment = <1%	EPI	

2,4-BPS CASRN 5397-34-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**MODERATE: Evaluation of the persistence of 2,4-BPS is based entirely on QSARs for aerobic and anaerobic biodegradation. Results from these models estimate primary biodegradation in days-weeks and ultimate degradation in weeks. The persistence of 2,4-BPS is supported by an estimated half-life of 30 days in soil. 2,4-BPS is expected to partition primarily to soil. 2,4-BPS is not expected to partition to sediment and removal under anaerobic conditions is not anticipated to be a significant fate process. 2,4-BPS is not expected to undergo hydrolysis since it does not contain hydrolyzable functional groups. 2,4-BPS does not absorb UV light at environmentally significant wavelengths. The vapor phase reaction of 2,4-BPS with atmospheric hydroxyl radicals is estimated at 8.8 hours, although it is expected to exist primarily in the particulate phase in air. Consideration of all of these factors indicates that the persistence concern is Moderate for 2,4-BPS.**		
Water	**Aerobic Biodegradation**	Days-weeks (primary survey model) Weeks (ultimate survey model)	EPI	
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (anaerobic-methanogenic biodegradation probability model)	EPI	
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	8.8 hours (Estimated)	EPI	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	Substance does not contain functional groups that would be expected to absorb light at wavelengths >290 nm.
	Hydrolysis	Not a significant fate process (Estimated)	Wolfe and Jeffers, 2000; Professional judgment	Substance does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.
	Pyrolysis			No data located.

2,4-BPS CASRN 5397-34-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Environmental Half-Life		30 days (Estimated)	EPI; PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**LOW: The low potential for bioaccumulation is based on an estimated BCF for fish that is less than the low criteria cutoff of 100. In addition, the estimated BAF of 3.5, which accounts for metabolism, suggests that 2,4-BPS will not bioaccumulate in higher trophic levels.**		
	Fish BCF	5.7 (Estimated)	EPI	
	BAF	3.5 (Estimated)	EPI	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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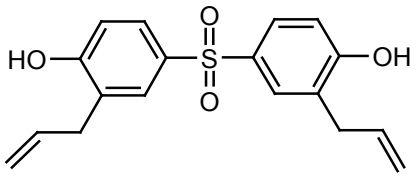
TGSA



CASRN: 41481-66-7

MW: 330.40

MF: $C_{18}H_{18}O_4S$

Physical Forms:
Neat: Solid

Use: Developer for thermal paper

SMILES: S(c1cc(CC=C)c(cc1)O)(c1cc(CC=C)c(cc1)O)(=O)=O

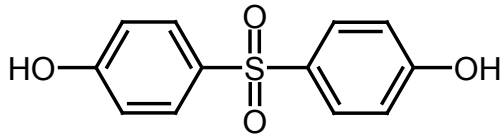
Synonyms: Phenol, 4,4'-sulfonylbis[2-(2- propen-1-yl)-; bis-(3-Allyl-4-hydroxyphenyl) sulfone; Phenol, 4,4'-sulfonylbis(2-(2-propenyl)-; 2,2'-diallyl-4,4'-sulfonyldiphenol; 2-allyl-4-(3-allyl-4-hydroxyphenyl)sulfonylphenol; 4-(4-hydroxy-3-prop-2-enyl-phenyl)sulfonyl-2-prop-2-enyl-phenol

Polymeric: No
Oligomers: Not applicable

Metabolites, Degradates and Transformation Products: Potential for epoxide formation on terminal double bonds.

Analog: Bisphenol S (80-09-1)
Endpoint(s) using analog values: Reproductive and developmental toxicity.

Analog Structure:



Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)

Risk Phrases: 43 - May cause sensitization by skin contact; 51/53 - Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (ESIS, 2011).

Risk Assessments: None identified

TGSA CASRN 41481-66-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES				
Melting Point (°C)		151-155 ±1 (Measured)	Nippon Kayaku Co., 1992b	Adequate; guideline study.
		144 (Measured)	Submitted confidential study	Adequate.
Boiling Point (°C)		Decomposed prior to boiling (Measured)	Nippon Kayaku Co., 1992b	Adequate; decomposition occurs before the boiling point is reached.
Vapor Pressure (mm Hg)		$9.5x10^{-10}$ (Measured)	Nippon Kayaku Co., 1992b	Adequate; guideline study.
Water Solubility (mg/L)		4.79 at 20.3°C ±0.5 (Measured)	Nippon Kayaku Co., 1992b	Adequate; guideline study.
Log K_{ow}		3.22 (Measured)	Nippon Kayaku Co., 1992b	Adequate; guideline study.
Flammability (Flash Point)		Not highly flammable (Measured)	Nippon Kayaku Co., 1992b	Adequate; guideline study.
Explosivity		Not explosive (Measured)	Nippon Kayaku Co., 1992b	Adequate; guideline study.
pH				No data located.
pK_a		8.3-8.5 (Estimated)	SPARC	
HUMAN HEALTH EFFECTS				
Toxicokinetics		**TGSA as a neat material is not estimated to be absorbed through the skin and is expected to have poor skin absorption when in solution. It is estimated to be absorbed via the lungs and gastrointestinal tract based on data for BPA. TSGA is a potential cross-linking agent because it has two terminal double bonds that are expected to be oxidized in the body via an epoxide intermediate.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Not absorbed through the skin as neat material and has poor absorption in solution. Can be absorbed through the lung and gastrointestinal tract. (Estimated by analogy) Oxidation of the terminal double bonds in the body via an epoxide intermediate is expected. TGSA is a potential cross-linking agent because it has two terminal double bonds. (Estimated by analogy)	Professional judgment	Estimate based on reported experimental data for the analog BPA; the potential for crosslinking is based on a mechanistic analysis.

TGSA CASRN 41481-66-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Mammalian Toxicity		**LOW: Based on experimental values for oral and dermal exposure. Experimental data indicated that the acute oral and dermal toxicity of TGSA is low. No data were located regarding the acute inhalation hazard.**		
Acute Lethality	**Oral**	Sprague-Dawley rat LD_{50} >2,000 mg/kg	Nippon Kayaku Co., 1991f	Adequate guideline study (OECD 401).
	Dermal	Rat dermal LD_{50} >2,000 mg/kg	Nippon Kayaku Co., 1991d	Adequate guideline study (OECD 402).
	Inhalation			No data located.
Carcinogenicity		**MODERATE: Estimated to be a concern for carcinogenicity based on data reported for the epoxide oxidation product. In addition, there is uncertainty due to the lack of data located for this substance. Carcinogenic effects cannot be ruled out.**		
	OncoLogic Results			No data located; not amenable to available estimation method.
	Carcinogenicity (Rat and Mouse)	Concern for carcinogenicity (Estimated)	Professional judgment	Estimated based on potential for the epoxide oxidation product.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
Genotoxicity		**LOW: Based on experimental data showing that TGSA did not induce gene mutations or chromosomal aberrations *in vitro,* and was negative in a mammalian erythrocyte micronucleus assay in mice.**		
	Gene Mutation *in vitro*	Negative, Ames assay (standard plate) in *S. typhimurium* strains TA98, TA100, TA1537, TA1535, and *E. coli* WP2*uvr*A$^-$ with and without metabolic activation	Nippon Kayaku Co., 1991g	Test conducted in accordance with OECD 471; test substance purity: 96.2%.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Negative for chromosome aberrations in human lymphocytes	Nippon Kayaku Co., 2000c	Test conducted in accordance with OECD 473.
		Negative for sister chromatid exchanges	Submitted confidential study	Adequate.
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Other (Mitotic Gene Conversion)	Negative, mammalian erythrocyte micronucleus test in mice (gavage)	Nippon Kayaku Co., 1991i	Test conducted in accordance with OECD 474; test substance purity: 96.2%.
Reproductive Effects		**MODERATE: Estimated based on analogy to bisphenol S. In a reproductive/developmental toxicity screening test, oral exposure of parental rats to the analog bisphenol S resulted in marked systemic effects and the NOAEL for reproductive effects is 60 mg/kg-day (prolonged estrous cycle, decreased fertility index and decreased number of live offspring). Based on the NOAEL for reproductive effects, a Moderate hazard designation is selected.**		
	Reproduction/ Developmental Toxicity Screen	Parental toxicity: NOAEL = 10 mg/kg bw-day LOAEL = 60 mg/kg bw-day Reproductive toxicity: NOAEL = 60 mg/kg bw-day LOAEL = 300 mg/kg bw-day (Estimated by analogy)	ECHA, 2011; Professional judgment	Using the analog bisphenol S, data are for an adequate guideline study (OECD 421) reported in a secondary source.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	Concern for male reproductive toxicity (Estimated)	Professional judgment	Estimated based on reported data for the epoxide oxidation product and on reported experimental data for the analog bisphenol S.
Developmental Effects		**MODERATE: Estimated based on analogy to bisphenol S. In a reproductive/developmental toxicity screening test, oral exposure of parental rats to the analog bisphenol S resulted in marked systemic effects and decreased number of live offspring (PND 4) at the highest dose level (300 mg/kg-day) with a NOAEL of 60 mg/kg-day. Based on the NOAEL, a Moderate hazard designation is selected.**		
	Reproduction/ Developmental Toxicity Screen	Concern for developmental toxicity (Estimated)	Professional judgment	Estimated based on reported data for the epoxide oxidation product and on reported experimental data for the analog bisphenol S.

TGSA CASRN 41481-66-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Parental toxicity: NOAEL = 10 mg/kg bw-day LOAEL = 60 mg/kg bw-day Reproductive toxicity: NOAEL = 60 mg/kg bw-day LOAEL = 300 mg/kg bw-day (Estimated by analogy)	ECHA, 2011; Professional judgment	Using the analog bisphenol S, data are for an adequate guideline study (OECD 421) reported in a secondary source.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on structural alert.
Repeated Dose Effects		**HIGH: Based on experimental data for a 28-day oral exposure to TGSA in rats. A NOAEL of 15 mg/kg-day and a LOAEL of 150 mg/kg-day was identified for repeated dose effects that would indicate a MODERATE hazard designation based on a 90-day study. Based on the DfE criteria, when the study duration is less than 90-days, this study is to be evaluated using modified criteria at 3 times the threshold values. The NOAEL value of 15 mg/kg-day is within the High hazard designation range (< 30 mg/kg-day). In addition, there is concern for liver and kidney toxicity based on data for the epoxide oxidation product.**		

TGSA CASRN 41481-66-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	28-day repeated-dose oral exposure study, Sprague-Dawley rats; There was no mortality and no clinical signs of toxicity; increased salivation with wet fur and red/brown staining of body surface at doses of 150 mg/kg-day and higher; Decreased body weight gain in females administered 1,000 mg/kg-day; no treatment related effects on hematology, serum chemistry, necropsy, or organ weights; increased incidence of basophilic tubules and interstitial mononuclear cell infiltrates in kidneys of males in the 1,000 mg/kg-day group; similar but less pronounced effect occurred at 150 mg/kg-day in males. NOAEL = 15 mg/kg-day LOAEL = 150 mg/kg-day (microscopic renal changes)	Nippon Kayaku Co., 1991j	Test conducted in accordance with OECD 474; test substance purity: 96.2%.; 28-day study was evaluated and applied to the DfE criteria using modified criteria at 3 times the thresholds because the standard thresholds are based on 90-day studies.
Skin Sensitization	**MODERATE: There is moderate concern that TGSA is a weak skin sensitizer based on test concentrations and positive incidence rates in the guinea pig maximization test and on negative results for the Buehler test and local lymph node assay.**		

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Skin Sensitization	Weak skin sensitizer in guinea pigs; produced a positive result of 70% (14/20) sensitization rate in guinea pigs.	Nippon Kayaku Co., 1991h	Test conducted in accordance with OECD 406 skin sensitization Magnusson and Kligman maximization test; test substance purity: 96.2%; intradermal induction: 25% in arachis oil B.P, topical induction: 50% in arachis oil B.P., topical challenge: 50% in arachis oil B.P.; categorized as a weak skin sensitizer based on criteria for skin sensitization for guinea pig maximization test (Kimber et al., 2003; as cited in CERI, 2012).
		Did not produce skin sensitization in guinea pigs in Buehler test.	Nippon Kayaku Co., 1992b	Test conducted in accordance with EEC methodology 84/449/EEC (OJ No. L251, 19.9.84), Part B, test substance purity: 97.9 %; Method B.6; Induction: 60% Alembicol D; challenge: 60% in Alembicol D.
		Classified as non-sensitizer in local lymph node assay in female CBA/JN mice; applied to dorsum of ears for 3 days; all stimulation indexes were below 3.	Nippon Kayaku Co., 2010	Test conducted in accordance with OECD TG429; test substance purity: 97.8%.
Respiratory Sensitization		**MODERATE: There is concern that TGSA is a respiratory sensitizer based on the epoxide oxidation product.**		
	Respiratory Sensitization	Concern for respiratory sensitization	Professional judgment	Estimated based on reported data for the epoxide oxidation product.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Eye Irritation		**LOW: Based on experimental data suggesting that TGSA is a minimal irritant to rabbit eyes.**		
	Eye Irritation	Minimal irritant, rabbit	Nippon Kayaku Co., 1991e	Test conducted in accordance with OECD 405; test substance purity: 96.2%.
Dermal Irritation		**VERY LOW: Based on experimental data indicating that TGSA is not an irritant to rabbit skin.**		
	Dermal Irritation	Non-irritant, rabbit	Nippon Kayaku Co., 1991c	Test conducted in accordance with OECD 404; test substance purity: 96.2%.
Endocrine Activity		**There was no evidence that TGSA elicits estrogenic activity. TGSA did not bind to estrogen receptors in yeast, and did not have estrogenic effects on uterus of immature rats *in vivo*.**		
		Did not cause significant estrogenic activity in a recombinant yeast screen assay in *Saccharomyces cerevisiae;* did not bind to estrogen receptor in recombinant yeast; there was an estrogenic response that was 4 orders of magnitude less than 17B-estradiol and 1 order of magnitude less than BPA.	Nippon Kayaku Co., 1999a	Adequate study details provided.
		Uterotrophic assay in immature rat; No evidence of estrogenic effects on uterus of immature rats at oral doses up to 100 mg/kg bd. Wt.	Nippon Kayaku Co., 1999b	Adequate study details provided; TGSA also did not provide a synergistic effect when administered in combination with diethylstilbestrol (positive control).
Immunotoxicity		**No data located.**		
	Immune System Effects			No data located.
ECOTOXICITY				
ECOSAR Class		Phenols, poly		

TGSA CASRN 41481-66-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Toxicity	**HIGH: Based on experimental acute aquatic toxicity values for fish and Daphnid which are in the range of 1-10 mg/L.**		
Fish LC_{50}	*Oncorhynchus mykiss* (rainbow trout) 96 hour LC_{50} = 4.0 mg/L; NOEC – 96 hour = 1.8 mg/L (Experimental)	Nippon Kayaku Co., 1991b	Test conducted in accordance with OECD 203.
	Oryzias latipes (medaka) 96 hour LC_{50} >9.8 mg/L (Experimental)	Nippon Kayaku Co., 2011b	Test conducted in accordance with OECD 203; test substance purity: 98%.
	Fish 96-hour LC_{50} = 1.17 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
	Fish 96-hour LC_{50} = 2.22 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid LC_{50}	Daphnia (*Daphnia magna*) 48-hour EC_{50} = 5.5 mg/L (immobilization); 24-hour EC_{50} = 7.8 mg/L (immobilization); NOEC – 48-hour = 3.2 mg/L (Experimental)	Nippon Kayaku Co., 1991a	Test conducted in accordance with OECD 202.
	Daphnia (*Daphnia magna*) 48-hour EC_{50} >12 mg/L (immobilization); 24-hour EC_{50} >12 mg/L (immobilization); (Experimental)	Nippon Kayaku Co., 2011a	Test conducted in accordance with OECD 202; test substance purity: 98%.

TGSA CASRN 41481-66-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Daphnid 48-hour LC_{50} = 1.72 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid 48-hour LC_{50} = 1.87 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
Green Algae EC_{50}	Green algae (*Scenedesmus subspicatus*) 72-hour EC_{50} = >100 mg/L (Experimental)	Nippon Kayaku Co., 2000b	Test conducted in accordance with OECD 201; test substance purity: 50% TGSA, 4%PVA, 46% water.
	Green algae 96-hour EC_{50} = 1.71 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
	Green algae 96-hour EC_{50} = 2.01 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

TGSA CASRN 41481-66-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Chronic Aquatic Toxicity	**MODERATE: Based on experimental LOEC/NOEC and chronic EC_{50} values for fish and Daphnid that are in the range of 1.0-10 mg/L. There were no experimental chronic toxicity data for algae available, though estimated values fall within the High and Moderate hazard designation categories.**		
Fish ChV	Fish ChV = 0.20 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Fish ChV = 0.24 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
	Oryzias latipes (Madeka) 28-day NOEC (growth) = >8.0 mg/L (highest dose tested) LOEC ≥8.0 mg/L	CERI, 2011	Test conducted in accordance with OECD 215; test substance purity: 98%; impurities: 2% unknown organic constituents.
Daphnid ChV	Daphnia (*Daphnia magna*) 14-day EC_{50} = 4.1 mg/L (immobilization) (Experimental)	Nippon Kayaku Co., 2000a	Test conducted in accordance with OECD 211; 14-day value determined during 21-day reproduction test in parental daphnia generation; based on time-weighted mean measured test concentrations of the filtered test substance.
	Daphnia (*Daphnia magna*) 21-day EC_{50} = 2.8 mg/L (immobilization) (Experimental)	Nippon Kayaku Co., 2000a	Test conducted in accordance with OECD 211; 21-day reproduction test in parental daphnia generation; Based on time-weighted mean measured test concentrations of the filtered test substance.

TGSA CASRN 41481-66-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Daphnia (*Daphnia magna*) 21-day EC_{50} = 2.0 mg/L (reproduction) (Experimental)	Nippon Kayaku Co., 2000a	Test conducted in accordance with OECD 211; 21-day reproduction test; Based on time-weighted mean measured test concentrations of the filtered test substance.
	Daphnia (*Daphnia magna*) LOEC = 1.6 mg/L (reproduction) NOEC = 0.50 mg/L (Experimental)	Nippon Kayaku Co., 2000a	Test conducted in accordance with OECD 211; 21-day reproduction test; based on time-weighted mean measured test concentrations of the filtered test substance.
	Daphnid ChV = 0.25 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid ChV = 0.61 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
Green Algae ChV	Green algae ChV = 0.20 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
	Green algae ChV = 1.14 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

TGSA CASRN 41481-66-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL FATE				
Transport		**TGSA is expected to exist in both the neutral and anionic forms at environmentally-relevant pH. TGSA is expected to have moderate mobility in soil. Anionic TGSA may have higher mobility due to enhanced water solubility. However, leaching through soil to groundwater is not expected to be an important transport mechanism. In the atmosphere, TGSA is expected to exist in the particulate phase, which will be deposited back to the soil and water surfaces through wet or dry deposition. The Level III fugacity model indicates that TGSA will partition primarily to soil.**		
	Henry's Law Constant (atm-m^3/mole)	$8.6x10^{-8}$ (Estimated)	EPI	
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	996 (Measured) HPLC screening method using cyanopropyl packed column; GLP compliance	TSCATS	Adequate, nonguideline study yet established method considered to have higher reliability than QSAR-based estimations.
		>30,000 (Estimated)	EPI; U.S. EPA, 2004	Cutoff value for nonmobile compounds.
	Level III Fugacity Estimations	Air = <1% (Estimated) Water = 9.8% Soil = 58.2% Sediment = 31.9%	EPI	
Persistence		**HIGH: The persistence of TGSA is based on an estimated half-life of 75 days in soil. TGSA is expected to partition primarily to soil. Experimental biodegradation data for TGSA were not located. Evaluation of the biodegradation potential for TGSA is based entirely on QSARs of aerobic and anaerobic biodegradation. Results from these models estimate ultimate biodegradation in weeks-months and primary degradation in days-week. Biodegradation under anaerobic methanogenic conditions is not probable based on results from estimation models. TGSA does not contain functional groups that absorb light at environmentally-relevant wavelengths. Therefore, it is not expected to be susceptible to direct photolysis. It is not expected to undergo hydrolysis as it does not contain hydrolyzable functional groups. The atmospheric half-life of TGSA is estimated at 1.8 hours, although it is expected to exist primarily as a particulate in air. Therefore, biodegradation is expected to be the main degradation pathway for TGSA.**		
Water	**Aerobic Biodegradation**	Days-weeks (primary survey model) Weeks-months (ultimate survey model)	EPI	

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (anaerobic-methanogenic biodegradation probability model)	EPI	
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	1.8 hours (Estimated)	EPI	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	Substance does not contain functional groups that would be expected to absorb light at wavelengths >290 nm.
	Hydrolysis	<10% in 5 days at 50°C, pH 4	Nippon Kayaku Co., 1992b	Adequate; guideline study.
	Pyrolysis			No data located.
Environmental Half-life		75 days	EPI; PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**LOW: The estimated fish BAF and BCF is <100.**		
	Fish BCF	62 (Estimated)	EPI	Estimate performed using experimental log K_{ow}.
	BAF	18 (Estimated)	EPI	Estimate performed using experimental log K_{ow}.
	Metabolism in Fish			No data located.

TGSA CASRN 41481-66-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL MONITORING AND BIOMONITORING			
Environmental Monitoring	No data located.		
Ecological Biomonitoring	No data located.		
Human Biomonitoring	This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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Nippon Kayaku Co. *TG-SA: Acute dermal toxicity (limit test) in the rat.* Nippon Kayaku Co. Limited, Tokyo Japan. Project number: 189/315. **1991d**.

Nippon Kayaku Co. *TG-SA: Acute eye irritation test in the rabbit.* Nippon Kayaku Co. Limited, Tokyo Japan. Project number 189/317. **1991e**.

Nippon Kayaku Co. *TG-SA: Acute oral toxicity (limit test) in the rat.* Nippon Kayaku Co. Limited, Tokyo Japan. Project number: 189/314. **1991f**.

Nippon Kayaku Co. *TG-SA: Determination of Physico-Chemical Properties.* Nippon Kayaku Co. Limited, Tokyo Japan. Project number: 189/324. **1992a**.

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Nippon Kayaku Co. *TG-SA: Magnusson & Kligman maximization. Study in the guinea pig.* Nippon Kayaku Co. Limited, Tokyo Japan. Project number: 189/318. **1991h**.

Nippon Kayaku Co. *TG-SA: Micronucleus test.* Nippon Kayaku Co. Limited, Tokyo Japan. Project number: 189/323. **1991i**.

Nippon Kayaku Co. *TG-SA: Twenty-eight day sub-acute oral toxicity study in the rat.* Nippon Kayaku Co. Limited, Tokyo Japan. Project number 189/325. **1991j**.

Nippon Kayaku Co. *TG-SA: Skin sensitisation in the guinea-pig.* Nippon Kayaku Co. Limited, Tokyo Japan. 920596D/NKU 268/SS. **1992b**.

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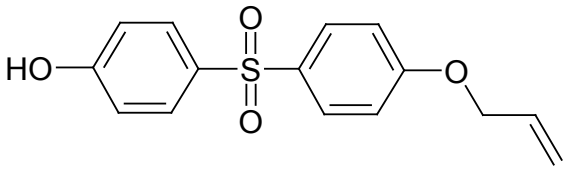
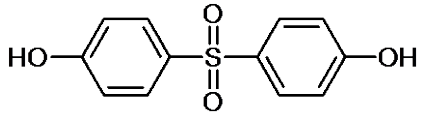
BPS-MAE



	CASRN: 97042-18-7
	MW: 290.34
	MF: $C_{15}H_{14}O_4S$
	Physical Forms: **Neat:** Solid
	Use: Developer for thermal paper
SMILES: C=CCOc2ccc(cc2)S(=O)(=O)c1ccc(O)cc1	
Synonyms: BPS-MAE; bis(4-Hydroxyphenyl) sulfone monoallyl ether; 4-[[4-(2-Propenyloxy)phenyl]sulfonyl]phenol; 4-{[4-(allyloxy)phenyl]sulfonyl}phenol	
Polymeric: No **Oligomers:** Not applicable	
Metabolites, Degradates and Transformation Products: Potential for epoxide formation on terminal double bond.	
Analog: Bisphenol S (80-09-1) **Endpoint(s) using analog values:** Boiling point, carcinogenicity, reproductive and developmental toxicity.	**Analog Structure:** 
Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)	
Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2011).	
Risk Assessments: None identified	

BPS-MAE CASRN 97042-18-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	172 (Measured)	Submitted confidential study	Adequate.
Boiling Point (°C)	>300 (Estimated)	EPI; U.S. EPA, 1999	Decomposition may occur before the boiling point is reached based on the experimental decomposition temperature of 315°C for an analogous structure, bisphenol S. Cutoff value for high boiling point compounds according to HPV assessment guidance.
Vapor Pressure (mm Hg)	$<1x10^{-8}$ (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for nonvolatile compounds according to HPV assessment guidance.
Water Solubility (mg/L)	83 (Estimated)	EPI	
Log K_{ow}	3.1 (Estimated)	EPI	
Flammability (Flash Point)			No data located.
Explosivity			No data located.
pH			No data located.
pK_a	8.2 (Estimated)	SPARC	

BPS-MAE CASRN 97042-18-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**BPS-MAE is estimated not to be absorbed through the skin as the neat material and have poor skin absorption when in solution. BPS-MAE is estimated to have good absorption via the lungs and gastrointestinal tract based on data for the analog BPA. BPS-MAE is a potential cross-linking agent because it has two terminal double bonds that are expected to be oxidized in the body via an epoxide intermediate.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Estimated to be poorly absorbed as neat material and in solution through the skin. Absorption through lungs and gastrointestinal tract is expected to be good. The terminal double bonds have the potential be oxidized metabolically to the epoxide. (Estimated by analogy)	Professional judgment	Estimated based on reported experimental data for the analog BPA; the potential for epoxide formation is based on a mechanistic analysis.
Acute Mammalian Toxicity		**LOW: BPS-MAE was not toxic following acute oral exposure based on the acute oral LC_{50} value of >2,000 mg/kg-bw in rats.**		
Acute Lethality	**Oral**	Rat (Sprague-Dawley CD) oral LD_{50} >2,000 mg/kg-bw, no mortalities or signs of systemic toxicity at the highest dose tested (2,000 mg/kg-bw).	Submitted Confidential Study	Adequate; guideline study (OECD 423).
	Dermal			No data located.
	Inhalation			No data located.
Carcinogenicity		**MODERATE: Estimated to have potential for carcinogenicity based on data reported for the epoxide oxidation product and structural analogy to bisphenol S. In addition, there is uncertainty due to the lack of data for this substance. Carcinogenic effects cannot be ruled out.**		
	OncoLogic Results			Not amenable to available estimation method.
	Carcinogenicity (Rat and Mouse)	Potential for carcinogenicity (Estimated)	Professional judgment	Estimated based on potential for the epoxide oxidation product and based on analogy to bisphenol S.
	Combined Chronic Toxicity/Carcinogenicity			No data located.

BPS-MAE CASRN 97042-18-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Genotoxicity		**MODERATE: BPS-MAE was clastogenic in CHL/IU cells with metabolic activation, but did not cause mutations in bacterial cells nor cause an increase in the induction of micronucleated immature erythrocytes or bone marrow cells in CD-1 mice.**		
	Gene Mutation *in vitro*	Negative, Reverse Mutation assay in *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537 and *Escherichia coli* WP2 uvrA/pKM101 with and without metabolic activation. Cytotoxicity was observed in *Salmonella typhimurium* strains TA98, TA1535, and TA1537 in the presence of activation at 5000 µg/plate.	Submitted Confidential Study	Adequate; guideline study (OECD 471).
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Positive for chromosome aberrations with activation in the CHL/IU cell line; the incidences of cells with structural chromosome aberrations was 6.0% (1250 µg/mL), 7.5% (2500 µg/mL) and 11% (5000 µg/ml) with metabolic activation.	Submitted Confidential Study	Adequate; guideline study (Japanese Guidelines on Industrial Chemicals (1997) and OECD Guideline (1997)).
	Chromosomal Aberrations *in vivo*	BPS-MAE did not cause an increase in the induction of micronucleated immature erythrocytes or bone marrow cells following oral gavage exposure to CD-1 mice.	Submitted Confidential Study	Adequate; guideline study (OECD 474).
	DNA Damage and Repair			No data located.
	Other (Mitotic Gene Conversion)			No data located.
Reproductive Effects		**MODERATE: Estimated based on analogy to bisphenol S. In a reproduction/developmental toxicity screening test, oral exposure of parental rats to the analog bisphenol S resulted in marked systemic effects and the NOAEL for reproductive effects is 60 mg/kg-day (prolonged estrous cycle, decreased fertility index and decreased number of live offspring). Based on the NOAEL for reproductive effects, a Moderate hazard designation is selected.**		

BPS-MAE CASRN 97042-18-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction/ Developmental Toxicity Screen	Parental toxicity: NOAEL = 10 mg/kg bw-day LOAEL = 60 mg/kg bw-day Reproductive toxicity: NOAEL = 60 mg/kg bw-day LOAEL = 300 mg/kg bw-day (Estimated by analogy)	ECHA, 2011; Professional judgment	Using the analog bisphenol S, data are for an adequate guideline study (OECD 421) reported in a secondary source.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	Potential for male reproductive toxicity (Estimated)	Professional judgment	Estimated based on reported data for the epoxide oxidation product and on reported experimental data for the analog bisphenol S.
Developmental Effects		**MODERATE: Estimated based on analogy to bisphenol S. In a reproduction/developmental toxicity screening test, oral exposure of parental rats to the analog bisphenol S resulted in marked systemic effects and decreased number of live offspring (PND 4) at the highest dose level (300 mg/kg-day with a NOAEL of 60 mg/kg-day. Based on the NOAEL, a Moderate hazard designation is selected.**		
	Reproduction/ Developmental Toxicity Screen	Parental toxicity: NOAEL = 10 mg/kg bw-day LOAEL = 60 mg/kg bw-day Reproductive toxicity: NOAEL = 60 mg/kg bw-day LOAEL = 300 mg/kg bw-day (Estimated by analogy)	ECHA, 2011; Professional judgment	Using the analog bisphenol S, data are for an adequate guideline study (OECD 421) reported in a secondary source.

BPS-MAE CASRN 97042-18-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Potential for developmental toxicity (Estimated)	Professional judgment	Estimated based on reported data for the epoxide oxidation product and on reported experimental data for the analog bisphenol S.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert. (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on structural alert.
Repeated Dose Effects		**LOW: Effects from BPS-MAE were limited to increased kidney weights at 1,000 mg/kg/day in a 28-day repeated-dose toxicity study in rats.**		
		Adverse effects were limited to higher absolute and relative kidney weights in female Crj:CD (SD) IGS rats at 1,000 mg/kg-bw; NOEL = 1,000 mg/kg-bw/day (males) and 200 mg/kg-bw/day (females).	Submitted Confidential Study	Adequate; guideline study (OECD 407).
Skin Sensitization		**LOW: BPS-MAE was not a skin sensitizer in one study of guinea pigs.**		
	Skin Sensitization	Negative for skin sensitization in Dunkin Hartley guinea pigs.	Submitted Confidential Study	Adequate; guideline study (OECD 406).
Respiratory Sensitization		**MODERATE: BPS-MAE is estimated to have potential to be a respiratory sensitizer based on the epoxide oxidation product.**		
	Respiratory Sensitization	Potential for respiratory sensitization	Professional judgment	Estimated based on reported data for the epoxide oxidation product.

BPS-MAE CASRN 97042-18-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Eye Irritation		**LOW: Minimal conjunctival irritation was observed that cleared by the 24-hour observation.**		
	Eye Irritation	Slight irritant (maximum group mean score: 2.7) in New Zealand White rabbits, minimal conjunctival irritation, treated eyes appeared normal at the 24-hour observation.	Submitted Confidential Study	Adequate; guideline study (OECD 405).
Dermal Irritation		**VERY LOW: BPS-MAE was not a dermal irritant in one study of rabbits.**		
	Dermal Irritation	Non-irritant (primary irritation index: 0) in New Zealand White rabbits.	Submitted Confidential Study	Adequate; guideline study (OECD 404).
Endocrine Activity		**No data located.**		
				No data located.
Immunotoxicity		**No data located.**		
	Immune System Effects			No data located.
ECOTOXICITY				
ECOSAR Class		Phenols; Vinyl/allyl ethers		
Acute Toxicity		**HIGH: Based on measured EC_{50} values for fish, daphnia, and algae of 4.5, 13.5, and 4.5 mg/L, respectively.**		
Fish LC_{50}		Rainbow trout (*Oncorhynchus mykiss*) 96-hour LC_{50} = 4.5 mg/L; mean measured concentrations; static-renewal test system; solvent: dimethylformamide (DMF); sub-lethal effects included loss of equilibrium, hyperventilation, lying on base of tank, increased pigmentation, and erratic swimming.	Submitted Confidential Study	Adequate; guideline study (OECD 203).
		Fish 96-hour LC_{50} = 27 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

BPS-MAE CASRN 97042-18-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Fish 96-hour LC_{50} = 8 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.11	
	Fish 96-hour LC_{50} = 1.7 mg/L (Estimated) ECOSAR: Vinyl/allyl ethers	ECOSAR version 1.11	
Daphnid LC_{50}	*Daphnia magna* 48-hour EC_{50} = 13.5 mg/L; mean measured concentrations; static test system; solvent: DMF.	Submitted Confidential Study	Adequate; guideline study (OECD 202).
	Daphnid 48-hour LC_{50} = 17 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid 48-hour LC_{50} = 3.8 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.11	
	Daphnid 48-hour LC_{50} = 7.9 mg/L (Estimated) ECOSAR: Vinyl/allyl ethers	ECOSAR version 1.11	
Green Algae EC_{50}	*Pseudokirchneriella subcapitata* 72-hour EC_{50} = 4.5 mg/L (biomass), 7.8 mg/L (growth rate); mean measured concentrations; solvent: DMF.	Submitted Confidential Study	Adequate; guideline study (OECD 201).
	Green algae 96-hour EC_{50} = 19 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

BPS-MAE CASRN 97042-18-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Green algae 96-hour EC_{50} = 16 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.11	
	Green algae 96-hour EC_{50} = 18 mg/L (Estimated) ECOSAR: Vinyl/allyl ethers	ECOSAR version 1.11	
Chronic Aquatic Toxicity	**HIGH: Based on measured fish and Daphnid ChV values of 0.162 mg/L and 0.102 mg/L, respectively.**		
Fish ChV	Fathead minnow (*Pimephales promelas*) 32-day NOEC = 0.0939 mg/L, LOEC = 0.28 mg/L, ChV (MATC) = 0.162 mg/L; mean measured concentrations; flow-through test system; solvent: tetrahydrofuran (THF); basis of effect level: survival.	Submitted Confidential Study	Adequate; guideline study (OECD 210).
	Fish ChV = 3 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Fish ChV = 0.940 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.11	
	Fish ChV = 0.047 mg/L (Estimated) ECOSAR: Vinyl/allyl ethers	ECOSAR version 1.11	

BPS-MAE CASRN 97042-18-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid ChV	*Daphnia magna* 21-day NOEC= 0.0664 mg/L, LOEC= 0.157 mg/L, ChV = 0.102 mg/L; mean measured concentrations; static-renewal test system; solvent: DMF; basis of effect level: parental survival and reproduction.	Submitted Confidential Study	Adequate; guideline study (OECD 211).
	Daphnid ChV = 2.2 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid ChV = 0.73 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.11	
	Daphnid ChV = 1.9 mg/L (Estimated) ECOSAR: Vinyl/allyl ethers	ECOSAR version 1.11	
Green Algae ChV	*Pseudokirchneriella subcapitata* 72-hour NOEC = 1.8 mg/L, LOEC = 3.7 mg/L, ChV = 2.6 mg/L; mean measured concentrations; solvent: DMF.	Submitted Confidential Study	Adequate; guideline study (OECD 201).
	Green algae ChV = 6.1 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

BPS-MAE CASRN 97042-18-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Green algae ChV = 7.4 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.11	
		Green algae ChV = 3.5 mg/L (Estimated) ECOSAR: Vinyl/allyl ethers	ECOSAR version 1.11	
Earthworm Subchronic Toxicity		Earthworm 14-day LC_{50} = 100.029 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.11	
ENVIRONMENTAL FATE				
Transport		**BPS-MAE is expected to exist in both neutral and anionic forms at environmentally-relevant pH, based on its estimated pKa. The neutral form of BPS-MAE is expected to be immobile in soil based on its estimated K_{oc}. The anionic form may be more mobile although leaching of BPS-MAE through soil to groundwater is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that it will be nonvolatile from surface water. Volatilization from dry surface is also not expected based on its estimated vapor pressure. In the atmosphere, BPS-MAE is expected to exist solely in the particulate phase based on its estimated vapor pressure. Particulates may be removed from air by wet or dry deposition. Level III fugacity models incorporating the available experimental property data indicate that the unionized form of BPS-MAE is expected to partition primarily to soil.**		
	Henry's Law Constant (atm-m^3/mole)	<$1x10^{-8}$ (Estimated)	EPI; Professional judgment	Cutoff value for nonvolatile compounds.
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	$3.0x10^3$ (Estimated)	EPI	
	Level III Fugacity Model	Air = <1% (Estimated) Water = 11% Soil = 87% Sediment = 2%	EPI	

BPS-MAE CASRN 97042-18-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**HIGH: High persistence concern for BPS-MAE results from an estimated half-life of 75 days in soil, the compartment where according to fugacity models; it is expected to primarily partition. Evaluation of QSARs models estimate ultimate biodegradation in weeks to months, which suggest a biodegradation half-life of <60 days with no persistent metabolites in aquatic environments. Biodegradation under anaerobic methanogenic conditions is not probable based on results from estimation models. BPS-MAE is not expected to undergo hydrolysis since it does not contain hydrolyzable functional groups. The atmospheric half-life of BPS-MAE is estimated at 3 hours although it is expected to exist primarily in the particulate phase in air.**		
Water	**Aerobic Biodegradation**	Days-weeks (primary survey model) Weeks-months (ultimate survey model)	EPI	
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (anaerobic-methanogenic biodegradation probability model)	EPI	
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	3.0 hours (Estimated)	EPI	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	Substance does not contain functional groups that would be expected to absorb light at wavelengths >290 nm.
	Hydrolysis	Not a significant fate process (Estimated)	Wolfe and Jeffers, 2000; Professional judgment	Substance does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.
	Pyrolysis			No data located.

BPS-MAE CASRN 97042-18-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Environmental Half-life		75 days (Estimated)	EPI; PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**LOW: The estimated BCF and BAF are both <100.**		
	Fish BCF	48 (Estimated)	EPI	
	BAF	76 (Estimated)	EPI	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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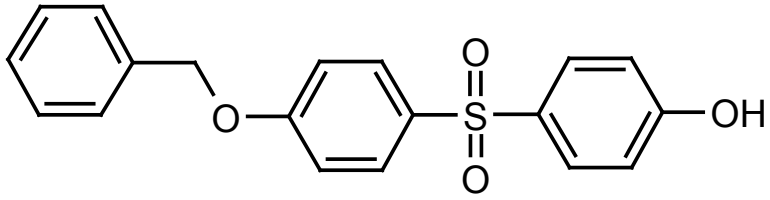
BPS-MPE



CASRN: 63134-33-8

MW: 340.4

MF: $C_{19}H_{16}O_4S$

Physical Forms:
Neat: Solid

Use: Developer for thermal paper

SMILES: O=S(=O)(c(ccc(OCc(cccc1)c1)c2)c2)c(ccc(O)c3)c3

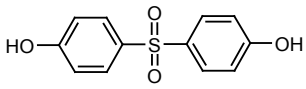
Synonyms: Phenol, 4-[[4-(phenylmethoxy)phenyl]sulfonyl]-; 4-Benzyloxy-4'-hydroxydiphenyl sulfone; 4-Hydroxy-4'-benzyloxydiphenylsulfone

Polymeric: No
Oligomers: Not applicable

Metabolites, Degradates and Transformation Products: None

Analog: Bisphenol S (80-09-1)
Endpoint(s) using analog values: Boiling point, reproductive and developmental toxicity, repeated dose toxicity, genotoxicity

Analog Structure:



Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)

Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2011).

Risk Assessments: None identified

BPS-MPE CASRN 63134-33-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	170	ChemSpider, 2010	Secondary source; study details and test conditions were not provided.
Boiling Point (°C)	>300 (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for high boiling point compounds according to the HPV assessment guidance; decomposition may occur before the boiling point is reached based on the experimental decomposition temperature of 315°C for the analog bisphenol S (80-09-1).
Vapor Pressure (mm Hg)	$<1x10^{-8}$ (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for nonvolatile compounds according to the HPV assessment guidance.
Water Solubility (mg/L)	10 (Estimated)	EPI	
Log K_{ow}	3.9 (Estimated)	EPI	
Flammability (Flash Point)			No data located.
Explosivity			No data located.
pH			No data located.
pK_a	8.2 (Estimated)	SPARC	

BPS-MPE CASRN 63134-33-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**One experimental study indicated that BPS-MPE was not absorbed through the skin in guinea pigs. BPS-MPE is estimated not to be absorbed through the skin as a neat material and to have poor skin absorption when in solution. BPS-MPE is estimated to have good absorption via the lungs and gastrointestinal tract based on data for the analog BPA.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral**	Not absorbed through the skin as a neat material and has poor absorption in solution; can be absorbed through the lung and gastrointestinal tract (Estimated by analogy)	Professional judgment	Estimated based on experimental data for the analog BPA.
	Dermal	No evidence of skin absorption at 1,000 mg/kg; three guinea pigs, solid-moist with water	Eastman Kodak, 1991	Adequate.
Acute Mammalian Toxicity		**LOW: Based on acute oral LD_{50} values >2,000 mg/kg in rats and mice. The acute dermal lethality study in guinea pigs failed to identify an LD_{50}, although the results indicated that the LD_{50} was >1,000 mg/kg, the highest dose tested.**		
Acute Lethality	**Oral**	Rat LD_{50} >3,200 mg/kg; 10 male rats, moderate weakness and diarrhea	Eastman Kodak, 1991	Adequate.
		Mouse LD_{50} = 3,200 mg/kg; 10 male mice, moderate weakness, rough hair coats	Eastman Kodak, 1991	Adequate.
	Dermal	Guinea pig LD_{50} >1,000 mg/kg; slight edema, desquamation, slight to moderate alopecia	Eastman Kodak, 1991	Adequate.
	Inhalation			No data located.
Carcinogenicity		**MODERATE: There is uncertain potential for carcinogenicity due to the lack of data located for this substance. Carcinogenic effects cannot be ruled out.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)			No data located.

BPS-MPE CASRN 63134-33-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Combined Chronic Toxicity/Carcinogenicity			No data located.
Genotoxicity		**MODERATE: Estimated based on analogy to bisphenol S. Bisphenol S did not induce gene mutations in several *in vitro* assays and did not induce chromosomal aberrations *in vivo* in a mammalian erythrocyte micronucleus assay in NMRI mice or in Chinese hamster ovary (CHO) cells *in vitro* in the presence of exogenous metabolic activation. However, the analog bisphenol S did induce chromosomal aberrations in CHO cells *in vitro* in the absence of exogenous metabolic activation (at a noncytotoxic concentration). The positive result in the *in vitro* assay and negative result in the *in vivo* test suggest an equivocal response and therefore a Moderate hazard potential.**		
	Gene Mutation *in vitro*	Negative, mouse lymphoma L5178Y (TK+/TK-) cells, with and without metabolic activation (Estimated by analogy)	CCRIS database; Professional judgment	Adequate; based on experimental data measured for the analog bisphenol S.
		Negative, Ames assay (standard plate) in *Salmonella typhimurium* strains TA98, TA100, TA1537, TA1535, and TA1538 with and without metabolic activation (Estimated by analogy)	CCRIS database; Professional judgment	Adequate; based on experimental data measured for the analog bisphenol S.
		Negative, Salmonella/microsome test, *S. typhimurium* strains TA1535, TA100, TA1537, and TA98 with and without metabolic activation (Estimated by analogy)	Miles Inc., 1992; ECHA, 2011; Professional judgment	Adequate; based on experimental data measured for the analog bisphenol S in an adequate guideline study (OECD 471).
		Negative, Ames assay (preincubation) in *S. typhimurium* strains TA98, TA100, TA1537, TA1535 and *Escherichia coli* WP2UVRA with and without metabolic activation (Estimated by analogy)	CCRIS database, 2010; ECHA, 2011; Professional judgment	Adequate; based on experimental data measured for the analog bisphenol S in an adequate guideline study (OECD 471).
		Negative, umu test in *S.typhimurium* strain TA1335 (Estimated by analogy)	Chen, Michihiko et al., 2002; Professional judgment	Adequate; based on experimental data measured for the analog bisphenol S.

BPS-MPE CASRN 63134-33-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Negative, CHO HGPRT mutation assay, with and without metabolic activation (Estimated by analogy)	Amoco Corp., 1991a; Professional judgment	Adequate; based on experimental data measured for the analog bisphenol S.
		Potential for mutagenicity (Estimated by analogy)	Professional judgment	Estimated based on experimental data for the analog bisphenol S.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Positive, without metabolic activation; negative, with metabolic activation (Estimated by analogy)	Amoco Corp., 1991b; ECHA, 2011; Professional judgment	Adequate; based on experimental data measured for the analog bisphenol S in an adequate guideline study (similar to OECD 473).
	Chromosomal Aberrations *in vivo*	Negative, mammalian erythrocyte micronucleus assay in male NMRI mice (gavage) (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; based on experimental data measured for the analog bisphenol S in an adequate guideline study (OECD 474).
	DNA Damage and Repair			No data located.
	Other (Mitotic Gene Conversion)			No data located.
Reproductive Effects		**MODERATE: Estimated based on analogy to bisphenol S. In a reproductive/developmental toxicity screening test, oral exposure of parental rats to the analog bisphenol S resulted in marked systemic effects and the NOAEL for reproductive effects is 60 mg/kg-day (prolonged estrous cycle, decreased fertility index and decreased number of live offspring). Based on the NOAEL for reproductive effects, a Moderate hazard designation is selected.**		
	Reproduction/ Developmental Toxicity Screen	Parental toxicity: NOAEL = 10 mg/kg bw-day LOAEL = 60 mg/kg bw-day Reproductive toxicity: NOAEL = 60 mg/kg bw-day LOAEL = 300 mg/kg bw-day (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; based on experimental data measured for the analog bisphenol S in an adequate guideline study (OECD 421) reported in a secondary source.

BPS-MPE CASRN 63134-33-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	Potential for reproductive toxicity (Estimated by analogy)	Professional judgment	Estimated based on experimental data for the analog bisphenol S.
Developmental Effects		**MODERATE: Estimated based on analogy to bisphenol S. In a reproductive/developmental toxicity screening test, oral exposure of parental rats to the analog bisphenol S resulted in marked systemic effects and a decreased number of live offspring (PND 4) at the highest dose level (300 mg/kg-day) with a NOAEL of 60 mg/kg-day. Based on the NOAEL, a Moderate hazard designation is selected.**		
	Reproduction/ Developmental Toxicity Screen	Parental toxicity: NOAEL = 10 mg/kg bw-day LOAEL = 60 mg/kg bw-day Reproductive toxicity: NOAEL = 60 mg/kg bw-day LOAEL = 300 mg/kg bw-day (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; based on experimental data measured for the analog bisphenol S in an adequate guideline study (OECD 421) reported in a secondary source.
		Potential for developmental toxicity (Estimated by analogy)	Professional judgment	Estimated based on experimental data for the analog bisphenol S.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert. (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on structural alert.

BPS-MPE CASRN 63134-33-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects	**HIGH: Based on analogy to bisphenol S. In two adequately-designed repeated dose oral studies in rats, one study identified a NOAEL of 10 mg/kg-day and a LOAEL of 60 mg/kg-day for systemic effects and the other study identified a NOAEL of 40 mg/kg-day and a LOAEL of 200 mg/kg-day for systemic effects following exposure to the analog bisphenol S. The High hazard designation is based on uncertainty as to the potential systemic toxicity in the range of 40-60 mg/kg-day. Data located for BPS-MPE are inadequate to assess the hazard for repeated dose effects.**		
Oral	12-Day repeated dose oral (dietary) study, 5 male rats/group, test compound concentrations of 0, 0.1, and 1.0% in corn oil (~0, 100, and 980 mg/kg-day, respectively), slightly increased absolute (high dose) and relative (high and low dose) liver weights, no abnormalities or changes in body weight, clinical chemistry, gross pathology, or histopathology NOAEL = 100 mg/kg-day LOAEL = 980 mg/kg-day	Eastman Kodak, 1991	Inadequate; exposure duration only 12 days, and only one species tested.
	In a repeated-dose oral study, Sprague-Dawley rats, NOAEL = 40 mg/kg bw-day LOAEL = 200 mg/kg-bw-day (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; based on experimental data measured for the analog bisphenol S in an adequate 28-day repeat dose toxicity guideline study.
	In a reproduction/developmental toxicity screening test, Sprague-Dawley rats, NOAEL = 10 mg/kg bw-day LOAEL = 60 mg/kg bw-day (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; based on experimental data measured for the analog bisphenol S in an adequate guideline study (OECD 421).
	Potential for liver and kidney toxicity (Estimated by analogy)	Professional judgment	Estimated based on experimental data for the analog bisphenol S.

BPS-MPE CASRN 63134-33-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Dermal		10-Day repeated-dose dermal study, 5 guinea pigs; repeated dosing slightly exacerbated skin reaction; by day 10, severe erythema and minute eschar formation in 2/5 guinea pigs	Eastman Kodak, 1991	Inadequate; treatment period only 10 days, no dose level.
Skin Sensitization		**LOW: Not an apparent skin sensitizer in guinea pigs.**		
	Skin Sensitization	Negative for skin sensitization; 10 guinea pigs	Eastman Kodak, 1991	Adequate.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: Slightly irritating to rabbit eyes with clearing within 24 hours.**		
	Eye Irritation	Slight irritant, rabbits, clearing within 24 hours	Eastman Kodak, 1991	Adequate.
Dermal Irritation		**LOW: Slightly irritating to the skin of guinea pigs.**		
	Dermal Irritation	Slight irritant at 24 hours recovering within 2 weeks, guinea pigs	Eastman Kodak, 1991	Adequate.
Endocrine Activity		**No data located.**		
				No data located.
Immunotoxicity		**No data located.**		
	Immune System Effects			No data located.
ECOTOXICITY				
ECOSAR Class		Phenols		
Acute Toxicity		**VERY HIGH: Based on measured 96-hour LC_{50} values for fish and Daphnid in the range of 0.34-3.4 mg/L, although detailed study results were not provided.**		
Fish LC_{50}		Fathead minnow 96-hour LC_{50} = 0.34-3.4 mg/L (Experimental)	Eastman Kodak, 1991	Although experimental details were not provided, the study demonstrates the potential for adverse effects at concentrations corresponding to a Very High hazard concern.

BPS-MPE CASRN 63134-33-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Fish 96-hour LC_{50} = 2.01 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.11	
	Fish 96-hour LC_{50} = 6.28 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid LC_{50}	Daphnid 96-hour LC_{50} = 0.34-3.4 mg/L (Experimental)	Eastman Kodak, 1991	Although experimental details were not provided, the study demonstrates the potential for adverse effects at concentrations corresponding to a Very High hazard concern.
	Daphnid 48-hour LC_{50} = 1.46 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.11	
	Daphnid 48-hour LC_{50} = 4.57 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

BPS-MPE CASRN 63134-33-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae EC_{50}	Green algae 96-hour EC_{50} = 4.32 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Green algae 96-hour EC_{50} = 5.58 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.11	
Chronic Aquatic Toxicity	**HIGH: Based on an estimated fish 30-day ChV of 0.27 mg/L.**		
Fish ChV	Fish 30-day ChV = 0.27 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.11	
	Fish ChV = 0.57 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid ChV	Daphnid 21-day ChV = 0.28 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.11	

BPS-MPE CASRN 63134-33-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Daphnid ChV = 0.59 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Green Algae ChV	Green algae ChV = 2.22 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Green algae ChV = 2.56 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.11	
Earthworm Subchronic Toxicity	Earthworm 14-day LC_{50} = 52.09 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.11	chemical may not be soluble enough to measure this predicted effect

BPS-MPE CASRN 63134-33-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL FATE				
Transport		**Based on the Level III fugacity models incorporating the located experimental property data, BPS-MPE is expected to partition primarily to soil. BPS-MPE is expected to exist in both neutral and anionic forms at environmentally-relevant pH, based on its estimated pK_a. The neutral form of BPS-MPE is expected to be immobile in soil based on its estimated K_{oc}. The anionic form may be more mobile, as anions do not bind as strongly to organic carbon and clay as their neutral counterparts. However, leaching of BPS-MPE through soil to groundwater is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that it will be nonvolatile from surface water. Volatilization from dry surface is also not expected based on its estimated vapor pressure. In the atmosphere, BPE-MPE is expected to exist solely in the particulate phase, based on its estimated vapor pressure. Particulates may be removed from air by wet or dry deposition.**		
	Henry's Law Constant ($atm\text{-}m^3/mole$)	$<1x10^{-8}$ (Estimated)	EPI, Professional judgment	Cutoff value for nonvolatile compounds, based on professional judgment.
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	>30,000 (Estimated)	EPI; U.S. EPA, 2004	Cutoff value for nonmobile compounds.
	Level III Fugacity Model	Air = <1% (Estimated) Water = 8.5% Soil = 75% Sediment = 16%	EPI	
Persistence		**HIGH: Evaluation of the persistence of BPS-MPE is based entirely on QSARs for aerobic and anaerobic biodegradation. Results from these models estimate primary biodegradation in days-weeks and ultimate degradation in weeks-months. BPS-MPE is expected to partition primarily to soil. Based on these data, the biodegradation half-life is expected to be 75 days in soil. Biodegradation under anaerobic methanogenic conditions is not probable. BPS-MPE is not expected to undergo hydrolysis since it does not contain hydrolyzable functional groups. BPS-MPS does not absorb UV light at environmentally significant wavelengths. The vapor phase reaction of BPS-MPE with atmospheric hydroxyl radicals is estimated at 5.7 hours, although it is expected to exist primarily in the particulate phase in air. Considerations of all these factors indicate that the persistence concern is High for BPS-MPE.**		
Water	**Aerobic Biodegradation**	Days-weeks (Primary survey model) Weeks-months (Ultimate survey model)	EPI	

BPS-MPE CASRN 63134-33-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (anaerobic-methanogenic biodegradation probability model)	EPI	
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	5.7 hours (Estimated)	EPI	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	The substance does not contain functional groups that would be expected to absorb light at wavelengths >290 nm.
	Hydrolysis	Not a significant fate process (Estimated)	Wolfe and Jeffers, 2000; Professional judgment	The substance does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.
	Pyrolysis			No data located.
Environmental Half-life		75 days (Estimated)	EPI, PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**MODERATE: Both the estimated BCF for fish and the BAF are in the range from 100 to 1,000.**		
	Fish BCF	180 (Estimated)	EPI	
	BAF	110 (Estimated)	EPI	
	Metabolism in Fish			No data located.

BPS-MPE CASRN 63134-33-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL MONITORING AND BIOMONITORING			
Environmental Monitoring	No data located.		
Ecological Biomonitoring	No data located.		
Human Biomonitoring	This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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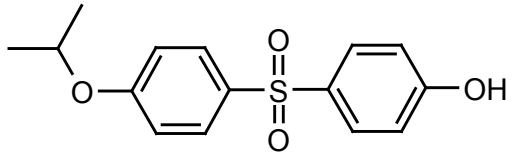
D-8



CASRN: 95235-30-6

MW: 292.35

MF: $C_{15}H_{16}O_4S$

Physical Forms:
Neat: Solid

Use: Developer for thermal paper

SMILES: O=S(=O)(c1ccc(O)cc1)c2ccc(OC(C)C)cc2

Name: 4-hydroxyphenyl 4-isoprooxyphenylsulfone

Synonyms: Phenol, 4-[[4-(1-methylethoxy)phenyl]sulfonyl]-; 4-(4-isopropoxyphenylsulfonyl)phenol; Phenol, 4-[[4-(1-methylethoxy)phenyl]sulfonyl]-; 4-Hydroxy-4-isopropoxydiphenylsulfone; D-8; DD-8; ALD-2000

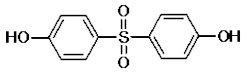
Polymeric: No
Oligomers: Not applicable

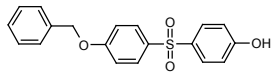
Metabolites, Degradates and Transformation Products: None identified

Analog: Bisphenol S (80-09-1)
Endpoint(s) using analog values: Reproductive effects, developmental effects, and repeated dose effects
Analog: BPS-MPE (63134-33-8)
Endpoint(s) using analog values: Acute mammalian toxicity; eye irritation; dermal irritation; skin sensitization

Analog Structures:

Structure:





Name: Bisphenol S (80-09-1) BPS-MPE (63134-33-8)

Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)

Risk Phrases: 51/53 - Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (ESIS, 2011).

Risk Assessments: None identified

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	129 (Measured)	Submitted confidential study	Adequate.
	129.3 (Measured) at 101.3 kPa; using capillary method	ECHA, 2013	Reported in a secondary source.
Boiling Point (°C)	>300 (Estimated)	EPI; U.S. EPA, 1999	Decomposition may occur before the boiling point is reached based on the experimental decomposition temperature. Cutoff value for high boiling point compounds according to HPV assessment guidance.
	260 (Measured) at 101.3 kPa	ECHA, 2013	Reported in a secondary source with limited study details.
	Decomposes (Measured) reported as 363 K at 2.128 kPa using Siwoloboff method	ECHA, 2013	Reported in a secondary source. This compound was found to decompose at a reduced pressure of 2.128 kPa.
Vapor Pressure (mm Hg)	$<1x10^{-8}$ (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for nonvolatile compounds according to HPV assessment guidance.
	$<7.5x10^{-7}$ (Measured) reported as < 0.0001 Pa at 27°C using gas saturation method	ECHA, 2013	Cutoff value reported in a secondary source.
	$<7.5x10^{-8}$ (Measured) reported as < 0.00001 Pa at 27°C	ECHA, 2013	
Water Solubility (mg/L)	21 (Measured)	Submitted confidential study	Adequate.
	19.7 (Measured) at pH of 6.85; 25°C	ECHA, 2013	Reported in a secondary source.
Log K_{ow}	3.36 (Measured) using shake-flask method	ECHA, 2013	Reported in a secondary source.
Flammability (Flash Point)	Auto flammability temperature: ≥129°C	ECHA, 2013	Cutoff value reported in a secondary source.
Explosivity			No data located.

D-8 CASRN 95235-30-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
pH				No data located.
pK_a		8.2 (Estimated)	SPARC	
HUMAN HEALTH EFFECTS				
Toxicokinetics		**D-8 is estimated not to be absorbed through the skin as the neat material and have poor skin absorption when in solution. D-8 is estimated to have good absorption via the lungs and gastrointestinal tract based on data for the analog BPA.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Estimated to not be absorbed through the skin as neat material and has poor absorption in solution. Can be absorbed through the lung and gastrointestinal tract (Estimated by analogy)	Professional judgment	Estimated based on reported experimental data for the analog BPA.
Acute Mammalian Toxicity		**LOW: Based on experimental oral, dermal and inhalation data.**		
Acute Lethality	**Oral**	Rat LD_{50} >3,200 mg/kg; 10 male rats, moderate weakness and diarrhea	Eastman Kodak, 1991	Adequate.
		Mouse LD_{50} = 3,200 mg/kg; 10 male mice, moderate weakness, rough hair coats	Eastman Kodak, 1991	Adequate.
		Rat, LD_{50} > 5,000 mg/kg	ECHA, 2013	Limited study details reported in a secondary source.
	Dermal	Guinea pig LD_{50} >1,000 mg/kg; slight edema, desquamation, slight to moderate alopecia	Eastman Kodak, 1991	Adequate.
		Rat LD_{50} > 2,000 mg/kg	ECHA, 2013	Limited study details reported in a secondary source.
	Inhalation	Rat LC_{50} > 5.04 mg/L	ECHA, 2013	Limited study details reported in a secondary source.

D-8 CASRN 95235-30-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Carcinogenicity		**MODERATE: There is uncertain potential for carcinogenicity due to the lack of data for this substance. Carcinogenic effects cannot be ruled out.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
Genotoxicity		**LOW: This substance is not mutagenic in bacteria and does not cause chromosome aberrations in Chinese hamster lung cells *in vitro*, or in mice *in vivo*.**		
	Gene Mutation *in vitro*	Potential for mutagenicity (Estimated)	Professional judgment	Estimated by analogy to confidential analog and professional judgment.
		Negative, reverse mutation assay in *S. typhimurium* TA98, TA100, TA1535, TA1538	Submitted confidential study; ECHA, 2013	Adequate.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Negative, chromosomal aberrations in Chinese hamster lung cells (Measured)	Submitted confidential study; ECHA, 2013	Adequate.
	Chromosomal Aberrations *in vivo*	Negative, chromosomal aberrations in male/female NMRI mice	ECHA, 2013	Limited study details reported in a secondary source.
	DNA Damage and Repair			No data located.
	Other (Mitotic Gene Conversion)			No data located.

D-8 CASRN 95235-30-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**MODERATE: Estimated based on analogy to bisphenol S. In a reproduction/developmental toxicity screening test, oral exposure of parental rats to the analog bisphenol S resulted in marked systemic effects and the NOAEL for reproductive effects is 60 mg/kg-day (prolonged estrous cycle, decreased fertility index and decreased number of live offspring). Based on the NOAEL for reproductive effects, a Moderate hazard designation is selected.**		
	Reproduction/ Developmental Toxicity Screen	Parental toxicity: NOAEL = 10 mg/kg bw-day LOAEL = 60 mg/kg bw-day Reproductive toxicity: NOAEL = 60 mg/kg bw-day LOAEL = 300 mg/kg bw-day (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; using the analog bisphenol S, data are for an adequate guideline study (OECD 421) reported in a secondary source.
		One-generation oral (gavage) study in rats Parental NOEL = 125 mg/kg-day F1 NOEL = 125 mg/kg-day	ECHA, 2013	No study details reported in a secondary source; administered doses not specified; unclear if a LOAEL was identified.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	Potential for reproductive toxicity (Estimated by analogy)	Professional judgment	Estimated based on reported experimental data for the analog bisphenol S.

D-8 CASRN 95235-30-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Developmental Effects		**MODERATE: Estimated based on analogy to bisphenol S. In a reproduction/developmental toxicity screening test, oral exposure of parental rats to the analog bisphenol S resulted in marked systemic effects and decreased number of live offspring (PND 4) at the highest dose level (300 mg/kg-day with a NOAEL of 60 mg/kg-day. Based on the NOAEL, a Moderate hazard designation is selected.**		
	Reproduction/ Developmental Toxicity Screen	Parental toxicity: NOAEL = 10 mg/kg bw-day LOAEL = 60 mg/kg bw-day Reproductive toxicity: NOAEL = 60 mg/kg bw-day LOAEL = 300 mg/kg bw-day (Estimated by analogy)	ECHA, 2011; Professional judgment	Adequate; using the analog bisphenol S, data are for an adequate guideline study (OECD 421) reported in a secondary source.
		Potential for developmental toxicity (Estimated by analogy)	Professional judgment	Estimated based on reported experimental data for the analog bisphenol S.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert. (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on structural alert.

D-8 CASRN 95235-30-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects		**MODERATE: There were no significant effects observed in a 90-day oral toxicity test in rats at doses ≤50 mg/kg-day (highest dose tested). This value falls within the Moderate hazard criteria (10-100 mg/kg-day). There is uncertainty if there would be adverse effects occurring at doses between 50 and 100 mg/kg-day so the hazard designation is assigned a Moderate for this endpoint.**		
		90-day repeated dose oral study in CLR: (WI) BR Wistar rats NOAEL = 50 mg/kg-day (highest dose tested) LOAEL = not established	Submitted confidential study; ECHA, 2013	Adequate; conducted to OECD guideline 408. A LOAEL could not be established because there were no effects.
		Subchronic oral (dietary) repeated dose study in F344 rats NOAEL = 10.9 mg/kg-day (males), 11.9 mg/kg-day (females); actual doses received	ECHA, 2013	Limited study details reported in a secondary source; administered doses not specified; unclear if a LOAEL was identified.
Skin Sensitization		**LOW: Estimated based on analogy to BPS-MPE. Not considered a skin sensitizer for guinea pigs based on analog data for BPS-MPE.**		
	Skin Sensitization	Negative for skin sensitization; 10 guinea pigs	Eastman Kodak, 1991	Adequate.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: Estimated based on analogy to BPS-MPE. The analog bisphenol BPS-MPE was non-irritating to slightly irritating to rabbit eyes.**		
	Eye Irritation	Slight irritant, rabbits, clearing within 24 hours	Eastman Kodak, 1991	Adequate.
		No eye irritation in rabbits	ECHA, 2013	Limited study details reported in a secondary source.

D-8 CASRN 95235-30-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Dermal Irritation		**LOW: Estimated based on analogy to BPS-MPE. The analog bisphenol BPS-MPE was slightly irritating to guinea pig skin.**		
	Dermal Irritation	Slight irritant at 24 hours recovering within 2 weeks, guinea pigs	Eastman Kodak, 1991	Adequate.
		No skin irritation reported in rabbits	ECHA, 2013	Limited study details reported in a secondary source.
Endocrine Activity		**Based on several in vitro studies, there is limited evidence of endocrine activity. D-8 was negative for estrogenicity in two ER binding assays and one competitive ER binding assay, and positive for anti-estrogenicity in a competitive binding assay in the presence of 17β-estradiol.**		
		Negative for ER binding in yeast two-hybrid assay using human and medaka fish estrogen receptor (hERα and medERα, respectively) and coactivator TIF2 in *Saccharomyces cerevisiae* with or without exogenous metabolic activation.	Terasaki et al., 2007	Adequate.
		Negative for competitive ER-binding affinity in ER-ELISA assay with or without exogenous metabolic activation.	Terasaki et al., 2007	Adequate.
		Positive for anti-estrogenic activity in cell proliferation assay of ERE-GFP-MCF7 cells treated with 17β-estradiol.	Kuruto-Niwa et al., 2005	Adequate.
		Negative for estrogenic activity in cell proliferation assay of ERE-GFP-MCF7 cells in the absence of 17β-estradiol.	Kuruto-Niwa et al., 2005	Adequate.
Immunotoxicity		**No data located.**		
	Immune System Effects			No data located.
ECOTOXICITY				
ECOSAR Class		Phenols		
Acute Toxicity		**HIGH: Based on an experimental EC_{50} for algae, which is in the range of 1-10 mg/L. Estimated LC_{50}s for fish and Daphnid also fall within the High hazard category criteria, while experimental data for fish and Daphnid are within the Moderate hazard criteria range.**		

D-8 CASRN 95235-30-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Fish LC_{50}	Oryzias latipes 96-hour LC_{50} = 18.8 mg/L (nominal) (semi-static test conditions)	ECHA, 2013	Limited study details reported in a secondary source.
	Fish 96-hour LC_{50} = 6.64 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.00	
	Fish 96-hour LC_{50} = 25.58 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid LC_{50}	*Daphnia magna* 48-hour EC_{50} = 12 mg/L (static test conditions)	ECHA, 2013	Limited study details reported in a secondary source.
	Daphnia magna 48-hour EC_{50} = 21 mg/L (static test conditions)	ECHA, 2013	Limited study details reported in a secondary source.
	Daphnid 48-hour LC_{50} = 3.56 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.00	
	Daphnid 48-hour LC_{50} = 16.89 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

D-8 CASRN 95235-30-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae EC_{50}	*Pseudokirchnerella subcapitata* 72-hour EC_{50} = 2.22 mg/L	ECHA, 2013	Limited study details reported in a secondary source.
	Green algae 96-hour EC_{50} = 11.52 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Green algae 96-hour EC_{50} = 14.70 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.00	
Chronic Aquatic Toxicity	**HIGH: Based on estimated ChVs for fish and Daphnid, which are in the range of 0.1-1 mg/L. One experimental study in Daphnia reported a 21-day LC_{50} value of 2.7 mg/L; however, a NOEC was not reported. No chronic aquatic toxicity studies were located for fish or algae.**		
Fish ChV	Fish 30-day ChV = 0.69 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.00	
	Fish 60-day ChV = 2.37 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid ChV	*Daphnia magna* 21-day LC_{50} = 2.7 mg/L (static test conditions) No NOEC reported	ECHA, 2013	Limited study details reported in a secondary source.
	Daphnid 21-day ChV = 0.68 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.00	

D-8 CASRN 95235-30-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Daphnid 21-day ChV = 1.90 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Green Algae ChV		Green algae ChV = 5.11 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
		Green algae ChV = 5.11 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.00	
Earthworm Subchronic Toxicity		Earthworm 14-day LC_{50} = 6.81 mg/L (Estimated) ECOSAR: phenols	ECOSAR version 1.00	
ENVIRONMENTAL FATE				
Transport		**Evaluation of D-8 transport is based entirely on estimations on QSARs for fugacity (level III), disassociation constant (pK_a), soil adsorption coefficient (K_{oc}), volatilization, and vapor pressure. If released to air, an estimated vapor pressure of $<1x10^{-8}$ mm Hg at 25°C indicates that D-8 will exist in the particulate phase in the atmosphere. Particulate-phase D-8 will be removed from the atmosphere by wet or dry deposition. If released to soil, D-8 is expected to have moderate mobility based upon an estimated K_{oc} of 2,500. Volatilization from water surfaces is not expected to be an important fate process based upon this compound's estimated Henry's Law constant.**		
	Henry's Law Constant ($atm\text{-}m^3/mole$)	$<1x10^{-8}$ (Estimated)	EPI	Cutoff value for nonvolatile compounds based on professional judgment.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Sediment/Soil Adsorption/ Desorption Coefficient – K_{oc}	$2.5x10^3$ (Estimated)	EPI	
	Level III Fugacity Model	Air = 0% (Estimated) Water = 11% Soil = 87% Sediment = 2%	EPI	
Persistence		**MODERATE: Based on experimental biodegradation study results that indicate D-8 will undergo aerobic biodegradation in domestic activated sludge. A Dissovled Organic Carbon (DOC) removal test demonstrated 85% degradation of D-8 after 81 days. D-8 was also found to have 31-60% degradation after 39 days in a CO_2 evolution test.**		
Water	**Aerobic Biodegradation**	Days-weeks (primary survey model) Weeks-months (ultimate survey model)	EPI	
		Study results: 31-60%/39 days Test method: CO_2 evolution 10-20 mg/L test material in domestic, activated sludge screening test (Measured)	ECHA, 2013	Nonguideline study reported in a secondary source.
				No data located.
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (anaerobic-methanogenic biodegradation probability model)	EPI	
	Soil Biodegradation w/ Product Identification			No data located.

D-8 CASRN 95235-30-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Sediment/Water Biodegradation	Study results: 85%/81 days Test method: DOC removal 15, 25, 50 mg/L test material in domestic, activated non-adapted sludge simulation test (Measured)	ECHA, 2013	Nonguideline study reported in a secondary source.
Air	**Atmospheric Half-life**	5.3 hours (Estimated)	EPI	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mills, 2000; Professional judgment	The substance does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.
	Hydrolysis	Not a significant fate process (Estimated)	Wolfe and Jeffers, 2000; Professional judgment	The substance does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.
		Reported as the recovery of test substance with no method indicated: >96% to <102% recovery at pH 4.07, 7.1 and 8.92; at 50°C after ≥24 to ≤120 hours (Measured)	ECHA, 2013	Nonguideline study reported in a secondary source with limited details.
	Pyrolysis			No data located.
Environmental Half-life		75 days	EPI; PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**MODERATE: The measured fish BCF values are less than 1000.**		
	Fish BCF	>27-<78 after 28 days >40-<132 after 42 days in Carp (Measured)	ECHA, 2013	Nonguideline study reported in a secondary source.
	BAF	83 (Estimated)	EPI	

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING			
Environmental Monitoring	No data located.		
Ecological Biomonitoring	No data located.		
Human Biomonitoring	This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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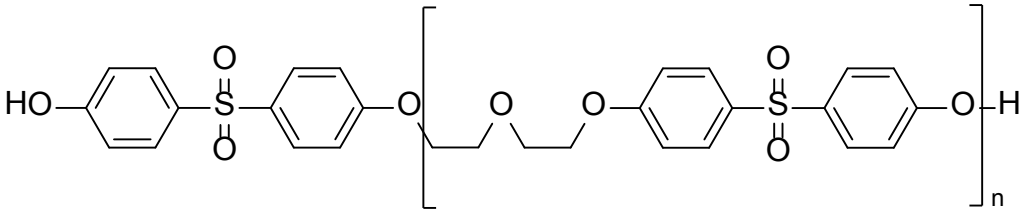
D-90



	CASRN: 191680-83-8
	MW: 570.63 (n = 1) 891.00 (n = 2)
	MF: $C_{28}H_{26}O_9S_2$ (n = 1) $C_{44}H_{42}O_{14}S_3$ (n = 2)
	Physical Forms: **Neat:** Solid
	Use: Developer for thermal paper

SMILES: (n = 1): O=S(C1=CC=C(OCCOCCOC2=CC=C(S(=O)(C3=CC=C(O)C=C3)=O)C=C2)C=C1)(C4=CC=C(O)C=C4)=O
(n = 2): O=S(C1=CC=C(OCCOCCOC2=CC=C(S(=O)(C3=CC=C(OCCOCCOC4=CC=C(S(=O)(C5=CC=C(O)C=C5)=O)C=C4)C=C3)=O)C=C2)C=C1)(C6=CC=C(O)C=C6)=O

Synonyms: Bis(2-chloroethyl)ether-4,4'-dihydroxydiphenyl sulfone copolymer; Ethane, 1,1'-oxybis(2-chloro-, polymer with 4,4'-sulfonylbis(phenol); Phenol, 4,4'-sulfonylbis-, polymer with 1,1'-oxybis(2-chloroethane); 4,4'-Dihydroxydiphenyl sulfone- 2,2'-dichlorodiethyl ether copolymer; 4,4'-Dihydroxydiphenyl sulfone-bis(2-chloroethyl) ether copolymer

Polymeric: Yes
Oligomers: Two representative structures for the low MW oligomers evaluated in this assessment are indicated above (n = 1 or 2). These representative structures are anticipated to be the predominant components of the polymeric mixture.

Metabolites, Degradates and Transformation Products: None identified

Analog: No analogs **Endpoint(s) using analog values:** Not applicable	**Analog Structure:** Not applicable

Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)

Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2011).

Risk Assessments: None identified

D-90 CASRN 191680-83-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)			No data located.
Boiling Point (°C)	>300 (Estimated for n = 1 and n = 2)	EPI; U.S. EPA, 1999	Estimates were performed on representative components of the polymer that have a MW <1,000; those with n = 1 or 2. Higher oligomers are expected to have a similar value. Cutoff value for high boiling point compounds according to HPV assessment guidance.
Vapor Pressure (mm Hg)	$<1x10^{-8}$ (Estimated for n = 1 and n = 2)	EPI; U.S. EPA, 1999	Estimates were performed on representative components of the polymer that have a MW <1,000; those with n = 1 or 2. Higher oligomers are expected to have a similar value. Cutoff value for nonvolatile compounds according to HPV assessment guidance.
Water Solubility (mg/L)	0.54 (n = 1) (Estimated)	EPI	Estimates performed on representative components of the polymer indicated.
	$<1x10^{-3}$ (n = 2) (Estimated)	EPI; U.S. EPA, 1999	Estimates performed on representative components of the polymer indicated. Cutoff value for non-soluble compounds according to HPV assessment guidance.
Log K_{ow}	3.8 (n = 1) (Estimated)	EPI	Estimates performed on representative components of the polymer indicated.
	5.9 (n = 2) (Estimated)	EPI	Estimates performed on representative components of the polymer indicated.

D-90 CASRN 191680-83-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Flammability (Flash Point)				No data located.
Explosivity				No data located.
pH				No data located.
pK_a		6.9-7.5 (Estimated, identical values obtained for both n = 1 and n = 2)	ACD/Labs, 2010	SMILES notation was too long for SPARC estimations, which were used for the other chemicals assessed, and an alternative estimation method was used.
HUMAN HEALTH EFFECTS				
Toxicokinetics		**No data located.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**			No data located.
Acute Mammalian Toxicity		**LOW: D-90 was not toxic following acute exposure, based on the acute oral and dermal LC_{50} values of >2,000 mg/kg-bw in rats.**		
Acute Lethality	**Oral**	Rat (Sprague-Dawley CD) oral LD_{50} >2,000 mg/kg bw; no mortalities or signs of systemic toxicity at the highest dose tested (2,000 mg/kg bw).	Submitted confidential study	Adequate; guideline study (OECD 401).
	Dermal	Rat (Sprague-Dawley CD) dermal LD_{50} >2,000 mg/kg bw; no mortalities or signs of systemic toxicity at the highest dose tested (2,000 mg/kg bw).	Submitted confidential study	Adequate; guideline study (OECD 402).
	Inhalation			No data located.
Carcinogenicity		**MODERATE: There is uncertainty due to the lack of data for this substance. Carcinogenic effects cannot be ruled out.**		
	OncoLogic Results			No data located.

D-90 CASRN 191680-83-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
Genotoxicity		**LOW: D-90 does not cause mutations in bacterial cells *in vitro* and is not clastogenic in human lymphocytes *in vitro*.**		
	Gene Mutation *in vitro*	Negative, reverse mutation assay in *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537 and *Escherichia coli* WP2 uvrA with and without metabolic activation.	Submitted confidential study	Adequate; non-standard guideline study (Japanese guideline for mutagenicity tests using microorganisms).
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Non-clastogenic, chromosome aberrations test in human lymphocytes with and without activation.	Submitted confidential study	Adequate; guideline study (OECD 473).
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.
	Other (Mitotic Gene Conversion)			No data located.
Reproductive Toxicity		**LOW: A combination of limited predicted absorption, low predicted metabolism, and lack of significant toxicological concerns from repeated dose testing suggests low potential for reproductive effects based on professional judgment.**		
	Reproduction/ Developmental Toxicity Screen	Low potential for reproductive toxicity (Estimated)	Professional judgment	Estimated based on predicted limited absorption, low metabolism, lack of evidence from repeated dose studies.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction and Fertility Effects			No data located.
Developmental Toxicity		**LOW: A combination of limited predicted absorption, low predicted metabolism, and lack of significant toxicological concerns from repeated dose testing suggests low potential for developmental effects based on professional judgment.**		
	Reproduction/ Developmental Toxicity Screen	Low potential for developmental toxicity (Estimated)	Professional judgment	Estimated based on predicted limited absorption, low metabolism, lack of evidence from repeated dose studies.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert. (Estimated)	U.S. EPA, 2010, Professional judgment	Estimated based on structural alert.

D-90 CASRN 191680-83-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects		**LOW: D-90 did not cause mortality or systemic effects at oral doses as high as 1,000 mg/kg-day in a 28-day repeated-dose toxicity study in rats.**		
		No adverse effects (e.g., mortality; clinical signs; and changes in body weights, food consumption, urinalysis data, hematology data, gross pathology, organ weights, organ-to-body weight ratios or histopathology) were observed in a 28-day oral (gavage) study in male and female Fischer 344 rats; increases in y-glutamyl transpeptidase was observed in females exposed to 300 and 1,000 mg/kg-bw-day, which did not correspond to histopathological effects. NOEL = 1,000 mg/kg-bw-day (highest dose tested)	Submitted confidential study	Adequate; not specified as a guideline study, but follows general OECD guidelines.
Skin Sensitization		**LOW: D-90 was not a skin sensitizer in one study of guinea pigs.**		
	Skin Sensitization	Negative for skin sensitization, Dunkin Hartley guinea pigs	Submitted confidential study	Adequate; guideline study (OECD 406).
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**MODERATE: Iridial inflammation and moderate conjunctival irritation were observed up to the 48- or 72-hour observation in one study of rabbits.**		
	Eye Irritation	Irritant (maximum group mean score: 13), iridial inflammation and moderate conjunctival irritation, treated eyes appeared normal at the 48- or 72-hour observation, New Zealand White rabbits	Submitted confidential study	Adequate; guideline study (OECD 405).
Dermal Irritation		**VERY LOW: D-90 was not a dermal irritant in one study of rabbits.**		
	Dermal Irritation	Non-irritant (primary irritation index: 0), New Zealand White rabbits	Submitted confidential study	Adequate; guideline study (OECD 404).

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Endocrine Activity		**No data located.**		
				No data located.
Immunotoxicity		**No data located.**		
	Immune System Effects			No data located.
ECOTOXICITY				
ECOSAR Class		Phenols, poly		
Acute Toxicity		**LOW: Based on estimated 96-hour LC_{50} for fish, 48-hour LC_{50} for Daphnid, and 96-hour EC_{50} for green algae that result in no effects at saturation (NES), as obtained for representative components of the polymer that have a MW <1,000. Higher MW components of the polymer are expected to have similar behavior.**		
Fish LC_{50}		Fish 96-hour LC_{50} = 4.76 mg/L (n = 1) (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.11	NES for representative component of the polymer with a MW <1,000.
		Fish 96-hour LC_{50} = 0.31 mg/L (n = 2) (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	NES for representative component of the polymer with a MW <1,000. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

D-90 CASRN 191680-83-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid LC_{50}	Daphnid 48-hour LC_{50} = 9.46 mg/L (n = 1) (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	NES for representative component of the polymer with a MW <1,000. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid 48-hour LC_{50} = 0.29 mg/L (n = 2) (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	NES for representative component of the polymer with a MW <1,000. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Green Algae EC_{50}	Green algae 96-hour EC_{50} = 3.36 mg/L (n = 1) (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.11	NES for representative component of the polymer with a MW <1,000.
	Green algae 96-hour EC_{50} = 0.63 mg/L (n = 2) (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.11	NES for representative component of the polymer with a MW <1,000.
Chronic Aquatic Toxicity	**LOW: Based on ChV values for fish, Daphnid, and green algae that result in no effects at saturation (NES), as obtained for representative components of the polymer that have a MW <1,000. Higher MW components of the polymer are expected to have similar behavior.**		
Fish ChV	Fish 30-day ChV = 1.08 mg/L (n = 1) (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.11	NES for representative component of the polymer with a MW <1,000.

D-90 CASRN 191680-83-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Fish 30-day ChV = 0.027 mg/L (n = 2) (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	NES for representative component of the polymer with a MW <1,000 Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis..
Daphnid ChV	Daphnid ChV = 1.20 mg/L (n = 1) (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	NES for representative component of the polymer with a MW <1,000. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid ChV = 0.054 mg/L (n = 2) (Estimated) ECOSAR: neutral organics	ECOSAR version 1.11	NES for representative component of the polymer with a MW <1,000. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Green Algae ChV	Green algae ChV = 0.51 mg/L (n = 1) (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.11	NES for representative component of the polymer with a MW <1,000.

D-90 CASRN 191680-83-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Green algae ChV = 0.206 mg/L (n = 2) (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.11	NES for representative component of the polymer with a MW <1,000.
ENVIRONMENTAL FATE				
Transport		**Evaluation of D-90 transport is based entirely on estimations on QSARs that were performed on two representative components of the polymer (n = 1 and n = 2) that are a MW <1,000, although the higher MW oligomers are anticipated to behave similarly. These representative structures are anticipated to be the predominate components of the polymeric mixture. D-90 is expected to have low mobility in soil based on its expected strong absorption to soil. If released to the atmosphere, D-90 is likely to exist solely as particulate. As a particulate, atmospheric oxidation is not expected to be a significant route of environmental removal. Level III fugacity models indicate that D-90 will partition predominantly to the soil and sediment.**		
	Henry's Law Constant (atm-m^3/mole)	<$1x10^{-8}$ (Estimated for n = 1 and n = 2)	Professional judgment; EPI	Estimates were performed on representative components of the polymer that have a MW <1,000; those with n = 1 or 2. Higher oligomers are expected to have a similar value. Cutoff value for nonvolatile compounds based on professional judgment.
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	>30,000 (Estimated for n = 1 and n = 2)	EPI; U.S. EPA, 2004	Estimates were performed on representative components of the polymer that have a MW <1,000; those with n = 1 or 2. Higher oligomers are expected to have a similar value. Cutoff value for nonmobile compounds.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Level III Fugacity Estimations	Estimated for n = 1: Air = 0% Water = 3% Soil = 57% Sediment = 40%	EPI	Estimates performed on representative components of the polymer indicated.
		Estimated for n = 2: Air = 0% Water = 1% Soil = 52% Sediment = 48%	EPI	Estimates performed on representative components of the polymer indicated.
Persistence		**VERY HIGH: Evaluation of D-90 persistence is based entirely on estimations that were performed on two representative components of the polymer (n = 1 and n = 2) that have a MW <1,000 and are anticipated to be the predominant component of the polymeric mixture. Primary aerobic degradation was estimated to be in the order of weeks for both representative structures. Ultimate biodegradation was estimated to be in the order of months for the n = 1 polymer, and the n = 2 polymer was estimated to be recalcitrant. Estimated volatilization half-lives of >1 year for both representative structures indicate that volatilization is not expected to occur. D-90 does not contain functional groups that absorb light at environmentally-relevant wavelengths, and is not expected to be susceptible to direct photolysis. Atmospheric hydroxyl-radical photooxidation half-lives were estimated to be 2.5 and 1.4 hours, respectively. However, this is not expected to be an important removal process since D-90 is expected to exist in the particulate phase in the atmosphere. Higher MW components of the polymer are expected to have similar persistence behavior.**		
Water	**Aerobic Biodegradation**	Weeks (primary survey model; n = 1) Months (ultimate survey model; n = 1) Weeks (primary survey model; n = 2) Recalcitrant (ultimate survey model; n = 2)	EPI	Estimates performed on representative components of the polymer indicated.
	Volatilization Half-life for Model River	>1 year (Estimated for n = 1 and n = 2)	EPI	Estimates performed on representative components of the polymer indicated.

D-90 CASRN 191680-83-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Volatilization Half-life for Model Lake	>1 year (Estimated for n = 1 and n = 2)	EPI	Estimates performed on representative components of the polymer indicated.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (anaerobic-methanogenic biodegradation probability model; for n = 1 and n = 2)	EPI	Estimates performed on representative components of the polymer that have a MW <1,000; those with n = 1 or 2; higher oligomers are expected to have a similar value.
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	2.5 hours (Estimated for n = 1 for hydroxyl radical reaction assuming a 12-hour day and a hydroxyl radical concentration of $1.5x10^6$ OH/cm^3); 1.4 hours (Estimated for n = 2 for hydroxyl radical reaction assuming a 12-hour day and a hydroxyl radical concentration of $1.5x10^6$ OH/cm^3)	EPI	Estimates performed on representative components of the polymer that have a MW <1,000; those with n = 1 or 2; higher oligomers are expected to have a similar value.
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	Substance does not contain functional groups that would be expected to absorb light at wavelengths >290 nm.
	Hydrolysis	Not a significant fate process (Estimated)	Wolfe and Jeffers, 2000; Professional judgment	Substance does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.
	Pyrolysis			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Environmental Half-life		120 days in soil 540 days in sediment (Estimated for n =1) 360 days in soil; 1,600 days in sediment (Estimated for n = 2)	EPI; PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology; estimates were performed on representative components of the polymer indicated.
Bioaccumulation		**HIGH: The estimated BAF value for the low MW oligomers with n = 2 is >1,000, indicating that this component has the potential to bioaccumulate.**		
	Fish BCF	149 (n = 1) (Estimated)	EPI	Estimates performed on representative components of the polymer indicated.
		166 (n = 2) (Estimated)	EPI	Estimates performed on representative components of the polymer indicated.
	BAF	163 (n = 1) (Estimated)	EPI	Estimates performed on representative components of the polymer indicated.
		4,270 (n = 2) (Estimated)	EPI	Estimates performed on representative components of the polymer indicated.
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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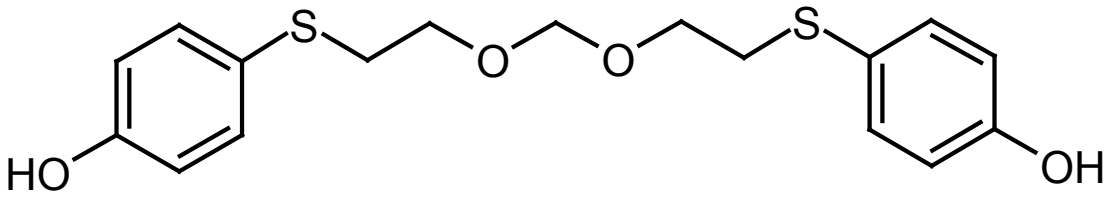
DD-70



	CASRN: 93589-69-6
	MW: 352.5
	MF: $C_{17}H_{20}O_4S_2$
	Physical Forms: **Neat:** Solid
	Use: Developer for thermal paper
SMILES: Oc1ccc(cc1)SCCOCOCCSc2ccc(cc2)O	
Synonyms: Phenol, 4,4'-(methylenebis(oxy-2,1-ethanediylthio))bis-	
Polymeric: No **Oligomers:** Not applicable	
Metabolites, Degradates and Transformation Products: None identified	
Analog: Confidential analog (structure not available) **Endpoint(s) using analog values:** Developmental toxicity, repeated dose toxicity, skin sensitization, and skin and eye irritation.	**Analog Structure:** Not applicable
Structural Alerts: Phenols, neurotoxicity (U.S. EPA, 2010)	
Risk Phrases: 51/53 - Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (ESIS, 2011).	
Risk Assessments: None identified	

DD-70 CASRN 93589-69-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	108 (Measured)	Submitted confidential study	Adequate.
Boiling Point (°C)	>350 (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for high boiling compounds according to HPV assessment guidance.
Vapor Pressure (mm Hg)	$<1x10^{-8}$ (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for nonvolatile compounds according to HPV assessment guidance.
Water Solubility (g/L)	0.13 (Estimated)	EPI	
Log K_{ow}	3.4 (Estimated)	EPI	
Flammability (Flash Point)			No data located.
Explosivity			No data located.
pH			No data located.
pK_a	9.6 (Estimated)	SPARC	

DD-70 CASRN 93589-69-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**DD-70, as a neat material, is estimated to not be absorbed through the skin and have poor skin absorption when in solution. DD-70 is expected to be poorly absorbed via the lungs and gastrointestinal tract.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Not absorbed through the skin as neat material and has poor absorption in solution. Poorly absorbed through the lung and gastrointestinal tract (Estimated by analogy)	Professional judgment	Based on closely related confidential analog with similar structure, functional groups, and physical/chemical properties.
Acute Mammalian Toxicity		**LOW: Acute mammalian toxicity is estimated for DD-70 based on high MW, lack of absorption, and the absence of structural alerts.**		
Acute Lethality	**Oral**	Low potential for acute mammalian toxicity (Estimated)	Professional judgment	Estimated based on professional judgment.
	Dermal			No data located.
	Inhalation			No data located.
Carcinogenicity		**MODERATE: Estimated using OncoLogic expert system, which describes a concern for this compound as a potential carcinogen or tumorigenesis promoter arising from its structural similarity to estrogenic/androgenic compounds, using the "phenols and phenolic compounds" structural alert**.		
	OncoLogic Results	Moderate (Estimated) OncoLogic class: phenols and phenolic compounds	OncoLogic	OncoLogic SAR analysis using the phenols and phenolic compounds class.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data
Genotoxicity		**LOW: Based on professional judgment, the absence of structural alerts suggests lower concern.**		
	Gene Mutation *in vitro*	Low potential for genotoxicity toxicity (Estimated)	Professional judgment	Estimated based on professional judgment.
	Gene Mutation *in vivo*			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Chromosomal Aberrations *in vitro*			No data located.
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.
	Other (Mitotic Gene Conversion)			No data located.
Reproductive Effects		**MODERATE: There are no data and no appropriate analog for this endpoint, however an analog for DD-70 is toxicologically active in repeated dose and developmental toxicity studies. Based on professional judgment, potential reproductive toxicity cannot be ruled out.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects			No data located.
Developmental Effects		**MODERATE: Based on confidential analog. Unspecified effects occurred at a dose of 100 mg/kg-day in a developmental study in rats.**		
	Developmental Toxicity Screen	Rabbit, oral, developmental study NOAEL = 300 mg/kg-day (Estimated by analogy)	Professional judgment	Estimated based on available test data for a confidential analog.
		Rat, oral, developmental study LOAEL = 100 mg/kg-day (NOAEL not established) (Estimated by analogy)	Professional judgment	Estimated based on available test data for a confidential analog.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on the presence of the phenol structural alert.**		
	Neurotoxicity Screening Battery (Adult)	There is potential for neurotoxicity effects based on the presence of the phenol structural alert. (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on structural alert.
Repeated Dose Effects		**MODERATE: Based on a confidential analog. Repeated dose effects including blood toxicity, severe gastrointestinal irritation and histopathological changes to the glandular stomach occurred at doses >50 mg/kg-day. Because the LOAEL is not specified, there is uncertainty as to the dose at which these effects occur. Using a conservative approach in the absence of a specified LOAEL, a Moderate hazard concern is selected because it is possible that effects can occur at doses between 50 and 100 mg/kg-day.**		
		Rat, 13-week oral exposure Blood toxicity, severe gastrointestinal irritation, histopathogical changes in the glandular stomach NOAEL = 50 mg/kg-day LOAEL = not identified (Estimated by analogy)	Professional judgment	Estimated based on available test data for a confidential analog.
Skin Sensitization		**MODERATE: Based on confidential analog. DD-70 may potentially cause dermal sensitization.**		
	Skin Sensitization	Positive for dermal sensitization in guinea pigs (Estimated by analogy)	Professional judgment	Estimated based on available test data for a confidential analog.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**HIGH: Based on confidential analog. DD-70 may potentially cause corrosion to eyes.**		
	Eye Irritation	Concern for potential corrosion to mucous membranes and eyes (Estimated by analogy)	Professional judgment	Estimated based on available test data for a confidential analog.
Dermal Irritation		**MODERATE: Based on confidential analog. DD-70 may have the potential to cause dermal irritation.**		
	Dermal Irritation	Concern for dermal irritation (Estimated by analogy)	Professional judgment	Estimated based on available test data for a confidential analog.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Endocrine Activity	**No data located.**		
			No data located.
Immunotoxicity	**No data located.**		
Immune System Effects			No data located.
ECOTOXICITY			
ECOSAR Class	Phenols, poly		
Acute Toxicity	**HIGH: Based on estimated 96-hour LC_{50} value for fish and 96-hour EC_{50} value for green algae that are in the range of 1-10 mg/L.**		
Fish LC_{50}	Fish 96-hour LC_{50} = 5.39 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
	Fish 96-hour LC_{50} = 19.6 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid LC_{50}	Daphnia 48-hour LC_{50} = 13.30 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnia 48-hour LC_{50} = 13.6 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
Green Algae EC_{50}	Green algae 96-hour EC_{50} = 2.28 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Green algae 96-hour EC_{50} = 9.98 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Chronic Aquatic Toxicity	**HIGH: Based on an estimated ChV of 0.42 mg/L for green algae.**		
Fish ChV	Fish 30-day ChV = 1.33 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
	Fish ChV = 1.80 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid ChV	Daphnid ChV = 1.56 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid ChV = 4.68 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	
Green Algae ChV	Green algae ChV = 0.422 mg/L (Estimated) ECOSAR: phenols, poly	ECOSAR version 1.00	

DD-70 CASRN 93589-69-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Green algae ChV = 4.62 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
ENVIRONMENTAL FATE				
Transport		**Based on the Level III fugacity models incorporating the available experimental property data, DD-70 is expected to partition primarily to soil. DD-70 is expected to exist in both neutral and anionic forms at environmentally-relevant pH, based on its estimated pK_a. The neutral form of DD-70 is expected to be immobile in soil based on its estimated K_{oc}. The anionic form may be more mobile, as anions do not bind as strongly to organic carbon and clay as their neutral counterparts. However, leaching of DD-70 through soil to groundwater is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that it will be nonvolatile from surface water. Volatilization from dry surface is also not expected based on its estimated vapor pressure. In the atmosphere, DD-70 is expected to exist solely in the particulate phase, based on its estimated vapor pressure. Particulates may be removed from air by wet or dry deposition.**		
	Henry's Law Constant ($atm\text{-}m^3/mole$)	$<1x10^{-10}$ (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for nonvolatile compounds according to HPV assessment guidance.
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	$3.3x10^4$ (Estimated)	EPI	
	Level III Fugacity Model	Air = <1% (Estimated) Water = 8.6% Soil = 75% Sediment = 16%	EPI	

DD-70 CASRN 93589-69-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**HIGH: Evaluation of the persistence of DD-70 is based entirely on QSARs for aerobic and anaerobic biodegradation. Results from these models estimate primary biodegradation in days-weeks and ultimate degradation in weeks-months. DD-70 is expected to partition primarily to soil; the half-life is estimated as 75 days. Biodegradation under anaerobic methanogenic conditions is not probable. DD-70 is not expected to undergo hydrolysis since it does not contain hydrolyzable functional groups. DD-70 does not contain chromophores that absorb at wavelengths >290 nm, and therefore, it is not expected to be susceptible to direct photolysis by sunlight. The vapor phase reaction of DD-70 with atmospheric hydroxyl radicals is estimated at 1.2 hours, although it is expected to exist primarily in the particulate phase in air. Considerations of all these factors indicate that the persistence concern is High for DD-70.**		
Water	**Aerobic Biodegradation**	Days-weeks (primary survey model) Weeks-months (ultimate survey model)	EPI	
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (anaerobic-methanogenic biodegradation probability model)	EPI	
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	1.2 hours (Estimated)	EPI	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	Substance does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.
	Hydrolysis	Not a significant fate process (Estimated)	Wolfe and Jeffers, 2000; Professional judgment	Substance does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.

DD-70 CASRN 93589-69-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Pyrolysis			No data located.
Environmental Half-life		75 days (Estimated)	EPI, PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**LOW: The estimated BCF for fish is less than the low criteria cutoff of 100. In addition, the estimated BAF of 35, which accounts for metabolism, suggests that DD-70 will not bioaccumulate in higher trophic levels.**		
	Fish BCF	75 (Estimated)	EPI	
	BAF	35 (Estimated)	EPI	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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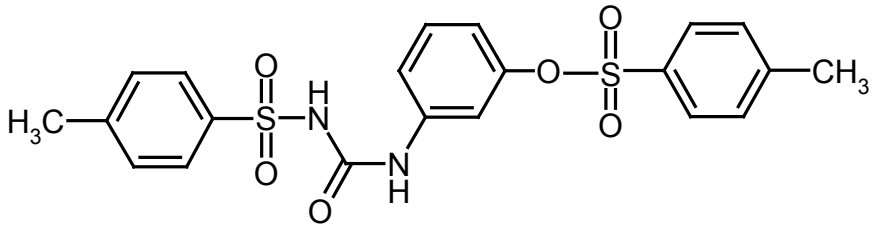
Pergafast 201



	CASRN: 232938-43-1
	MW: 460.5
	MF: $C_{21}H_{20}N_2O_6S_2$
	Physical Forms: **Neat:** Solid
	Use: Developer for thermal paper

SMILES: O=S(=O)(Oc1cccc(c1)NC(=O)NS(=O)(=O)c2ccc(C)cc2)c3ccc(C)cc3

Synonyms: Benzenesulfonamide, 4-Methyl-N-(((3-(((4-Methylphenyl)Sulfonyl)Oxy)Phenyl)Amino)Carbonyl)-;
N-(P-Toluenesulfonyl)-N'-(3-P-Toluenesulfonyloxyphenyl)Urea;
N-(4-Methylphenylsulfonyl)-N'-(3-(4-Methylphenylsulfonyloxy)Phenyl)Urea; N-P-Tolylsulfonyl-N'-3-(P-Tolylsulfonyloxy)Phenylurea;
Pergafast 201; PF 201

Polymeric: No
Oligomers: Not applicable

Metabolites, Degradates and Transformation Products: None identified

Analog: No **Endpoint(s) using analog values:** Not applicable	**Analog Structure:** Not applicable

Structural Alerts: Sulfonamides, photoreactions; Alkyl esters of sulfonic acids, toxicity caused by electrophiles (U.S. EPA, 2010)

Risk Phrases: 51/53 - Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (ESIS, 2011).

Risk Assessments: Risk assessment completed for Pergafast 201 by the Australian Department of Health and Ageing in 2004 (NICNAS, 2004).

Pergafast 201 CASRN 232938-43-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES				
Melting Point (°C)		157.7 (Measured)	NICNAS, 2004	Adequate; selected value.
		>155 (Measured)	BASF, 2010	Adequate; measured by chemical supplier.
Boiling Point (°C)		Decomposes at 250 (Measured)	NICNAS, 2004	Adequate.
Vapor Pressure (mm Hg)		$<1x10^{-8}$ (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for nonvolatile compounds according to HPV assessment guidance.
Water Solubility (mg/L)		35 (Measured)	NICNAS, 2004	Adequate; selected value.
		35 at 20 °C(Measured)	BASF, 2010	Adequate; measured by chemical supplier.
Log K_{ow}		2.6 (Measured)	NICNAS, 2004	Adequate.
Flammability (Flash Point)		Not highly flammable; not auto-flammable (Measured)	NICNAS, 2004	Adequate.
Explosivity		Non-explosive either by thermal or mechanical (shock and friction) stress. (Measured)	NICNAS, 2004	Adequate.
pH				No data located.
pK_a		pKa_1 = 12.5 pKa_2 = 5.3 pKa_3 = -3.8 pKa_4 = -13.6 (Estimated)	SPARC	
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Pergafast 201 is not estimated to be absorbed through the skin as the neat material and has poor absorption through the skin if in solution. Furthermore, Pergafast 201 has poor absorption from the lungs and gastrointestinal tract.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Not absorbed through the skin as the neat material poor absorption through the skin if in solution; poor absorption from the lungs and gastrointestinal tract.	Professional judgment	Based on closely related confidential analog with similar structure, functional groups, and physical/chemical properties.
Acute Mammalian Toxicity		**LOW: Based on acute oral and dermal LD_{50} values >2,000 mg/kg. No data were located regarding the acute inhalation hazard.**		

Pergafast 201 CASRN 232938-43-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Lethality	**Oral**	Rat oral LD_{50} >2,000 mg/kg	NICNAS, 2004	Adequate.
	Dermal	Rat dermal LD_{50} >2,000 mg/kg	NICNAS, 2004	Adequate.
	Inhalation			No data located.
Carcinogenicity		**MODERATE: There is uncertainty due to the lack of data for this substance. Carcinogenic effects cannot be ruled out.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
Genotoxicity		**LOW: Pergafast 201 did not cause gene mutations *in vitro* or chromosomal aberrations *in vivo*. Pergafast 201 did induce chromosomal aberrations in Chinese hamster V79 cells *in vitro*, but only at cytotoxic concentrations.**		
	Gene Mutation *in vitro*	Negative, Ames assay of *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and *Escherichia coli* WP2 uvrA both with and without metabolic activation	NICNAS, 2004	Adequate.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Positive, chromosomal aberrations in Chinese hamster V79 cells at cytotoxic concentrations	NICNAS, 2004	Adequate.
	Chromosomal Aberrations *in vivo*	Negative, *in vivo* micronucleus test in mouse, gavage exposure	NICNAS, 2004	Adequate.
	DNA Damage and Repair			No data located.
	Other			No data located.
Reproductive Effects		**MODERATE: There was a decrease in implantation sites in dams receiving 200 mg/kg, the highest dose tested, but the decrease was not statistically significant. Since significant reproductive toxicity cannot be ruled out at doses between 200 and 250 mg/kg, the hazard designation is Moderate.**		

Pergafast 201 CASRN 232938-43-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction/ Developmental Toxicity Screen	Rat, oral gavage; Males exposed for 29 days pre-mating, during mating, and up to sacrifice; Females exposed 42-46 days (2 weeks pre-mating, during mating, during post-coitum, up to LD 4. No statistically significant reproductive effects were observed, although there was a decrease in implantation sites in dams at 200 mg/kg, the highest dose tested. NOAEL (maternal toxicity): 50 mg/kg bw-day LOAEL (maternal toxicity): 100 mg/kg bw-day (hematology and accentuated lobular pattern of the liver) NOAEL (reproductive toxicity): >200 mg/kg (highest dose tested)	Submitted confidential study	Adequate; according to OECD guideline 421.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects			No data located.
Developmental Effects		**MODERATE: Rats orally exposed during mating, gestation, and lactation resulted in decreased pup body weight on days 1 & 4. There was a decrease in pup weights, compared to the control, at all doses, but taking into consideration the confounding of litter size, the NOAEL was determined to be 50 mg/kg-bw/day.**		
	Reproduction/ Developmental Toxicity	Rat, oral gavage; 0, 50, 100 or 200 mg/kg-bw/day:	Submitted confidential study	Adequate; according to OECD guideline 421.

Pergafast 201 CASRN 232938-43-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Screen	Males exposed for 29 days pre-mating, during mating, and up to sacrifice; Females exposed 42-46 days (2 weeks pre-mating, during mating, during post-coitum, up to lactation day 4. There was a significant decrease in pup body weight; on day 1, the significant decrease was seen in males, only at the highest dose, while in females, significant decreases were seen at all treatment levels. On day 4, significant decreases were observed in males and females at the highest dose. NOAEL (maternal toxicity): 50 mg/kg bw/day LOAEL (maternal toxicity): 100 mg/kg bw/day (accentuated lobular pattern of the liver, increased liver to body weight ratio) NOAEL (developmental toxicity): 50 mg/kg bw/day LOAEL (developmental toxicity): 100 mg/kg bw/day (decreased pup weights, days 1 & 4)		
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
Neurotoxicity		**LOW: No structural alerts or mechanistic pathways associated with neurotoxic effect identified.**		

Pergafast 201 CASRN 232938-43-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Neurotoxicity Screening Battery (Adult)	Low potential for neurotoxicity effects. (Estimated)	Professional judgment	Estimated based on no identified structural alerts or mechanistic pathways associated with neurotoxicity.
Repeated Dose Effects		**MODERATE: A 90-day study identified a LOAEL of 50 mg/kg bw-day and a NOAEL of 25 mg/kg bw-day; due to effects on the liver of female rats therefore a Moderate hazard designation is selected.**		
		28-Day repeated-dose study, rat, oral gavage, salivation, indications of hemolytic anemia, increased liver and kidney weights, microscopic changes including minimal hypertrophy of ventrilobular hepatocytes in liver of males and females and extramedullary haemopoiesis in spleen of females. NOAEL = 30 mg/kg bw-day, LOAEL = 150 mg/kg bw-day	NICNAS, 2004	Adequate.
		90-Day repeated-dose study, rat, oral gavage; Changes in hematology parameters and increased extramedullary hematopoiesis, increased absolute and relative organ weights with histopathological correlation in the liver; histopathological changes in spleen and adrenal glands. NOAEL = 25 mg/kg bw-day (increased liver weights and liver histopathological changes in females) LOAEL = 50 mg/kg bw-day NOAEL = 50 mg/kg bw-day (increased globulin B and liver hypertrophy in males) LOAEL = 150 mg/kg bw-day	Submitted confidential study	Adequate; according to OECD guideline 408.

Pergafast 201 CASRN 232938-43-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		5-Day range finding study, rat, oral gavage; decreased mean daily food consumption (male and female), decreased body weight gain (females), decreased absolute and relative thymus weights (males), increased absolute and relative liver weight (male and female). LOAEL = 200 mg/kg bw-day (lowest dose tested)	Submitted confidential study	Adequate.
Skin Sensitization		**LOW: Pergafast 201 did not appear to be a skin sensitizer in guinea pigs.**		
	Skin Sensitization	Skin irritation was observed in 1/10 guinea pigs at 24 hours (but not at 48 hours) following induction and subsequent challenge. The severity of the response was not described in the available source.	NICNAS, 2004	Inadequate; limited study details.
		Non-sensitizing, Guinea pig	BASF, 2010	Valid.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No located.
Eye Irritation		**LOW: Pergafast 201 was slightly irritating to rabbit eyes.**		
	Eye Irritation	Slightly irritating, rabbits	NICNAS, 2004	Adequate.
		Non-irritating, rabbits	BASF, 2010	Valid.
Dermal Irritation		**VERY LOW: Pergafast 201 was not irritating to rabbit skin.**		
	Dermal Irritation	Non-irritating, rabbits	NICNAS, 2004	Adequate.
Endocrine Activity		**A single study showed Pergafast 201 to be non-estrogenic with a relative potency substantially low compared to 17-beta-estradiol.**		

Pergafast 201 CASRN 232938-43-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Negative for estrogenic activity; Increased luciferase activity in a human estrogen receptor-α transcriptional activation assay. Relative potency was estimated to be about 10^7 times less than estrogen.	Submitted confidential study	Adequate; similar to OECD guideline 455.
Immunotoxicity		**There is uncertain concern for immunotoxicity based on effects to the spleen and adrenal glands.**		
	Immune System Effects	90-day repeated-dose study, rat, oral gavage; changes in spleen and adrenal glands. NOAEL = 25 mg/kg bw-day LOAEL = 150 mg/kg bw-day	Submitted confidential study	Adequate; according to OECD guideline 408.
ECOTOXICITY				
ECOSAR Class		Esters, Amides, Sulfonyl ureas		
Acute Aquatic Toxicity		**HIGH: Based on the 72-hour EC_{50} of 3 mg/L (nominal) for decreased growth rate in green algae. The level of concern for green algae varies from Moderate to Very High based on metric. The 96-hour assay using zebrafish and the 48-hour assay using Daphnids both yielded threshold results in the Low to Moderate range.**		
Fish LC_{50}		Zebra fish 96-hour LC_{50} >63 mg/L, NOEC = 63 mg/L (Experimental)	NICNAS, 2004	Chemical may not be soluble enough to measure this effect; LC_{50} value exceeds water solubility.
		Brachydanio rerio 96-hour LC50 ≥100 mg/L (Experimental)	BASF, 2010	Chemical may not be soluble enough to measure this effect; LC_{50} value exceeds water solubility.
		Fish 96-hour LC_{50} = 19.88 mg/L (Estimated) ECOSAR: amides	ECOSAR version 1.00	
		Fish 96-hour LC_{50} = 28.42 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Fish 96-hour LC_{50} = 110.21 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Chemical may not be soluble enough to measure this predicted effect; LC_{50} value exceeds water solubility. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid LC_{50}	*Daphnia magna* 48-hour EC_{50} = 57 mg/L (Experimental)	NICNAS, 2004	Inadequate (OECD 202). Chemical may not be soluble enough to measure this effect; EC_{50} value exceeds water solubility.
	Daphnid 48-hour LC_{50} = 13.78 mg/L (Estimated) ECOSAR: amides	ECOSAR version 1.00	
	Daphnid 48-hour LC_{50} = 54.07 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	Chemical may not be soluble enough to measure this predicted effect; LC_{50} value exceeds water solubility.
	Daphnid 48-hour LC_{50} = 40.69 mg/L (Estimated) ECOSAR: Sulfonyl ureas	ECOSAR version 1.00	Chemical may not be soluble enough to measure this predicted effect; LC_{50} value exceeds water solubility.
	Daphnid 48-hour LC_{50} = 68.38 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	
Saltwater Invertebrate LC_{50}	Mysid shrimp 96-hour LC_{50} = 29.89 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	

Pergafast 201 CASRN 232938-43-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae EC_{50}	*Scenedesmus subspicatus* 72-hour EC_{50} = 0.77 mg/L (nominal) (biomass); 72-hour EC_{50} = 3 mg/L (nominal) (growth rate) (Experimental)	NICNAS, 2004; Submitted confidential study	Adequate; OECD 201.
	Scenedesmus subspicatus 72-hour EC_{50} = 1.3 mg/L (nominal) (biomass); 72-hour EC_{50} = 3.2 mg/L (nominal) (growth rate) Static conditions (Experimental)	Submitted confidential study	Adequate; OECD 201.
	Scenedesmus subspicatus 96-hour EC_{50} = 6.3 mg/L (nominal) (biomass); 96-hour EC_{50} >10 mg/L (nominal) (growth rate) Static conditions (Experimental)	Submitted confidential study	Addition of sediment is not appropriate for this chemical class.
	Scenedesmus subspicatus; static conditions in the presence of sediment 96-hour EC_{50} = 5 mg/L (biomass) 96-hour EC_{50} = 7.4 mg/L (growth rate) 96-hour NOEC = 1.6 mg/L 96-hour LOEC = 3.6 mg/L 96-hour ChV = 2.4 mg/L (Experimental)	Submitted confidential study	Addition of sediment is not appropriate for this chemical class.
	Green algae 96-hour EC_{50} = 21.60 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	

Pergafast 201 CASRN 232938-43-1			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Green algae 96-hour EC_{50} = 0.69 mg/L (Estimated) ECOSAR: amides	ECOSAR version 1.00	
	Green algae 96-hour EC_{50} = 0.05 mg/L (Estimated) ECOSAR: sulfonyl ureas	ECOSAR version 1.00	
	Green algae 96-hour EC_{50} = 37.71 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Chemical may not be soluble enough to measure this predicted effect; EC_{50} value exceeds water solubility. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Chronic Aquatic Toxicity	**HIGH: Based on the 72-hour toxicity test using green algae (*Scenedesmus subspicatus*), which yielded a chronic toxicity value of 0.270 mg/L. Results for fish and Daphnid range from Low to High.**		
Fish ChV	*Pimephales promelas*, flow through conditions. 32-day NOEC ≥ 0.89 mg/L (highest dose tested) (Experimental)	Submitted confidential study	Adequate; EPA OPPTS 850.1400 guidelines; LOEC not identified.
	Fish ChV = 0.12 mg/L (Estimated) ECOSAR: amides	ECOSAR version 1.00	
	Fish 32/33-day ChV = 2.21 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Fish ChV = 10.32 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid ChV	*Daphnia magna* 21-day EC_{50} = 21 mg/L (Experimental)	NICNAS, 2004	Adequate; LOEC not identified.
	Daphnid ChV = 0.18 mg/L (Estimated) ECOSAR: amides	ECOSAR version 1.00	
	Daphnid 21-day ChV = 29.23 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
	Daphnid ChV = 4.11 mg/L (Estimated) ECOSAR: sulfonyl ureas	ECOSAR version 1.00	
	Daphnid ChV = 7.02 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnia magna 21-day NOEC = 10.2 mg/L (Experimental)	BASF, 2010	Valid; LOEC not identified.
	Daphnia Magna; semi-static conditions; 21-day NOEC = 10.2 mg/L 21-day LOEC = 34.5 mg/L (for immobilization) (Experimental)	Submitted confidential study	Adequate; OECD 211; Chemical may not be soluble enough to measure this predicted effect; LOEC value is at the level of water solubility.

Pergafast 201 CASRN 232938-43-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Saltwater Invertebrate ChV		Mysid shrimp ChV = 640 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	Chemical may not be soluble enough to measure this predicted effect.
Green Algae ChV		Green algae ChV = 0.013 mg/L (Estimated) ECOSAR: sulfonyl ureas	ECOSAR version 1.00	
		Green algae ChV = 6.62 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	
		Green algae ChV = 0.77 mg/L (Estimated) ECOSAR: amides	ECOSAR version 1.00	
		Green algae ChV = 15.23 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Terrestrial Ecotoxicity	**Earthworm Subchronic Toxicity**	Earthworm 14-day LC_{50} = 3,500 mg/L (Estimated) ECOSAR: esters	ECOSAR version 1.00	NES for measured water solubility of 35 mg/L.
	Toxicity to Terrestrial Plants	*Avena sativa, Pisum sativum and Brassica napus*: NOEC (21 d) = >1000 mg/kg (nominal) soil dw test material (based on: seedling emergence) *Avena sativa, Pisum sativum and Brassica napus*: NOEC (21 d) = >1000 mg/kg (nominal) soil dw test material. (based on: growth)	Submitted confidential study	Study conducted according to OECD guideline 208.

Pergafast 201 CASRN 232938-43-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL FATE				
Transport		**The transport evaluation for Pergafast 201 is based on available experimental and estimated physical and chemical properties. Based on the Level III fugacity models incorporating the available experimental property data, Pergafast 201 is expected to partition primarily to soil. Pergafast 201 is expected to have slight mobility in soil based on its estimated K_{oc}. However, leaching of Pergafast 201 through soil to groundwater is not expected to be an important transport mechanism. Estimated volatilization half-lives indicate that it will be nonvolatile from surface water. In the atmosphere, Pergafast 201 is expected to exist in the particulate phase, based on its estimated vapor pressure. Particulates will be removed from air by wet or dry deposition.**		
	Henry's Law Constant ($atm\text{-}m^3/mole$)	$<1x10^{-8}$ (Estimated)	EPI; Professional judgment	Cutoff value for nonvolatile compounds, based on professional judgment.
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	12,000 (Estimated)	EPI	
	Level III Fugacity Estimations	Air = <1% (Estimated) Water = 8% Soil = 85% Sediment = 7%	EPI	
Persistence		**VERY HIGH: Experimental guideline studies indicate that little or no biodegradation was observed under aerobic conditions.**		
Water	**Aerobic Biodegradation**	OECD TG 301 F Ready Biodegradability: Manometric Respirometry Test. Pergafast 201 is not readily biodegradable; 1.5% degradation of the test substance occurred after 28 days (Measured)	NICNAS, 2004	Adequate; guideline study described in secondary source.
		OECD 302B: Not readily biodegradable; >99% after 28 days (Measured)	BASF, 2010	Adequate, guideline study.
		No biodegradation occurred after 28 days. Ready biodegradability test with non-adapted, activated sludge. (Measured)	Submitted confidential study	Adequate; nonguideline study reported in secondary source.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**	Half-life of 4.9 days according to OECD 307; decreased to 14% of applied amount in 30 days (Measured)	Submitted confidential study	Inadequate as reported in a secondary source. The cited source indicated that the material did not mineralize over the course of the study, although no mass balance information was provided. These are results are not consistent with other biodegradation results.
	Anaerobic Biodegradation	Not probable (anaerobic-methanogenic biodegradation probability model)	EPI	
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	0.64 hours (Estimated)	EPI	
Reactivity	**Photolysis**	Not a significant fate process	Professional judgment	Qualitative assessment based on functional groups.
	Hydrolysis	Half-life >1 year at pH 4, 7, and 9 OECD 111; <10% hydrolysis after 5 days (Measured)	NICNAS, 2004	Adequate; guideline study described in secondary source.
	Pyrolysis			No data located.
Environmental Half-life		120 days (Estimated)	EPI; PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**LOW: The measured BCF in fish is <100.**		

Pergafast 201 CASRN 232938-43-1				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Fish BCF	<1 (0.2 mg/L) (Measured); <8 (0.02 mg/L) (Measured) according to guideline study OECD 305	Submitted confidential study	Adequate; guideline study described in a secondary source.
		30 (Measured)	NICNAS, 2004	Reported in a secondary source, although the resulting hazard is consistent with other studies.
	BAF	18 (Estimated)	EPI	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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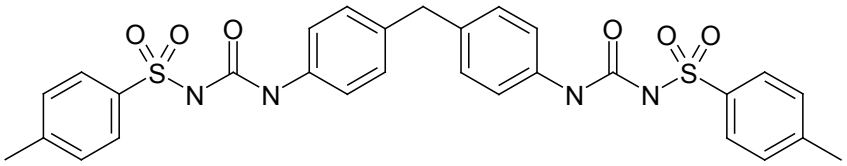
BTUM



	CASRN: 151882-81-4
	MW: 592.70
	MF: $C_{29}H_{28}N_4O_6S_2$
	Physical Forms: **Neat:** Solid
	Use: Developer for thermal paper
SMILES: O=C(NS(C1=CC=C(C)C=C1)(=O)=O)NC(C=C2)=CC=C2CC3=CC=C(NC(NS(C4=CC=C(C)C=C4)(=O)=O)=O)C=C3	
Synonyms: Benzenesulfonamide, N,N'-[methylenebis(4,1-phenyleneiminocarbonyl)]bis[4-methyl-; 4,4'-bis(*N*-carbamoyl-4-methylbenzenesulfonamide)diphenylmethane	
Polymeric: No **Oligomers:** Not applicable	
Metabolites, Degradates and Transformation Products: None identified	
Analog: None **Endpoint(s) using analog values:** Not applicable	**Analog Structure:** Not applicable
Structural Alerts: None identified	
Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2011).	
Risk Assessments: None identified	

BTUM CASRN 151882-81-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES				
Melting Point (°C)		154-156 (Measured)	Non-confidential PMN submission	Adequate.
Boiling Point (°C)		>300 (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for high boiling compounds according to HPV assessment guidance.
Vapor Pressure (mm Hg)		$<1x10^{-8}$ (Estimated)	EPI; U.S. EPA, 1999	Cutoff value for nonvolatile compounds according to HPV assessment guidance.
Water Solubility (mg/L)		0.77 (Measured)	Non-confidential PMN submission	Adequate.
Log K_{ow}		2.61 (Measured)	Non-confidential PMN submission	Adequate.
Flammability (Flash Point)				No data located.
Explosivity				No data located.
pH				No data located.
pK_a		4.8-5.4 (Estimated)	SPARC	
HUMAN HEALTH EFFECTS				
Toxicokinetics		**BTUM is not absorbed through the skin and will have poor absorption from the lungs and gastrointestinal tract.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Not absorbed through the skin; poor absorption through the lung and gastrointestinal tract	Professional judgment	Based on closely related confidential analog with similar structure, functional groups, and physical/chemical properties.

BTUM CASRN 151882-81-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Mammalian Toxicity		**LOW: The acute oral and dermal toxicity concern of BTUM is low based on experimental data in animals. Data indicate no mortality or signs of toxicity at doses up to 2,000 mg/kg.**		
Acute Lethality	**Oral**	Rat, LD_0 = 2,000 mg/kg No signs of toxicity	Non-confidential PMN submission	Adequate.
	Dermal	Rat, LD_0 = 2,000 mg/kg No signs of toxicity	Non-confidential PMN submission	Adequate.
	Inhalation			No data located.
Carcinogenicity		**MODERATE: There is uncertainty due to the lack of data for this substance. Carcinogenic effects cannot be ruled out.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
Genotoxicity		**LOW: BTUM did not cause mutations in bacteria or chromosomal aberrations in human lymphocytes.**		
	Gene Mutation *in vitro*	Negative for mutations in *Salmonella typhimurium* and *Escherichia coli* with and without activation	Non-confidential PMN submission	Adequate.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Negative for chromosomal aberrations in human lymphocytes	Non-confidential PMN submission	Adequate.
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.
	Other (Mitotic Gene Conversion)			No data located.

BTUM CASRN 151882-81-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**LOW: A combination of poor predicted absorption through all routes, low predicted metabolism, and lack of significant toxicological concerns from repeated dose testing suggests low potential hazard based on professional judgment.**		
	Reproduction/ Developmental Toxicity Screen	Low potential for reproductive effects (Estimated)	Professional judgment	Estimated based on professional judgment.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects			No data located.
Developmental Effects		**LOW: A combination of poor predicted absorption through all routes, low predicted metabolism, and lack of significant toxicological concerns from repeated dose testing suggests low potential hazard based on professional judgment.**		
	Reproduction/ Developmental Toxicity Screen	Low potential for reproductive effects (Estimated)	Professional judgment	Estimated based on professional judgment.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
Neurotoxicity		**LOW: No structural alerts or mechanistic pathways associated with neurotoxic effect identified.**		
	Neurotoxicity Screening Battery (Adult)	Low potential for neurotoxicity effects (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on no identified structural alerts or mechanistic pathways associated with neurotoxicity.

BTUM CASRN 151882-81-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects		**MODERATE: Blood toxicity and liver changes resulted in rats at a dose of 1,000 mg/kg-day following a 28-day exposure to BTUM. While the LOAEL identified in the study indicates a Low hazard concern (>300 mg/kg-day), the NOAEL is within the Moderate hazard concern range for a 28-day study duration (30-300 mg/kg-day). The uncertainty of where effects might occur warrants a Moderate hazard concern.**		
		Rat, 28-day oral (gavage) blood toxicity and liver changes. NOAEL = 200 mg/kg-day LOAEL = 1,000 mg/kg-day	Non-confidential PMN submission	Adequate.
Skin Sensitization		**LOW: BTUM did not cause dermal sensitization in one study of guinea pigs.**		
	Skin Sensitization	No skin sensitization in guinea pigs using the Magnusson Kligman assay	Non-confidential PMN submission	Adequate.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: BTUM was slightly irritating to eyes in one study of rabbits.**		
	Eye Irritation	Mild eye irritation in rabbits	Non-confidential PMN submission	Adequate.
Dermal Irritation		**LOW: BTUM did not cause dermal irritation in one study of rabbits.**		
	Dermal Irritation	No skin irritation in rabbits	Non-confidential PMN submission	Adequate.
Endocrine Activity		**No data located.**		
				No data located.
Immunotoxicity		**No data located.**		
	Immune System Effects			No data located.
ECOTOXICITY				
ECOSAR Class		Sulfonyl ureas		
Acute Toxicity		**HIGH: Based on an estimated acute toxicity value of <1.0 mg/L for algae, although there is a high degree of uncertainty and limited confidence in the estimation.**		

BTUM CASRN 151882-81-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Fish LC_{50}	Fish 96-hour LC_{50} = 37 mg/L ECOSAR: sulfonyl ureas (Estimated)	ECOSAR version 1.00	NES; estimated LC_{50} is greater than the measured water solubility (0.77 mg/L).
	Fish 96-hour LC_{50} = 137 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	NES; estimated LC_{50} is greater than the measured water solubility (0.77 mg/L). Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid LC_{50}	Daphnid 48-hour LC_{50} = 34 mg/L (Estimated) ECOSAR: sulfonyl ureas	ECOSAR version 1.00	NES; estimated LC_{50} is greater than the measured water solubility (0.77 mg/L).
	Daphnid 48-hour LC_{50} = 82 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	NES; estimated LC_{50} is greater than the measured water solubility (0.77 mg/L). Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Green Algae EC_{50}	Green algae 96-hour EC_{50} = 0.188 mg/L (Estimated) ECOSAR: sulfonyl ureas	ECOSAR version 1.00	There is some uncertainty to the estimated value for this compound since all chemicals in the training set for the sulfonyl urea class equation consists solely of triazine herbicides.

BTUM CASRN 151882-81-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Green algae 96-hour EC_{50} = 76 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	NES; estimated EC_{50} is greater than the measured water solubility (0.77 mg/L). Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Chronic Aquatic Toxicity	**HIGH: Based on an estimated ChV of 0.73 mg/L for daphnid and 0.035 for algae, although there is a high degree of uncertainty and limited confidence in the estimations.**		
Fish ChV	Fish ChV = 2.5 mg/L (Estimated) ECOSAR: sulfonyl ureas	ECOSAR version 1.00	NES; estimated ChV is greater than the measured water solubility (0.77 mg/L).
	Fish ChV = 14 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	NES; estimated ChV is greater than the measured water solubility (0.77 mg/L). Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid ChV	Daphnid ChV = 0.73 mg/L (Estimated) ECOSAR: sulfonyl ureas	ECOSAR version 1.00	There is a high degree of uncertainty for this estimate since the chemical may not be soluble enough to measure this predicted effect; ChV value is near the water solubility.

BTUM CASRN 151882-81-4			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Daphnid ChV = 9.4 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	NES; estimated ChV is greater than the measured water solubility (0.77 mg/L). Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Green Algae ChV	Green algae ChV = 0.035 mg/L (Estimated) ECOSAR: sulfonyl ureas	ECOSAR version 1.00	There is some uncertainty to the estimated value for this compound since all chemicals in the training set for the sulfonyl urea class equation consists solely of triazine herbicides.
	Green algae ChV = 76 mg/L (Estimated) ECOSAR: neutral organics	ECOSAR version 1.00	NES; estimated ChV is greater than the measured water solubility (0.77 mg/L). Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
ENVIRONMENTAL FATE			
Transport	**Evaluation of BTUM transport is based entirely on estimations based on QSARs for fugacity (level III), disassociation constant (pK_a), soil adsorption coefficient (K_{oc}), volatilization, and vapor pressure. It is expected to exist in both the neutral and anionic form at environmentally-relevant pH. BTUM is expected to have low mobility in soil. Anionic BTUM may have higher mobility due to enhanced water solubility. However, leaching through soil to groundwater is not expected to be an important transport mechanism. In the atmosphere, BTUM is expected to exist in the particulate phase, which will be deposited back to the soil and water surfaces through wet or dry deposition.**		

BTUM CASRN 151882-81-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Henry's Law Constant (atm-m^3/mole)	<$1x10^{-8}$ (Estimated)	EPI; Professional judgment	Cutoff value for nonvolatile compounds, based on professional judgment.
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	>30,000 (Estimated)	EPI; U.S. EPA, 2004	Cutoff value for nonmobile compounds.
	Level III Fugacity Model	Air = <1% Water = 2 % Soil = 72% Sediment = 26% (Estimated)	EPI	
Persistence		**HIGH: Evaluation of the persistence of BTUM is based entirely on QSARs of aerobic and anaerobic biodegradation. Results from these models estimate ultimate biodegradation in months and primary degradation in weeks. Biodegradation under anaerobic methanogenic conditions is not probable based on results from estimation models. BTUM does not contain chromophores that absorb light at wavelengths >290 nm. Therefore, it is not expected to be susceptible to direct photolysis. BTUM is not expected to undergo hydrolysis as it does not contain hydrolyzable functional groups. The atmospheric half-life of BTUM is estimated at 1.2 hours, although it is expected to exist primarily as a particulate in air. Therefore, biodegradation is expected to be the main degradation pathway for BTUM.**		
Water	**Aerobic Biodegradation**	Weeks (primary survey model); Recalcitrant (ultimate survey model)	EPI	
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (anaerobic-methanogenic biodegradation probability model)	EPI	
	Soil Biodegradation w/ Product Identification			No data located.

BTUM CASRN 151882-81-4				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	1.2 hours (Estimated)	EPI	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	Substance does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.
	Hydrolysis	Not a significant fate process (Estimated)	Wolfe and Jeffers, 2000; Professional judgment	Substance does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.
	Pyrolysis			No data located.
Environmental Half-life		120 days (Estimated)	EPI; PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**LOW: Based on both the estimated BCF and BAF that are <100.**		
	Fish BCF	25 (Estimated)	EPI	
	BAF	4 (Estimated)	EPI	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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SPARC On Line Calculator pKa/property server. Ver 4.5 September, 2009. Available from, http://ibmlc2.chem.uga.edu/sparc/ (accessed on August 12, 2010.

U.S. EPA (Environmental Protection Agency). High Production Volume (HPV) Challenge. Determining the Adequacy of Existing Data. U.S. Environmental Protection Agency: Washington D.C. **1999**. http://www.epa.gov/hpv/pubs/general/datadfin.htm

U.S. EPA (Environmental Protection Agency). **2004**. The Pollution Prevention (P2) Framework, EPA-748-B-03-001. Office of Pollution Prevention and Toxics 7403M, U.S. Environmental Protection Agency, Washington, DC. 20460. October 2003 version updated in January 2004. Latest version available at http://www.epa.gov/opptintr/newchems/pubs/sustainable/p2frame-june05a2.pdf

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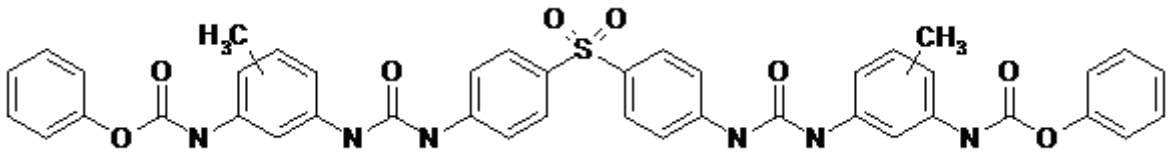

	CASRN: 321860-75-7
	MW: 784.9 (for representative structure)
	MF: $C_{42}H_{36}N_6O_8S$ (for representative structure)
	Physical Forms: **Neat:** Solid
	Use: Developer for thermal paper

SMILES: c1(NC(=O)Oc6ccccc6)c(C)cc(NC(=O)Nc2ccc(S(=O)(=O)c3ccc(NC(=O)Nc4c(C)cc(NC(=O)Oc5ccccc5)cc4)cc3)cc2)cc1 (for representative structure)

Synonyms: Urea Urethane Compound

Polymeric: Yes
Oligomers: A representative structure for the low molecular weight oligomer evaluated in this assessment is drawn above.

Metabolites, Degradates and Transformation Products: None

Analog: Confidential analog **Endpoint(s) using analog values:** Eye and skin irritation, respiratory and skin sensitization, immunotoxicity, neurotoxicity, genotoxicity, repeated dose	**Analog Structure:** Not applicable

Structural Alerts: None identified

Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2011).

Risk Assessments: None identified

UU CASRN 321860-75-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)			No data located.
Boiling Point (°C)	>300 (Estimated)	EPI; U.S. EPA, 1999	Estimates were performed on a representative component of the polymer shown above. This representative structure is anticipated to be the predominant component of the polymeric mixture. Cutoff value for high boiling point compounds according to HPV assessment guidance.
Vapor Pressure (mm Hg)	$<1x10^{-8}$ (Estimated)	EPI; U.S. EPA, 1999	Estimates were performed on a representative component of the polymer shown above. This representative structure is anticipated to be the predominant component of the polymeric mixture. Cutoff value for nonvolatile compounds according to HPV assessment guidance.
Water Solubility (mg/L)	$<1x10^{-3}$ (Estimated)	EPI; U.S. EPA, 1999	Estimates were performed on a representative component of the polymer shown above. This representative structure is anticipated to be the predominant component of the polymeric mixture. Cutoff value for nonsoluble compounds according to HPV assessment guidance.

UU CASRN 321860-75-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Log K_{ow}		6.5 (Estimated)	EPI	Estimates were performed on a representative component of the polymer shown above. This representative structure is anticipated to be the predominant component of the polymeric mixture.
Flammability (Flash Point)				No data located.
Explosivity				No data located.
pH				No data located.
pK_a		10.3 (Estimated)	SPARC	Estimates were performed on a representative component of the polymer shown above. This representative structure is anticipated to be the predominant component of the polymeric mixture.
HUMAN HEALTH EFFECTS				
Toxicokinetics		**UU is not absorbed by skin, poorly absorbed by the lung, and can be absorbed in the gastrointestinal tract.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal, or Inhaled**	No absorption through skin, poor absorption by lung, and can be absorbed by the gastrointestinal tract.	Professional judgment	Based on closely related confidential analog with similar structure, functional groups, and physical/chemical properties.
Acute Mammalian Toxicity		**LOW: No acute mammalian toxicity observed at oral and dermal exposure doses of less than or equal to 2,000 mg/kg.**		
Acute Lethality	**Oral**	Rat oral LD_0=2,000 mg/kg (Measured)	Submitted Confidential Study	Adequate.
	Dermal	Rat dermal LC_0=3161 mg/kg (Measured)	Submitted Confidential Study	Adequate.
	Inhalation			No data located.

UU CASRN 321860-75-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Carcinogenicity		**MODERATE: There is uncertainty due to the lack of data located for this substance. Carcinogenic effects cannot be ruled out.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
Genotoxicity		**LOW: UU was negative in bacterial mutagenicity assays and negative for chromosomal aberration in mammalian cells.**		
	Gene Mutation *in vitro*	Negative, Ames Assay, with and without activation (Measured)	Submitted Confidential Study	Adequate.
		Negative, *E. coli* reverse mutation assay, with and without activation (Measured)	Submitted Confidential Study	Adequate.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*			No data located.
	Chromosomal Aberrations *in vivo*	Negative, chromosomal aberration in CHL cells, with and without activation (Measured)	Submitted Confidential Study	Adequate.
	DNA Damage and Repair			No data located.
	Other (Mitotic Gene Conversion)			No data located.
Reproductive Effects		**LOW: Based on professional judgment. A combination of limited predicted absorption, low predicted metabolism, and lack of significant toxicological concerns from repeated dose testing on a close analog suggests low potential hazard, with lower confidence.**		
	Reproduction/ Developmental Toxicity Screen	Low potential for reproductive effects (Estimated)	Professional judgment	Estimated based on professional judgment.

UU CASRN 321860-75-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects			No data located.
Developmental Effects		**LOW: Based on professional judgment. A combination of limited predicted absorption, low predicted metabolism, and lack of significant toxicological concerns from repeated dose testing on a close analog suggests low potential hazard, with lower confidence.**		
	Reproduction/ Developmental Toxicity Screen	Low potential for developmental effects (Estimated)	Professional judgment	Estimated based on professional judgment.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
Neurotoxicity		**LOW: No structural alerts or mechanistic pathways associated with neurotoxic effect identified.**		
	Neurotoxicity Screening Battery (Adult)	Low potential for neurotoxicity effects (Estimated)	U.S. EPA, 2010; Professional judgment	Estimated based on no identified structural alerts or mechanistic pathways associated with neurotoxicity.
Repeated Dose Effects		**LOW: There were no repeated dose effects at oral doses ≤1,000 mg/kg-day.**		
		28-Day repeated-dose study, rat, oral, gavage, no clinical signs, no macroscopic or histopathological abnormalities, NOAEL = 1000 mg/kg-day. (Measured)	Submitted Confidential Study	Adequate.
Skin Sensitization		**LOW: Based on closely related confidential analog with similar structure, functional groups, and physical/chemical properties.**		
	Skin Sensitization	Non-sensitizing, Guinea pigs (Measured)	Submitted Confidential Study	Adequate.

UU CASRN 321860-75-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: UU is not an eye irritant.**		
	Eye Irritation	Slight irritation, rabbits (Measured)	Submitted Confidential Study	Adequate.
Dermal Irritation		**LOW: UU is not a dermal irritant.**		
	Dermal Irritation	Non-irritating, rabbits (Measured)	Submitted Confidential Study	Adequate.
Endocrine Activity		**No data located.**		
				No data located.
Immunotoxicity		**No data located.**		
	Immune System Effects			No data located.
ECOTOXICITY				
ECOSAR Class		Substituted ureas; Amides; Carbamate esters		
Acute Toxicity		**LOW: Based on measured 96-hour LC_{50} for fish and on estimated 96-hour LC_{50} for fish, 48-hour LC_{50} for Daphnid, and 96-hour EC_{50} for green algae that result in no effects at saturation (NES), as obtained for a representative component of the polymer that has a MW <1,000.**		
Fish LC_{50}		Fish 96-hour LC_{50}>250 mg/L (Measured)	Submitted Confidential Study	Adequate
		Fish 96-hour LC_{50} = 0.028 mg/L (Estimated) ECOSAR: amides	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.
		Fish 96-hour LC_{50} = 0.118 mg/L (Estimated) ECOSAR: substituted ureas	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.
		Fish 96-hour LC_{50} = 0.061 mg/L (Estimated) ECOSAR: carbamate esters	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.
Daphnid LC_{50}		Daphnid 48-hour LC_{50} = 0.074 mg/L (Estimated) ECOSAR: amides	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.

UU CASRN 321860-75-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Daphnid 48-hour LC_{50} = 0.088 mg/L (Estimated) ECOSAR: substituted ureas	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.
	Daphnid 48-hour LC_{50} = 0.958 mg/L (Estimated) ECOSAR: carbamate esters	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.
Green Algae EC_{50}	Green algae 96-hour EC_{50} = 0.096 mg/L (Estimated) ECOSAR: amides	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.
	Green algae 96-hour EC_{50} = 0.288 mg/L (Estimated) ECOSAR: substituted ureas	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.
	Green algae 96-hour EC_{50} = 0.223 (Estimated) ECOSAR: carbamate esters	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.
Chronic Aquatic Toxicity	**LOW: Based on ChV values for fish, Daphnid, and green algae that result in no effects at saturation (NES), as obtained for a representative component of the polymer that has a MW <1,000.**		
Fish ChV	Fish ChV = 0.00016 mg/L (Estimated) ECOSAR: amides	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.
	Fish ChV = 0.003 mg/L (Estimated) ECOSAR: substituted ureas	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.
	Fish ChV = 0.005 mg/L (Estimated) ECOSAR: carbamate esters	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.
Daphnid ChV	Daphnid ChV = 0.00098 mg/L (Estimated) ECOSAR: amides	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.

UU CASRN 321860-75-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Daphnid ChV = 0.019 mg/L (Estimated) ECOSAR: substituted ureas	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.
		Daphnid ChV = 0.006 mg/L (Estimated) ECOSAR: carbamate esters	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.
Green Algae ChV		Green algae ChV = 0.046 mg/L (Estimated) ECOSAR: substituted ureas	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.
		Green algae ChV = 1.311mg/L (Estimated) ECOSAR: amides	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.
		Green algae ChV = 0.488 mg/L (Estimated) ECOSAR: carbamate esters	ECOSAR version 1.00	NES; estimates were performed for the representative component of the polymer shown above.
ENVIRONMENTAL FATE				
Transport		**Evaluation of UU transport is based entirely on QSAR estimations that were performed on a representative component of the polymer that has a MW <1,000. This representative structure is anticipated to be the predominant component of the polymeric mixture. UU is expected to have low mobility in soil based on its expected strong absorption to soil. If released to the atmosphere, UU is likely to exist solely as particulate. As a particulate, atmospheric oxidation is not expected to be a significant route of environmental removal. Based on the Henry's Law constant, volatilization from water or moist soil is not expected to occur at an appreciable rate. Level III fugacity models indicate that UU will partition predominantly to the soil and sediment.**		
	Henry's Law Constant (atm-m^3/mole)	<$1x10^{-8}$ (Estimated)	EPI	Estimates were performed on a representative component of the polymer shown above. This representative structure is anticipated to be the predominant component of the polymeric mixture. Cutoff value for nonvolatile compounds based on professional judgment.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	>30,000 (Estimated)	EPI	Estimates were performed on a representative component of the polymer shown above. This representative structure is anticipated to be the predominant component of the polymeric mixture. Cutoff value for nonmobile compounds.
	Level III Fugacity Model	Air = <1% (Estimated) Water = 1% Soil = 52% Sediment = 47%	EPI	Estimates were performed on a representative component of the polymer shown above. This representative structure is anticipated to be the predominant component of the polymeric mixture.
Persistence		**VERY HIGH: UU is not ready biodegradable based on a Japanese MITI test. Further evaluation of the persistence of UU is based on predictive QSAR models for the representative component estimates UU to be recalcitrant to ultimate biodegradation, and suggest a biodegradation half-life of >180 days. In addition, the larger oligomers in the polymeric mixture with a MW>1,000 are expected to have Very High persistence potential based on DfE assessment guidance as they are likely too large and too water insoluble to be bioavailable.**		
Water	**Ready Biodegradability**	Not ready biodegradable in Japanese MITI test (OECD 301C). 1% (by BOD) and 2% (by HPLC) biodegradation in 28 days. (Measured)	Submitted Confidential Study	Adequate.
	Aerobic Biodegradation	Weeks (primary survey model) Recalcitrant (ultimate survey model))	EPI	Estimates were performed on a representative component of the polymer shown above. This representative structure is anticipated to be the predominant component of the polymeric mixture.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	Estimates were performed on a representative component of the polymer shown above. This representative structure is anticipated to be the predominant component of the polymeric mixture.
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	Estimates were performed on a representative component of the polymer shown above. This representative structure is anticipated to be the predominant component of the polymeric mixture.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation			No data located.
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	0.64 hours (Estimated)	EPI	The estimated half-life is for a gas-phase reaction; UU is expected to exist as a particulate in the atmosphere and the rate of this process will be highly attenuated.
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	Substance does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Hydrolysis	42 minutes at pH 8; 7 hours at pH 7 (Estimated)	EPI	Limited confidence in the estimated half-lives given the limited solubility anticipated for this material. Hydrolysis is not expected to occur to an appreciable extent and UU is anticipated to lie outside the domain of this model.
	Pyrolysis			No data located.
Environmental Half-life		360 days (Estimated)	EPI; PBT Profiler	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology for the representative component of the polymer shown above.
Bioaccumulation		**LOW: The measured BCF for UU is <100 (4.6). The estimated BAF for the representative component of the polymer is <100 (7.9). Although the BCF model results in a higher hazard concern, the BAF model is anticipated to better account for metabolism for this class of compounds. In addition, the polymeric components of the mixture that have a MW >1,000 are not expected to be bioaccumulative because, in general, substances with a MW >1,000 are not bioaccumulative due to their large size.**		
	Fish BCF	0.46-4.6 (Measured)	Submitted Confidential Study	Adequate.
	Fish BCF	9,100 (Estimated)	EPI	Estimates were performed on a representative component of the polymer shown above. This representative structure is anticipated to be the predominant component of the polymeric mixture.
	BAF	7.9 (Estimated)	EPI	Estimates were performed on a representative component of the polymer shown above. This representative structure is anticipated to be the predominant component of the polymeric mixture.

UU CASRN 321860-75-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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